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### 2021 - VOLUME 5, JANUARY ISSUE 1

#### ORIGINAL ARTICLE

**COMPARATIVE STUDY BETWEEN SURGICAL TREATMENT AND DILTIAZEM 2% GEL APPLICATION IN THE MANAGEMENT OF CHRONIC ANAL FISSURE**

\*Ammar Khiatah, Ahmad Saad and Sajieh Massoud


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**INFLUENCE OF SYSTEM QUALITY, INFORMATION QUALITY, AND SERVICE QUALITY ON ORGANIZATION AT PUBLIC HEALTH CENTER PASURUAN CITY**

Nita Dwi Nur Aini\*, Farida Wahyu Ningtyias and Dewi Rokhmah

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**PREVALENCE OF OBESITY AMONG CHILDREN UNDER 5 YEARS ATTENDED TO PRIMARY HEALTH**

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\*Akintoye Emily Obside, Akintoye Onome Pearl and Adjene Josiah Obaghwarhievw


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Nita Dwi Nur Aini\*, Farida Wahyu Ningtyias and Dewi Rokhmah

**ABSTRACT**

Health policy in Indonesia requires every public health center to organize a Puskesmas Management Information System (SIMPUS). SIMPUS implementation in Pasuruan City aims to improve the quality of health services, but in its implementation SIMPUS still faces many obstacles so that it has not run optimally. The purpose of this study is to identify and determine the effect of system quality, information quality and service quality on the organization. This type of research used analytic observational with cross sectional design. Total population 268 officers with a sample of 160 officers at the public health center. The results showed that the quality of the system had no effect on the organization. Meanwhile, information quality and service quality have an effect on the organization. Suggestions that can be given are improving network quality, holding training and technical guidance, evaluating and maintaining devices.

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## COMPARATIVE STUDY BETWEEN SURGICAL TREATMENT AND DILTIAZEM 2% GEL APPLICATION IN THE MANAGEMENT OF CHRONIC ANAL FISSURE

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### ABSTRACT

**Introduction:** The surgical intervention on chronic anal fissure is still the first line of treatment for this disease. The importance of this research lies in finding a new treatment for one of the most common anal lesions, and to choose a safe and effective method in the treatment of chronic anal fissure, avoiding the risks of anesthesia and surgery. **Objective:** To compare the surgical treatment (Lateral Internal Sphincterotomy) and topical treatment (Diltiazem Gel 2%), in terms of the ability to heal, studying the degree of symptoms regression after the treatment (bleeding/pain), and studying the incidence of gas / fecal incontinence. **Materials and Methods:** A prospective pilot study, which included 60 patients divided into two groups equally, Group A (30 patients who underwent surgical treatment), Group B (30 patients who underwent topical drug treatment with Diltiazem 2% gel), and the study was conducted at Tishreen University Hospital in Latakia – Syria, in the period between 2019-2020. **Results:** In group A, complete recovery occurred in 29 patients (96.6%), anal bleeding decreased in all patients (100%), pain feeling decreased in all patients (100%), and gas incontinence occurred only in 4 patients (13.3%). Fecal incontinence didn't occur. In group B, complete recovery occurred in 17 patients (56.6%), anal bleeding decreased in 17 patients (68%), pain feeling decreased in 17 patients (65.3%), and gas / fecal incontinence didn't occur at all. **Conclusion:** Lateral internal Sphincterotomy is still the first line of treatment in patients with a chronic anal fissure, but drug therapy with (Diltiazem 2% gel) can be applied to patients who refuse surgical treatment, or for those who have contraindications for surgical intervention.

**KEYWORDS:** Anal Fissure, lateral sphincterotomy, Topical diltiazem.

### INTRODUCTION

An anal fissure is one of the most common lesions to be considered in the differential diagnosis of anal pain. The commonly accepted definition of an anal fissure is "A linear ulcer of the anoderm, distal to the dentate line, generally located in the posterior midline".<sup>[1-4]</sup> It typically causes episodic pain that occurs during defecation and persists for 1 to 2 hours afterward.<sup>[5]</sup> The most consistent finding in typical fissures is the spasm of the internal anal sphincter, which is so severe that the pain caused by the fissure is thought to be due to ischemia of the sphincter.<sup>[6]</sup> Chronic fissures, by definition, are those that persist beyond six weeks. The pathogenesis is not fully clear,<sup>[7]</sup> though reduced consumption of dietary fiber and constipation may be important risk factors.<sup>[8]</sup> Another hypothesis, supported by both anatomical and anal manometry studies, is that

the relative ischemia of the posterior midline anal canal leads to poor healing of the fissure.<sup>[9]</sup>

Regarding the treatment aspect, there are two options, Conservative method which is most readily accepted by patients, and Secondly, surgical method of treatment,<sup>[10]</sup> The American Society of Colon and Rectal Surgeons (ASCRS) recommend conservative management with stool softeners, high fiber diet and sitz bath as the initial line of management.<sup>[11]</sup> A Cochrane review of anal fissure treatment had shown that topical and injected therapies are only marginally effective to placebo therapy and recommended lateral internal sphincterotomy (LIS) as the gold standard for chronic anal fissure (CAF).<sup>[12]</sup> The main drawback of LIS is the potential complication of incontinence to flatus or fecal matter. This is the reason for trying alternative pharmacologic agents (chemical sphincterotomy) in the treatment of CAF. An evidence-based summary

regarding the role of topical diltiazem had been recently issued by the National Institute for Health and Care Excellence (NICE, UK) organization in the UK.<sup>[13]</sup>

The aim of this randomized study was to compare the efficacy of topical 2 % diltiazem with the traditional LIS in the treatment of CAF.

## METHODS

This was a hospital-based prospective study containing 2 groups, group A, where patients will be treated with the surgical approach and group B with the conservative approach. The study was carried out at the Department of General Surgery, at Tishreen University Hospital in Latakia – Syria, over a period of one calendar year, from September 2019 - September 2020. All patients presenting to the outpatient department of General Surgery, Tishreen University Hospital in Latakia – Syria, with symptoms of anal fissure were examined thoroughly, and a detailed history was taken as per the proforma.

### Inclusion criteria

1. Patients with a confirmed diagnosis of chronic anal fissure.
2. Patients' age ranging from 18years to 50years of both the sexes.
3. Patients were willing to be part of the present study.

### Exclusion criteria

1. Patients with co-morbidities of severe nature.
2. Age <18years and >50years.
3. Patients were not willing to be part of the present study.
4. Patients who were bedridden and were not able to participate in the present study.
5. Pregnant women.

During the study period, a total of 60 patients were selected, matching the inclusion and exclusion criteria. After the history and general examination, the local examination was carried out, which included the digital rectal examination to assess the extent and the degree of the anal fissure. These patients were randomly assigned to group A and group B with 30 patients for each group. Group A patients were treated on an in-patient basis. They were operated on using the lateral internal sphincterotomy method. Group B patients were treated for anal fissure on an outpatient base, and they were given 2% topical diltiazem with application instruction. All patient were they were asked to apply it twice a day foreight8 weeks.

All Patients were included after providing a written informed consent.

### Follow up

All patients were followed for ten weeks in the outpatient clinic and a physical exam was performed with subjective data provided by the patients, and an outcome

like flatus incontinence and fecal incontinence was noted in both the group patients.

### Statistical analysis

The data were expressed as proportions and means. Chi-square test and students T-test was used to determine the efficacy of the treatment groups.

## RESULTS

Both groups were comparable in terms of the distribution of males and females in the present study. The p-value was more than 0.05. The number of males and females in both groups was also not much different from each other. So, annal fissure can affect both sexes equally.

Both groups were comparable in terms of average age in the present study. The mean age in group A patients was 26.56 years, and the mean age of patients from group B was 25.96 years. The difference was statistically, not significant.

### Symptoms

Both Pain and Bleeding per rectum were the most common presenting symptoms in both the groups affecting about 90% of the patients. Hence pain, bleeding were the presenting symptoms in the present study for patients from both the groups. Both groups were comparable in terms of symptoms.

Posterior midline anal fissure was seen in all patients.

### Comparison of Healing in Both Groups at Different Weeks of Follow Up

Healing at 10th week was significantly higher in surgical treatment group A (96.6 %) than that of in medical treatment group B (56.6%). The p-value was less than 0.05.

### Comparison of Pain Relief in Both Groups at Different weeks of Follow Up

Pain relief was more in the surgical treatment group than in the medical treatment group at the 10th week of follow up. Significant pain relief was seen in both the groups as duration progresses from 2nd to 10th week.

### Comparison of Bleeding PR in Both Groups at Different Weeks of Follow Up

Bleeding PR has regressed more in the surgical treatment group than in the medical treatment group at the 10th week of follow up. Significant regression of bleeding was seen in both the groups as duration progresses from 2nd to 10th week.

### Comparison of incontinence incidence in Both Groups

No incontinence was present in the medical treatment group (B) throughout the study period. But four patients among surgical treatment group (A) had gas incontinence in 2nd week, and by the end, the of 10 end them, all of them were healed.



**Table 1: Distribution as per sex.**

Sex	Group		Chi-square	P-value
	A	B		
Males	17 (56.66%)	16 (53.33%)	0.0673	0.795
Females	13 (43.33%)	14 (46.66%)		

**Table 2: Comparison of the mean age between the two groups.**

Group	Mean	SD	T - value	P-value
A	26.56	4.95	0.41	0.68
B	25.96	6.13		

**Table 3: Comparison of symptoms between the two groups.**

Symptoms	Group	
	A	B
Anal pain	28 (93.3%)	26 (86.6%)
Bleeding PR	27 (90%)	25 (83.3%)
Anal Itching	20 (66.6%)	19 (63.3%)
Anal Oozing	21 (70%)	23 (76.6%)
Constipation	18 (60%)	20 (66.6%)

**Table 4: Comparison of healing rates between the groups**

Time of follow up	Group		Chi-square	P-value
	A	B		
2 <sup>nd</sup> week	12 (40%)	1 (3%)	11.882	0.0005
6 <sup>th</sup> week	20 (66.6%)	9 (30%)	8.075	0.0044
10 <sup>th</sup> week	29 (96.6%)	17 (56.6%)	13.416	0.0002

**Table 5: Comparison of pain relief between the groups.**

Time of follow up	Group		Chi-square	P-value
	A	B		
2nd week	12 (42.8%)	1 (3%)	11.224	0.0008
6th week	20 (71.4%)	9 (34.6%)	7.348	0.006
10th week	28 (100%)	17 (65.3%)	11.63	0.0006

**Table 6: Comparison of bleeding PR regression between the groups.**

Time of follow up	Group		Chi-square	P-value
	A	B		
2 <sup>nd</sup> week	12 (44.4%)	1 (4%)	11.324	0.0007
6 <sup>th</sup> week	20 (74%)	9 (36%)	7.628	0.0057
10 <sup>th</sup> week	27 (100%)	17 (68 %)	10.219	0.0013

**Table 7: Comparison of incontinence incidence in Both Groups.**

Type	Group		Chi-square	P-value
	A	B		
Flatus incontinence	4 (13.3%)	-	4.285	0.0384
Fecal incontinence	-	-	-	-

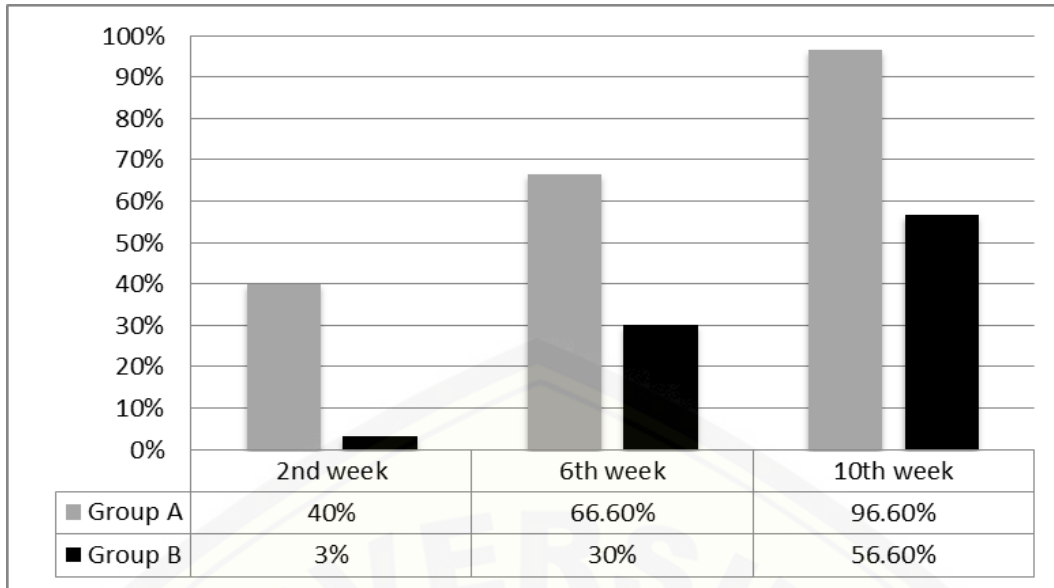


Figure-1: Comparison of healing rates between the groups.

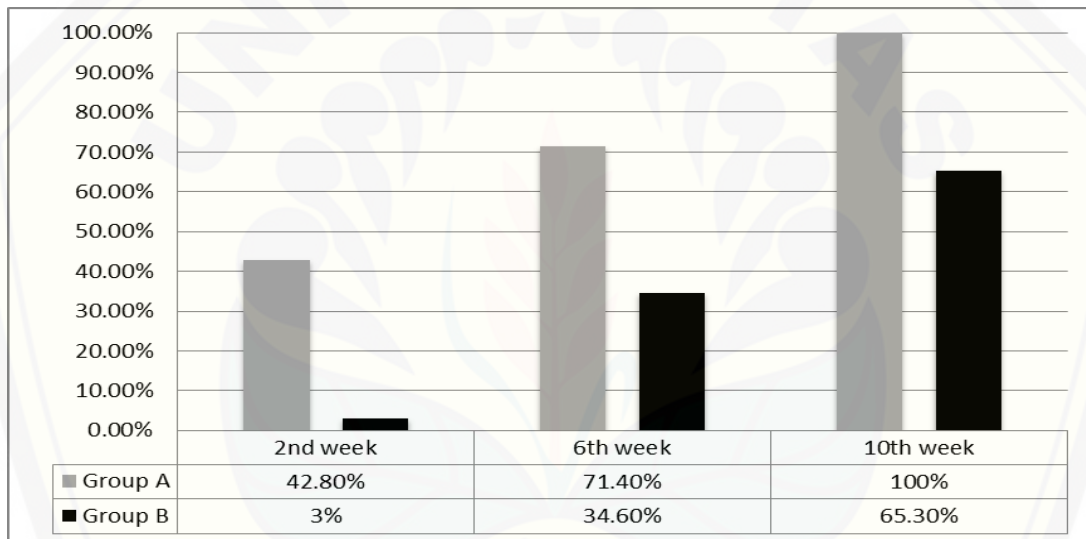


Figure 2: Comparison of pain relief between the groups.

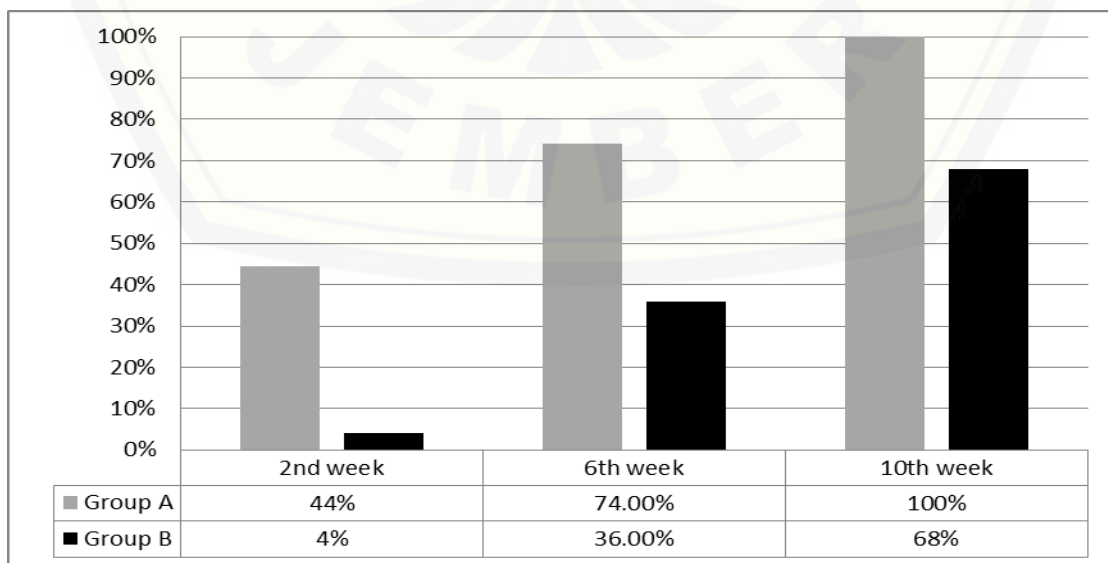


Figure 3: Comparison of Bleeding PR regression between the groups.



## DISCUSSION

Anal fissure is a very common problem across the world. It causes considerable morbidity and adversely affects the quality of life. Anal fissure is usually encountered in young or middle aged adults.<sup>[14,15]</sup> and is equally common in both sexes.<sup>[14]</sup> It is commonly found in the posterior position, although anterior fissure is comparatively common in females.<sup>[16]</sup>

Therapy focuses on breaking the cycle of pain, spasm, and ischemia thought to be responsible for the development of fissure in ano. Operative management includes anal dilatation and lateral internal sphincterotomy. Lateral sphincterotomy is perhaps the operation of choice to perform in patients with chronic anal fissure needing surgical treatment. Postoperative management is simple and rate of healing is faster. However complication such as permanent anal incontinence is associated with the surgery. Chemical sphincterotomy is now the first line of treatment in many centers.<sup>[17-19]</sup> Calcium channel blockers like nifedipine and diltiazem have been shown to lower resting anal pressure,<sup>[20]</sup> promote fissure healing and are associated with good healing rate,<sup>[17,21,22]</sup> They are associated with side effects such as headache and perianal dermatitis.<sup>[17]</sup>

Knight et al. 2001,<sup>[23]</sup> from the UK observed that 75% of their cases had fissure healed with topical 2% diltiazem ointment. Giridhar et al. 2014,<sup>[24]</sup> reported a healing rate of 88.46% in 4 weeks, with 2% diltiazem gel and a 100% healing rate by four weeks with LIS. Vaithianathan R et al. 2015,<sup>[25]</sup> explored the role of diltiazem as an alternative to surgical intervention in patients with a fissure in ano. They found that in the diltiazem group, the healing rate was 71% compared to 96% in the surgery group. Abhivardan D et al. 2017,<sup>[26]</sup> carried out a prospective study in 80 patients and assigned 40 patients each randomly in two groups; one group with diltiazem and the other group patients underwent surgery. They noted that in the diltiazem group, 37 out of 40 patients had complete healing. In this diltiazem group, only three patients had a recurrence. They concluded that 2% diltiazem should be preferred only for acute fissure in ano, and for the management of the chronic fissure in ano, surgery is better than topical diltiazem. In a study by Gupta et al. 2018,<sup>[27]</sup> anal bleeding decreased by 93.3% in patients with surgical treatment, compared to 56.6% of medical treatment patients. Babu et al. 2016,<sup>[28]</sup> reported that bleeding PR has regressed in 91.4% of patients with surgical treatment, compared to 85.7% of medical treatment patients. Acar et al. study 2020,<sup>[29]</sup> showed the percentage of anal pain reduction in surgically treated patients of 91%, compared to 68% in medically treated patients. Pain relief of 100% in the surgical treatment group and 83% in the medical treatment group was reported in Motie et al. 2015.<sup>[30]</sup> While in Gupta et al. 2018,<sup>[27]</sup> the percentage of anal pain reduction in surgically treated patients was 96%, and the rate among medically treated patients was 56.6%. Yucel et al. 2009,<sup>[31]</sup> observed that rectal bleeding improved in

84.6% of patients who underwent surgery. Flatus incontinence occurred in 1% and 8.5% of the surgically treated patients without fecal incontinence, and flatus incontinence did not occur at all in drug-treated patients as reported by Babu et al and Acar et al. and. Respectively,<sup>[28-29]</sup>

In our study, we found that the healing rate was 96.6% in the surgical group compared to 56.6% in the diltiazem group, bleeding PR decreased by 100% in Group A patients, and in 68% of group B patients, pain relief was 100% in group A, compared to 65.3% in group B, and we observed that the rates of anal pain regression after treatment with the surgical intervention were higher than drug-treated patients with a statistically significant difference ( $P < 0.05$ ), at all times. Flatus incontinence occurred in 13.3% of group A patients, while they had no fecal incontinence, and in group B, gas incontinence did not occur at all. The incidence of gas incontinence in patients treated with the surgical intervention was higher than in drug-treated patients by a statistically significant difference ( $P < 0.05$ ).

## CONCLUSION

Lateral Internal Sphincterotomy is found to be a better treatment modality for chronic Fissure-in-Ano Topical Diltiazem ointment in this study. However, Topical Diltiazem ointment can be used as the initial modality of treatment in patients unwilling or unfit for surgery.

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## INFLUENCE OF SYSTEM QUALITY, INFORMATION QUALITY, AND SERVICE QUALITY ON ORGANIZATION AT PUBLIC HEALTH CENTER PASURUAN CITY

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### ABSTRACT

Health policy in Indonesia requires every public health center to organize a Puskesmas Management Information System (SIMPUS). SIMPUS implementation in Pasuruan City aims to improve the quality of health services, but in its implementation SIMPUS still faces many obstacles so that it has not run optimally. The purpose of this study is to identify and determine the effect of system quality, information quality and service quality on the organization. This type of research used analytic observational with cross sectional design. Total population 268 officers with a sample of 160 officers at the public health center. The results showed that the quality of the system had no effect on the organization. Meanwhile, information quality and service quality have an effect on the organization. Suggestions that can be given are improving network quality, holding training and technical guidance, evaluating and maintaining devices.

**KEYWORDS:** SIMPUS, system quality, information quality, service quality, organization.

### INTRODUCTION

Every health care facilities are required to manage health information systems as part of a management system to support and ensure better health services at the first level and the advanced level. Based on Permenkes No.31 of 2019 concerning of the public health center Information System, which states that every public health center is required to organize a Puskesmas Management Information System or called by SIMPUS. SIMPUS is a health center management applications where the primary function is to organize patient data starts from registration, examination, and treatment of patients. SIMPUS used to support the recording and documentation of health services at the health center using a computer and software (Thenu et al, 2016).

Based on the preliminary survey at the Pasuruan city public health centers in implementing the SIMPUS application, there are still several obstacles in terms of technology, namely the patient registration process at SIMPUS usually lasts 1-2 minutes now becomes 4-5 minutes, frequent errors occur at SIMPUS and slow connections due to SIMPUS connected in all Pasuruan city public health centers. Users also still ignore the SIMPUS operation procedures by not using it continuously and not filling in data completely. The lack of teamwork and management support for the use of

SIMPUS can be seen from the absence of training or technical guidance related to SIMPUS operations for all users at the Pasuruan city public health centers.

Support from top management is also very meaningful to provide motivation in using SIMPUS. This study was conducted to identify and observe the effect of system quality, information quality and service quality of the organization of management support, teamwork and organizational culture in public health centers Pasuruan city. The results of this study are expected to be repair SIMPUS for the future so the implementation can be optimized and can improve the quality of service Pasuruan city public health centers.

### METHOD

This research uses observational analytic with cross sectional study carried out by observation and measurement of the variables studied simultaneously at the same time. Place of research conducted at the public health centers in Pasuruan city health department, amounting to 8 health center on July 2020 to September 2020. The total sample consisted of 160 people using proportional random sampling. Variables consist of system quality, information quality, service quality and organization.

Sources of data in the study included the primary data and secondary data. The primary data consist of the results of the questionnaire obtained directly from respondents about the assessment and documentation of information systems. Secondary data is SIMPUS regulations issued by the Pasuruan city health department. The results of the study are presented in tables and narrative. Analysis of the data in this study were analyzed using program Partial Least Square (PLS) 3.0 with the analysis of SEM (Structural Equation Modeling). SEM is a statistical analysis technique which has the ability to analyze the pattern of the relationship between the latent variables and indicators (Wibisono et al, 2015).

## RESULT

### Identification System Quality, Information Quality, Service Quality SIMPUS

Assessment of system quality: 101 respondents (63%) said it was enough and 9 respondents (6%) said it was bad. Information quality: 99 respondents (62%) said it was enough and 6 respondents (4%) said that it was bad. Service quality: 81 respondents (51%) said it was enough and 5 respondents (3%) said it was bad. From the respondent's assessment above, it can be concluded that the system quality variable, the information quality variable, the service quality variable are in the enough category.

**Table 1: Identification System Quality, Information Quality, Service Quality.**

Variable	Category	N	%
System Quality	Bad	9	6
	Enough	101	63
	Good	50	31
	Total	160	100
Information Quality	Bad	6	4
	Enough	99	62
	Good	55	34
	Total	160	100
Service Quality	Bad	5	3
	Enough	81	51
	Good	74	46
	Total	160	100

### Identification of Organization SIMPUS

The assessment of organization, the highest value, 90 respondents (56%) said that it was good and 4 respondents (3%) said it was bad.

**Table 2: Identification of Organization.**

Variable	Category	N	%
Organization	Bad	4	3
	Enough	90	56
	Good	66	41
	Total	160	100

Based on the respondent's assessment, the organization was in the enough category 66 respondent (41%).

**Table 3: Result Test Direct Effect.**

Exogenous Variable	Endogenous Variable	T Statistics (IO/STDEV)	P Values	Information
System Quality	Organization	1,136	0,432	Not Significant
Information Quality	Organization	3,152	0,002	Significant
Service Quality	Organization	3,826	0,000	Significant

## DISCUSSION

Quality is the most important criteria for the success of an information system which refers to the desired features of an information system such as ease of access, flexibility, system integration, system response time, system reliability, the use of new technologies, the detection of user expectations, ease of learning and use. The quality of the system is in the moderate category (63%) because SIMPUS is easy to learn and easy to use in data entry, flexible in providing information and safe because SIMPUS is equipped with a username and password. In term speed of access, because the SIMPUS application is accessed simultaneously in all public health centers in Pasuruan city, sometimes it causes the internet connection to be slow and errors so that the work of the officers is slightly disrupted.

The quality of information generated by SIMPUS in the category enough (62%) because in terms of completeness, there are several columns of information that are not filled in completely and not appropriate with the user's needs for example, only at the pharmacy because of lack

of information about the amount of drug stocks at SIMPUS then the officer did check manually. The information that is generated or required must have good completeness because it will influence the decision making or determine the overall action. The quality of good information that includes a complete, accurate, timely and consistent.

Service quality is the level of satisfaction from service interactions received by users. Service quality consists of indicators of response speed, assurance and empathy. In response speed indicator, service providers SIMPUS always fast response in serving users. But sometimes service providers are also slow in dealing with certain problems that occur in SIMPUS. On the assurance indicators, service providers is already provides technicians who are competent in dealing with problems that occur in SIMPUS and always do a reconsideration after repair on SIMPUS. The success of information systems depends on the importance of technology resource infrastructure, technical skills and the quality of service provided by the developer.



Organizational factors can be assessed through leadership, top management support, and team work procedures. In terms of organizational culture, data re-checking is often forgotten because of the large number of patient queues. But, until now, data errors are still rare. Management support provided by the leadership is still not optimal because it tends to be indifferent and does not pay much attention to the implementation of SIMPUS. In addition, to support the successful implementation of SIMPUS, there has never been any training or socialization related to SIMPUS so that users feel that they are not very good at operating SIMPUS. It is important for management to understand the structure and needs of users in the successful implementation of the system that will have an impact on the performance and organization.

The result of the calculation of system quality to organization generate statistical value  $1.136 > 1.96$ , which means do not show the influence and the p-value  $0.432 < 0.05$ , which indicates that the value is not significant. This study proves that system quality have no effect on organization. The benefits of the system quality that are not implemented by users are related to several functions and features that exist in SIMPUS which causes organizations to make less strategies, especially in terms of training and evaluation for the implementation of SIMPUS.

Information quality have a positive influence on organization. The results of the calculation show that the t statistical value is  $3.152 > 1.96$ , which means there is an influence between the two variables. Meanwhile, the p value is  $0.002 < 0.05$ , which means that the value is significant. The higher quality of information produced by SIMPUS it will facilitate the organization in decision making.

Service quality also affects the organization. The result of the calculation produces a value of t statistic of  $3.826 > 1.96$ , which means that there is influence between the quality of service to the organization. The p value is  $0.000 < 0.05$ , which means that the resulting value is significant. This research shows that the better the quality of services provided by the service provider SIMPUS it can allow organizations to define a better strategy.

## CONCLUSION

Based on the identification results, the system quality, information quality, service quality and organization are in the sufficient category because there are still some factors that are still less than optimal, including speed of access, completeness, speed of response, and management support. Therefore, it should be an improvement on the factors that are lacking to support the successful implementation of SIMPUS.

Advice can be given to improve the quality SIMPUS to fit the vision and mission of the organization in terms of

decision making and improve the quality of health services is improve the quality of the network or internet connection so that the connection is running fast, providing training and technical guidance on procedures for the operation of SIMPUS organized by public health center and health department every 3 months to all SIMPUS users in Pasuruan City to improve users' skills and knowledge about the SIMPUS application. In addition, it is necessary for evaluation and periodic maintenance on the hardware and software to support SIMPUS to run optimally.

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## PREVALENCE OF OBESITY AMONG CHILDREN UNDER 5 YEARS ATTENDED TO PRIMARY HEALTH CARE CENTERS IN MOSUL CITY

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### ABSTRACT

**Background:** Childhood obesity is a "condition in which excess body fat negatively affects a kid's health or wellbeing". Due to expanding the occurrence of Childhood obesity and its various health impacts, it is considered as a serious general wellbeing concern. **Aim:** To determine the prevalence of overweight and obesity among children under 5 years attended primary health care centers in the Mosul city. **Methods:** **Study Setting:** Primary health care centers were chosen as three centers from both right & left sectors of Mosul City. **Study Design:** Cross-section study, which is a descriptive observational study. **Sample Size:** Three hundred and ten (310) children of both sexes aged under 5 years attended primary health care centers were examined, this sample was distributed by multistage stratified simple random technique. **Data Analysis:** Descriptive and analytic statistical tools were applied. For comparison between two means, independent t-test was used and chi-square test was applied for comparison between two categorical variables. Questionnaire form was arranged utilizing summarized questions. **Results:** In the present study, prevalence of overweight and obesity was 10.32%, 56.4% of the study sample were males, the rest were females and 59.4% of obese children were males while 40.6% of them were females. Mean age was 24.6 months with a range of 2 – 60 months, mean weight was 11.6 kg with arrange of 4.5 – 25.5 kg, mean height 83 cm with a range of 58 – 120 cm. All of obese children ate jam and only 9.5% of normal children ate jam, 40% of obese children moderately active and 27% of normal children moderate active, whereas 40% of obese not active and 26% of normal also not active. About half of normal children were active (47%) and only 20% of obese child were active. **Conclusion:** The present study concludes that there was a powerful association between eating some items of feeds like jam, also there was a reverse relationship between obesity and physical activity.

**KEYWORDS:** About half of normal children were active (47%) and only 20% of obese child were active.

### INTRODUCTION

Obesity in children is a general wellbeing burden in numerous nations. The first problem happen in obese kids are passionate or psychological.<sup>[1]</sup> Studies have shown that child overweight prompts the advancement of biomarkers of severe illnesses later in life. type II diabetes among Hispanic kids, for instance, is on the ascent because of hereditary susceptibility joined with obesity.<sup>[2]</sup> In addition to type II diabetes, overweight kids have an expanded danger for creating asthma, joint problems, cholesterol, depression, and anxiety. Physical and psychosocial effects of moderate to severe overweight include: obstructive apnea, hyperlipidemia, early onset of puberty in females, gallbladder disease,

hypertension, pancreatitis, polycystic ovary syndrome, and long-term damage to the cardiovascular system.<sup>[3]</sup> A systematic review of studies looking at the relationship between physical activity in children and obesity found about half had found no effect and the balance had a negative effect (i.e. Increased physical activity levels were protective).<sup>[4]</sup> Aim of study to determine the prevalence of overweight and obesity and associated factors among children under five years visited primary health care centers in Mosul City.

### SUBJECTS AND METHODS

Preceding to data collection (an official permit) was collected from the Nineveh Health Directorate (NHD) to

ease data collection from primary health care centers (PHCCs) that were to be participating in this study. also (informed oral consent) was collected from the concerned PHCCs managers, workers and participants.

**Sampling Technique:** To estimate the minimum sample size in the present study, Gorstein et al.,<sup>[5]</sup> sample size equation was used, which is

Where:

$$N = \frac{(z^2)(pq)}{d^2}$$

Z= z-value for 95% confidence (1.96).

P= prevalence of childhood obesity, which was 10 %.

q=1-p

d= is the desired level of absolute precision. In this work the value 0.05 was used. Since data collection was carried out from multiple PHC centers with different population size in the catchment areas; the estimated design effect (DEFF) used was to multiply the value given by the equation by 2. For the non-response or recording error the calculated sample size was inflated by 5%.

The sample of this study will be distributed by multistage Stratified Simple random method. 310 children were collected. Six health care centers spread across the Left and Right Sectors of Mosul City were undertaken. Right Sector PHC centers

- 1- AL-Yarmuke health center.
- 2- AL-Hadbaa health center.
- 3- Nablus health center.

Left Sector PHC centers

- 1- Al-Quds health center.
- 2- AL-Sharqy health center. 3- AL-Noor health center.

**Target Population**

- Under five years healthy male and female children attending primary health care centers for vaccination or accompany with their mothers.
- The period of data collection was three months: May-June and July 2013.
- All children included in the sample were examined by the investigator for the following

**Anthropometric Measurements**

- Body weight in Kg; baby was weighted with minimum amount of clothing, measurements was carried out using Seca scale/UNICEF.
- Height in cm, if the child was equal or older than two years (standing); height was taken by using wooden board of WHO/Seca.
- Length if the child was younger than two years (lying); In this measurements plastic or wooden board of WHO/Seca was used.
- Calculate the body mass index (BMI) = weight in

kg/[length(height)in m]<sup>2</sup> Then putting data in WHO Anthro program.

**Case definition of obesity in children whose Age from birth to age 5 according to WHO**

- **Obese child:** if the Body mass index (BMI) > 3 standard deviations (SD) above the WHO growth standard median.
- **Overweight child:** if the BMI > 2 standard deviations (SD) above the WHO growth standard median.<sup>[6]</sup>

**Data analysis and statistical test**

After the completion of the sample collection a dummy table with coding was performed, then data tabulation enters into the Excel software program.

Descriptive statistics and analytics statistics was done by using the Minitab statistical program. Chi-square test was used for comparison between categorical (qualitative) variables. For small frequency cells, Fisher-Exact test was used instead of Chi-square test. P-value ≤ 0.05 was considered significant throughout data analysis.

**RESULTS**

The sample of the present study includes 310 children. Table 1 describes the basic characteristics of study children. Out of the total sample 56.4% were males and the rest were females. Only 15.2% fell in the age group 0-6 months old, and less than half (44.8%) fell in the age group 7-24 months old, and two fifth (40.0%) were 25-60 months old.

**Table (1): Basic characteristics of study sampled children.**

Parameters	No. (n = 310)	%
<b>Sex</b>		
<b>Male</b>	175	56.4
<b>Female</b>	135	43.6
<b>Age groups (months)</b>		
<b>0 – 6</b>	47	15.2
<b>7 – 24</b>	139	44.8
<b>25 – 60</b>	124	40.0

Table 2 illustrates descriptive statistics like mean age was 24.6 months with a range of 2 – 60 months, mean wt. 11.6 kg with a range of 4.5 – 25.5 kg, height mean 83.0 cm with a range of 58.0 – 120.0 cm and child no. mean 3 with a range 1 – 9 children.



**Table (2): Mean parameters: Age, Weight, Height and Number of children.**

Variable (n=310)	Mean	SD	Minimum	Maximum
Age (m)	24.6	16.766	2.0	60.0
Weight (kg)	11.6	3.865	4.5	25.5
Height (cm)	83	14.897	58.0	120.0
Number of children	3	1.5308	1.0	9.0

In this study 32 children out of 310 were obese, so the prevalence of obesity was 10.32% as demonstrated in Table 3. The normal children were 259 about 82.55% of

the total sample of this study and underweight child where BMI  $\leq -2$  SD was 19 about 6.13%.

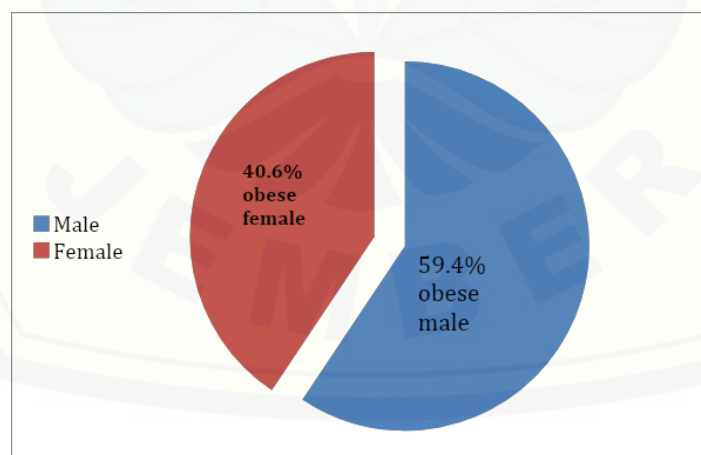
**Table (3): Prevalence of obesity according WHO growth assessment of "BMI to age".**

Z-score (n=310)	Classification	No.	%
$\geq +2$ SD	Overweight & Obese children	32	10.32
+1; $< +2$ SD	Normal BMI	62	20.00
0; $< +1$ SD	Normal BMI	95	30.64
$< 0$ ; -1 SD	Normal BMI	72	23.23
$< -1$ ; -2 SD	Normal BMI	30	9.68
$\leq -2$ SD	Underweight children	19	6.13

Table 4 describes the distribution of obesity (%) according to age group. The prevalence of this disorder was 4.26% in the age group 0-6 months old, followed by 12.23% in age groups 7-24 months old. Overall, 10.32% of the examined children were obese.

**Table (4): Prevalence of obesity in the three age groups according WHO classification for growth assessment.**

Age groups (months)	No.	%	Prevalence of obesity	
			No.	%
0 – 6	47	15.16	2	4.26
7 – 24	139	44.84	17	12.24
25 – 60	124	40.00	13	10.48
<b>Total</b>	310	100.00	32	10.32



**Figure 1: Obesity prevalence in both sexes.**

Table 5 demonstrates that there was no significant association between obesity prevalence and feeding before breakfast, while there was a significant association between obesity prevalence and eating jam during breakfast as well as drinking tea.

**Table (5): Comparison between obese and normal child according to the items of feeding before & during breakfast.**

Parameters	Obese children [n = 28]		Normal BMI [n = 200]		P-value*
	No.	%	No.	%	
<b>Before breakfast feeding</b>					
Milk	7	25.00	60	30.00	0.586
Biscuit	4	14.29	53	26.50	0.162
Nestle	4	14.29	48	24.00	0.251
<b>At breakfast feeding</b>					
Chesses	13	46.43	127	63.50	0.076
Bread	8	28.57	88	44.00	0.121
Egg	17	60.71	126	63.00	0.815
Jam	28	100.00	19	9.50	<b>0.000</b>
Tea	6	21.43	106	53.00	<b>0.002</b>

Chi-square test, d.f = 1. And Fisher-exact test for small frequency cells were used.

Table 6 comparison between obese and normal BMI child according to the physical activity where p –value significant (0.012) in moderate activity children, also

significant (0.009) in not-active children. About half of normal BMI children were active (47%) while only 20% of obese children were active.

**Table (6): Comparison between obese and normal child according to the physical activity.**

Physical activity	Obese children [n = 30]		Normal BMI [n = 202]		P-value*
	No.	%	No.	%	
Active	6	20	96	47	---
Moderate	12	40	54	27	<b>0.012</b>
Not-active	12	40	52	26	<b>0.009</b>

Chi-square test, d.f = 1. And Fisher-exact test for small frequency cells were used.

## DISCUSSION

The sample of the present study includes 310 children. Male account 56.4% and 43.6% were females. Mean age was 24.6 months with a range of 2– 60 months, 60% below two years and 40% were two to five years, this is because under two years attendant to the PHCC by their mothers to receive vaccine according to their immunization schedule.

The prevalence of overweight and obesity in the present study was 10.32%, which is higher than Matti study (3.5%).<sup>[7]</sup> (which was talking about the assessment of nutritional indicators among under five children at Al-Hamdaniya District, which is one of the biggest districts in Nineveh Governorate, on the south east of Mosul city North of Iraq) Pertaining to the nearby countries the prevalence of overweight and obesity for the period 2000-2009 was 4.7% in Jordon, 6.1% in Saudi Arabia, and in Egypt that was 20.5%.<sup>[8]</sup> The prevalence has increased at an alarming rate. Globally, in 2010 the number of overweight children under the age of five is calculated to be over 42 million. Close to 35 million of these are living in developing countries.<sup>[9]</sup>

The present study demonstrated no difference in the prevalence of risk of overweight and obesity among less than five children by age and sex this finding is logical with another study achieved in Canada.<sup>[10]</sup>

And differ from a study conducted by Kaur and co-

workers in India.<sup>[11]</sup> And study of Matti conducted by Al-Hamdaniya.<sup>[7]</sup> On the same topic Kamal et al.,<sup>[12]</sup> in Qatar recorded high levels of obesity among girls. The different figures recorded across studies may reflect different cultural habits and attitudes towards nutrition and physical activities. Bellisle et al.<sup>[13]</sup> have concluded that there does not appear to be a relationship between meal patterning and obesity; while the present study showed that children who ate jam during breakfast associated with overweight and obesity, the association was significant,  $p=0.000$ .

As we all know that the physical activity is most important in preventing obesity and also in decreasing it so there is adverse relationship between obesity and physical activity.

In the present study child who plays with ball and drive bicycle these consider active child and those who go into picnic consider moderate active child. Lastly, those children who watch TV consider not active child. There are several psychological effects of watching TV that encourage obesity. TV watching lowers physical activity. It was also found to lower the resting (basal) metabolic rate to a level related to that experienced during trancelike states.<sup>[14]</sup> In the present study we find significant association between these two variables  $p=0.012$  in those moderate active children and a higher significance in those not active, ( $p=0.009$ ) in comparison with active children.



A prospective study by Gortmaker et al.<sup>[15]</sup> showed a strong positive dose–response relationship between time watching television and prevalence of overweight.

## CONCLUSION

The present study concludes that there was a powerful association between eating some items of foods like jam, also there was a reverse relationship between obesity and physical activity.

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## PROGNOSIS OF HYPERREFLECTIVE FOCI (DOTS) ON OPTICAL COHERENCE TOMOGRAPHY IN PATIENTS WITH DIABETIC MACULAR EDEMA: ABOUT 30 CASES

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### INTRODUCTION

Diabetic macular edema (DME) is a thickening of the macular retina secondary to a rupture of the internal blood-retinal barrier. It is the leading cause of low vision in diabetic patients.<sup>[1]</sup> The functional prognosis depends on several anatomical factors. The spectral domain optical coherence tomography (SD-OCT) is an important tool for the diagnosis, therapeutic indication and monitoring of diabetic macular edema.

The aim of our study is firstly to assess the correlation between the number of intra-retinal hyper-reflective points (DOTS or FOCI) and the central thickness of the retina (CRT) and secondly to study the dynamics of DOTS during treatment by anti-VEGF.

### PATIENTS AND METHODS

We reviewed the medical files of patients with DME who were treated with intravitreal injections of bevacizumab at the department of Ophthalmology of the Cheikh Khalifa Ibn Zaid University Hospital in Casablanca, between January 2018 and December 2019.

All patients were followed for diabetic macular edema confirmed by follow-up OCT b scan and treated with IVT of Bevacizumab according to the Trait and Extend protocol.

The inclusion criteria are

- diabetic macular edema
- Treatment of 3 injections of anti-VEGF (Bevacizumab at a dose of 1.25 mg / IVT) with 4 week intervals
- Baseline and monitoring data available over 3 months.

The exclusion criteria are

- Previous treatment with focal laser or PPR
- Tractional retinal detachment or intravitreal hemorrhage
- Presence of other vascular pathologies (eg: OVR)

The Variables studied before and after treatment are

- Corrected visual acuity
- Central retinal thickness (CRT)

- Number of intra-retinal hyper-reflective points (DOTS) and their distribution in the retinal layers

The statistical study was carried out with SPSS version 20 software.

### RESULTS

The average age was 61, with extremes ranging from 55 to 76. The sex ratio was 1.3 (17 men and 13 women). The average duration of diabetes was 8 years.

The number of DOTS before treatment was 20.86 +/- 7.41 and after treatment 11.85 +/- 6.76.

2/3 of DOTS (68.33%) were located in the inner retinal layers. Their number significantly decreased after treatment at the level of the internal layers, going from 14.24 ± 5.01 to 8.86 ± 4.66 after treatment (p < 0.001).

1/3 of DOTS (31.67%) were located in the outer retinal layers, their number significantly decreased after treatment in the outer layers from 6.6 ± 3.28 to 3.05 ± 2.10 after treatment (p < 0.001). Central retinal thickness (CRT) increased from 461.91 ± 82.22 μm to 348.39 ± 73.44 μm after treatment (p < 0.001). (table 1)

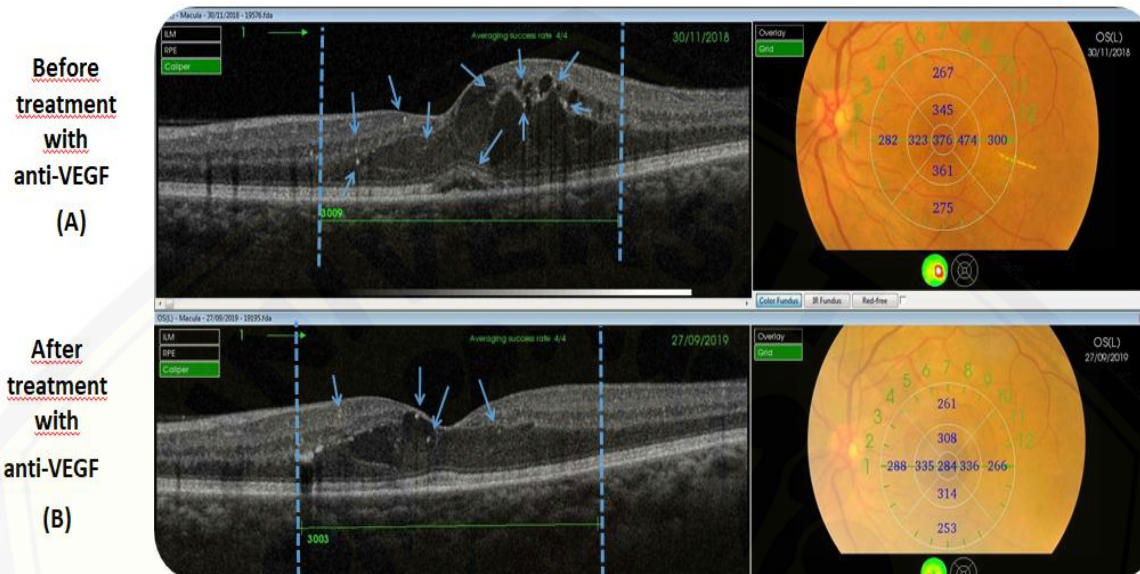
There is a significant correlation between the number of DOTS and the ECM. The correlation factor is 0.456 (p < 0.001) (figure 1)

The corrected visual acuity improved significantly after treatment, it went from 0.3 +/- 0.14 to 0.4 +/- 0.13 (p < 0.001) (table 1).

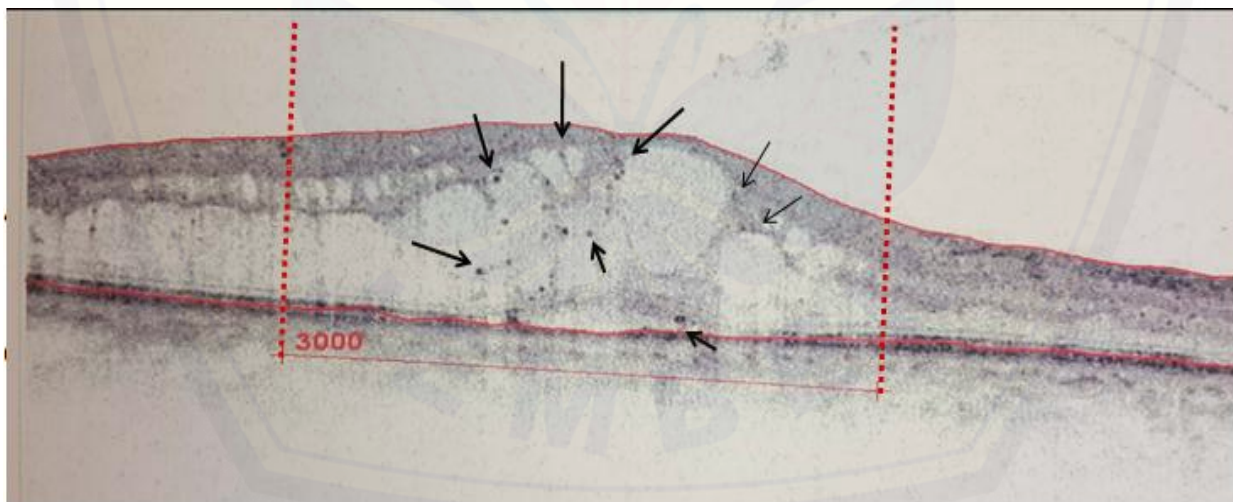


**Table 1: Differences between before and after treatment with anti-VEGF : Mean changes in central retinal thickness, visual acuity and number of hyperreflective foci at baseline and after 3 injections with anti-VEGF.**

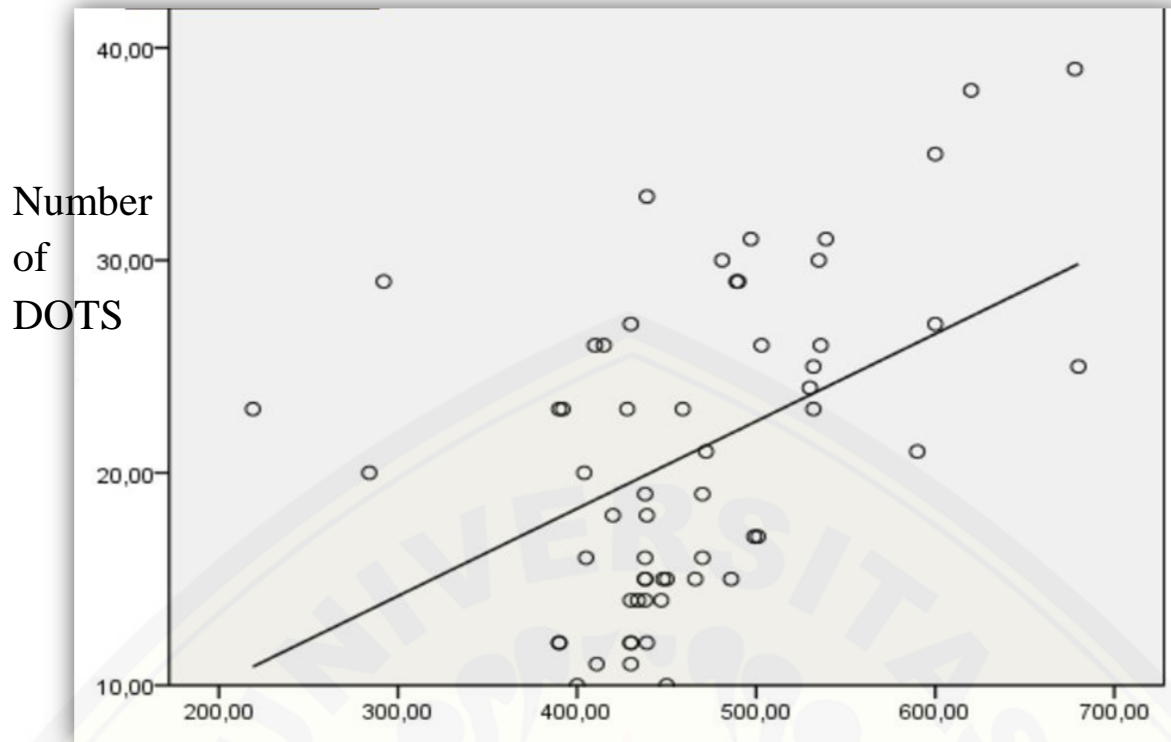
	Before treatment with anti-VEGF	After treatment with anti-VEGF
Number of DOTS	20,86 +/-7,41	11,85+/- 6,76
Number of DOTS in inner layers	14,24±5,01	8,86±4,66
Number of DOTS in outer layers	6,6±3,28	3,05 ±2,10
Central Retinal Thickness (CRT)	461,91 ±82.22 µm	348,39 ±73.44 µm
Corrected visual acuity	0.3 +/- 0.14	0.4+/- 0.13



**Figure 2: OCT B scan before (A) and after 3 months of IVT treatment of Bevacizumab centered on the fovea (B) showing the presence of DOTS in the central 3000 µm around the fovea.**



**Figure 3: Foveal centered spectral domain optical coherence tomography (SD-OCT) B-scan image of a patient with DME. Black arrows indicate hyperreflective foci, within 3000 µm of the fovea (dashed bars).**



**CRT before treatment of Bevacizumab**

**FIGURE 1:** Table showing a significant correlation between the number of DOTS and the ECM. The correlation factor is 0.456.

## DISCUSSION

Hyper-Reflective Points (DOTS) are small, dense, well-circumscribed round or oval particles less than 100  $\mu\text{m}$  in size.<sup>[2]</sup> Their reflectivity to OCT is higher than that of pigment epithelium. They can be present throughout the retinal thickness, in the walls of intra-retinal cubicles and at the edge of a serous retinal detachment.<sup>[3]</sup>

They are seen in diabetic retinopathy, AMD; OVRs; central serous chorioretinitis; retinal dystrophies and retinal detachment.<sup>[4]</sup>

Many authors have speculated on the pathophysiology and origin of hyper-reflective points. They can be either precursor of exudates, or secondary to a migration of the cells of the pigment epithelium, or correspond to degenerated Müller cells or else to the aggregation of activated immune cells such as microgliaocytes.<sup>[5]</sup>

Several studies<sup>[6]</sup> have reported the predominance of hyper-reflective points (DOTS) at the level of the inner layers of the retina (80%) compared to the outer layers. This result matches that of our study with a percentage of 68.33 percent at the level of the internal layers and 31.67 percent at the level of the external layers.

Hwang et al. Have<sup>[7]</sup> studied dots whose reflectivity is equal to that of EP, while we have used a reflectivity higher than the surrounding tissue, which, in our

experience, results in a more reliable detection of DOTS. In addition, proliferative diabetic retinopathy is associated with an exuberant increase and activation of microglia, and we therefore hypothesize that neovascularization could influence the number of HF.<sup>[8]</sup> For this reason, we excluded patients with neovascularization.

In addition, different treatment response criteria were used by different study groups: Kang et al.<sup>[9]</sup> chose a definition of response to treatment of CRT <300  $\mu\text{m}$  or a reduction of more than 50  $\mu\text{m}$ , while Vujosevic et al. defined it by the continuous variables: improvement in VA and reduction in CRT, respectively.<sup>[10, 11, 12, 13]</sup> As in the case of our study, we have an average decrease in ECM of 113  $\mu\text{m}$  after treatment with IVT of bevacizumab Hwang et al. Recently reported that a decrease in the number of FOCI was associated with a good ECM response after 3 months of treatment with bevacizumab.<sup>[14]</sup> The reason for this link is not clear, although there are substantial differences in the design of the study.

Our work shows that DOTS responds decrease after treatment to anti-VEGF (figure 2) and reside mainly in the inner layers of the retina, which is consistent with the behavior of microglial cells.<sup>[15]</sup> In addition, the decrease in the number of DOTS after 3 months of bevacizumab mainly concerned the inner retinal layers, which supports the hypothesis that DOTS in these layers corresponds to



activated microglia, and that DOTS in the outer retinal layers. may represent a different entity.<sup>[16, 17]</sup>

The hypothesis that DOTS are precursors of hard exudates is all the more possible given the equal reflectivity on OCT but also their situation in general at the level of the outer plexiform layer. Unlike microglial cells, which are not subject to rapid regression after only 3 months of treatment, although these dynamics are unknown for hard exudate precursors.<sup>[18, 19]</sup>

## CONCLUSION

In DME, Intra-retinal hyper-reflective DOTS are sensitive to anti-VEGF treatment. Their initial number correlates with the response to anti-VEGF treatment in terms of reduction of central retinal thickness and improvement of visual acuity. Therefore, they are a good predictor of the evolution of diabetic macular edema. Further studies are needed to analyze the evolution of DOTS in the retinal periphery.

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## THE PROGNOSTIC VALUE OF PERIPHERAL BLOOD ABSOLUTE LYMPHOCYTE TO MONOCYTE RATIO AT DIAGNOSIS IN HODGKIN'S LYMPHOMA PATIENTS

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### ABSTRACT

Determination of prognostic factors in Hodgkin's Lymphoma patients plays an important role in reducing intensive chemotherapy, decreasing economic costs, and improving the outcome of the patients. We conducted this study to determine the prognostic value of [lymphocyte/monocyte ratio (LMR)] in Classical Hodgkin's Lymphoma patients (cHL) [trying to establish a relationship between it, overall survival (OS) & progression free survival (PFS)]. Also, we wanted to study the relationship between LMR and other variables such as age, sex, histological type, white blood cells, absolute lymphocyte count, absolute monocyte count, hemoglobin, serum albumin, Ann Arbor Staging, B-Symptoms, early or advanced stages, bulky mediastinal mass, type of primary treatment if chemotherapy alone or radiochemotherapy and the effect of these variables on OS and PFS. A retrospective study included 242 patients with cHL admitted to the center of radiochemotherapy in Tishreen University Hospital in Lattakia from January 2011 to December 2015. We monitored the patients until 1<sup>st</sup> September 2020. An LMR at diagnosis of 2.9 or more was the best cut-off value for survival. In univariate analysis, patients with LMR < 2.9 had inferior OS and PFS. LMR had an important prognostic value in patients with limited or advanced stages. In multivariate analysis, LMR was an independent prognostic factor for survival and to predict clinical outcomes in patients with classical Hodgkin's lymphoma. In conclusion, LMR provides a simple model to assess clinical outcomes in cHL.

**KEYWORDS:** Hodgkin Lymphoma, Absolute lymphocyte count, Absolute monocyte count, Prognostic factors.

### INTRODUCTION

Hodgkin lymphoma (HL) is the most common subtype of lymphoid neoplasm in patients younger than 40 years old. Despite modern treatment strategies improved overall survival (OS); approximately 20% of patients with classical Hodgkin lymphoma (cHL) will develop relapsed/refractory disease and will die.<sup>[1]</sup> The International Prognostic Score (IPS) uses seven prognostic factors to predict clinical outcomes in patients with newly diagnosed classical Hodgkin's lymphoma. However, the IPS only applies to patients with advanced stage disease,<sup>[2]</sup> but it does not fully reflect all the biologic spectrum of cHL and is less suitable for patients with limited stage disease<sup>[3]</sup> [i.e., stages I and IIA, without constitutional symptoms and no bulky disease (i.e. not  $\geq 10$  cm in diameter)]. Pathologically, cHL is characterized by the presence of a small number of

diagnostic Reed-Sternberg cells in a background of reactive inflammatory cells composed of lymphocytes, neutrophils, macrophages, eosinophils, plasma cells, fibroblasts and collagen fibers.<sup>[4]</sup> Tumor-associated macrophages (TAMs) are derived from circulating monocytes and are recruited to the tumor site by soluble tumor-derived chemotactic factors.<sup>[5,6]</sup> Because TAMs originate from circulating monocytes, it is not surprising that the absolute monocyte count (AMC) or LMR may influence TAM content.<sup>[4]</sup> Recently, the peripheral blood absolute lymphocyte count (ALC)/absolute monocyte count (AMC) ratio at diagnosis in cHL patients was reported to be a prognostic factor for clinical outcomes.<sup>[7]</sup> How the peripheral blood AMC, LMR, and TAM content may interact with one another in cHL patients in conjunction with clinical outcome is unknown at the present.

We, therefore, studied the role of (LMR-DX), as a simple biomarker combining an estimate of host immune homeostasis [i.e., absolute lymphocyte count (ALC)/tumor-infiltrating lymphocytes]<sup>[8,9]</sup> and tumor microenvironment [i.e., absolute monocyte count (AMC)/tumor-associated macrophages], on clinical outcomes in patients with cHL.<sup>[2]</sup> Major efforts have been also made to avoid possible overtreatment and potential long-term toxicity in younger patients and to identify patients requiring more aggressive therapy in order to avoid the development of refractory disease. In this regard, to define a scoring system that could stratify patients, and possibly even predict outcome, would be both helpful and practical to apply in daily practice.<sup>[10]</sup>

## MATERIALS AND METHODS

We carried out a retrospective study of 242 patients with cHL who were admitted to the center of chemoradiotherapy in Tishreen University Hospital in Lattakia, between January 2011 and December 2015. We followed up the patients until 1st September 2020. Exclusion criteria were: Patients diagnosed with nodular lymphocyte predominant Hodgkin's lymphoma; age less than 14 years; previous history of malignancy, transplantation, or immunosuppression; positive for anti-HIV; and lack of laboratory data and follow-up information. Clinical characteristics were obtained from medical records. Patients or their guardians provided written informed consent to participate in the study. Routine follow-up imaging analyses were performed every 3 months for the first 2 years, then every 6 months for the next 3 years, and then annually or whenever clinically indicated. The ALC and AMC were obtained from the CBC examined at the time of the cHL diagnosis. The LMR was calculated by dividing the ALC by the AMC from the CBC.

### End-points

The primary end-point of this study was to determine the prognostic value of LMR in Classical Hodgkin Lymphoma (studying the relationship between LMR, overall survival and progression-free survival from the moment that classical Hodgkin's lymphoma was diagnosed). The secondary end-point was to determine whether LMR has a prognostic value on clinical outcomes in patients with limited or advanced stage at diagnosis. Limited-stage was defined as stage IA and IIA, without B-symptoms and absence of bulky disease defined as any mass of 10 cm or more in diameter.

### Prognostic Factors

The prognostic factors evaluated in the study included:

age > 45 years, male gender, albumin <4 g/dl, white blood cell count > 15,000/ $\mu$ l, ALC < 600/ $\mu$ l or < 8% of white cell count, hemoglobin  $\leq$  10.5 g/dl, stage IV, primary treatment (chemotherapy plus radiation versus chemotherapy alone), limited versus advanced disease, AMC at diagnosis, LMR at diagnosis, histopathology type, bulky mediastinal disease and B- Symptoms.

### Response and Survival

The OS was defined as the time from the first day of diagnosis to the date of death or date of interrupted follow-up. PFS was defined as the time from cHL diagnosis to the time to progression, relapse from complete response, death as a result of any cause, or last follow-up.

### Statistical analysis

OS and PFS were analyzed using the approach of Kaplan and Meier. Differences between survival curves were tested for statistical significance using the two-tailed log-rank test. The Cox proportional hazard model was used for the univariate and multivariate analyses to evaluate the variables under the prognostic factors' section to assess their impact on overall survival and progression-free survival. The choice of the best cutoff values of AMC-DX and the LMR ratio for assessing survival was based on their utility as a marker for the clinically relevant binary outcome of death/survival using the receiver operating characteristics curves (ROC) and area under the curve (AUC). Chi-square tests were used to determine relationships between categorical variables. The binary clinical outcome (death/survival) was established at 5 years after diagnosis. Patients were classified as "alive/censored" when the follow-up time was greater than 5 years and "death" for patients known to have died before this time point. All statistical analyses were performed using the IBM statistics (version20). The results were considered to be statistically significant when p-value < 0.05.

## RESULTS

### Patients' characteristics

Our study included 242 cHL patients, males were 141 patients (58.3%) and females were 101 patients (41.7%). The male to female ratio was 1.4:1. The median age at diagnosis was 31 years (range, 14-79 years). The distribution of additional baseline characteristics is presented in (Table 1). We recorded the death of 28 patients (11.6%) who died due to relapse/progression of lymphoma. The estimated 5-year OS rate was 88.4% and 5-year PFS was 75.6%.

**Table 1: Demographic and clinical characteristics of patients.**

Characteristic at diagnosis	No. of patients (%)
Age, median (range, years)	31 (14 – 97)
Male gender	58.3%
Histologic subtype	
Nodular sclerosis	65.3%

Mixed cellularity	30.2%
Lymphocyte-rich	2.9%
Lymphocyte-depleted	1.7%
Not classifiable	6.2 %
Ann Arbor stage	
I	5%
II	44.2%
III	33.1%
IV	17.8%
Stage (limited versus advanced)	
Limited	13.2%
Advanced	86.8%
B symptoms present	82.2%
Primary treatment	
Chemotherapy	59.1%
Chemoradiotherapy	40.9%
Mediastinal bulky disease	
≥10cm	9.9%
< 10cm	34.7%

#### Cut-off values for absolute monocyte count at diagnosis, ratio of absolute lymphocyte count to absolute monocyte count for survival analysis

The ROC curves of the LMR according to survival were generated to determine the appropriate cut-off value. For all patients, the area under the curve for the LMR was recorded as 0.62 [95% confidence interval (CI): 0.4 to 0.7]. An LMR value of 2.9 corresponded to the maximum joint sensitivity and specificity on the ROC curve for all patients (74% sensitivity and 76% specificity). An AMC-DX of 720 cells/mL or more had an AUC of 0.66 [95% confidence interval (CI): 0.4 to 0.6] with a sensitivity of 73% and specificity of 74%.

#### Comparison of patients with LMR values ≥ 2.9 to those with values < 2.9

Characteristics are summarized according to whether

patients presented with an LMR of 2.9 or more versus less than 2.9 in (Table 2). In this study, 70 patients (28.92%) had an LMR < 2.9, and 172 patients (71.08%) had an LMR ≥ 2.9. Higher numbers of patients in the group with LMR greater or equal to 2.9 had an albumin concentration of 4 g/dL or more (P=0.001). Fewer patients in the group with LMR of 2.9 or more presented with an ALC less than 600 cells/mL or less than 8% of the white blood cells (P=0.01), hemoglobin ≤ 10.5 g/dl (P=0.02), white blood cells > 15000×10<sup>9</sup> (P=0.0001) and also fewer numbers come with advanced stage (P=0.02), have B- Symptoms (P=0.006) and bulky mediastinal mass (P=0.04). No difference between the groups was observed regarding age (P=0.07), male gender (P=0.6), Stage IV (P=0.6), chemotherapy regimens (P=0.7), Ann Arbor Staging (P=0.6) and histopathological type (P=0.7).

**Table 2: Characteristics of the patients divided according to LMR ratio ≥ 2.9 versus < 2.9.**

Characteristics	LMR ≥ 2.9 (N =172)	LMR < 2.9 (N =70)	P- value
<b>At diagnosis</b>			
Age, years, median (range)	29 [14-65]	32 [14-79]	0.06
Gender	102 (59.3%)	39 (55.7%)	0.6
Male Female	70 (40.7%)	31 (44.3%)	
Histology			
Nodular sclerosis	109 (63.4%)	48 (68.6%)	
Mixed cellularity	54 (31.4%)	19 (27.1%)	0.7
Lymphocyte-depleted	6 (3.5%)	2 (2.9%)	
Lymphocyte-rich	3 (1.7%)	1 (1.4%)	
Stage			
I	10(5.8%)	2(2.9%)	
II	77(44.8%)	30(42.9%)	0.6
III	54(31.4%)	26(37.1%)	
IV	31(18%)	12(17.1%)	
Stage			
Limited	28(16.3%)	4(5.7%)	0.02
Advanced	144(83.7%)	66(94.3%)	



Mediastinal bulky disease			
≥10cm	13(7.6%)	11(15.7%)	0.04
< 10cm	62(36%)	22(31.4%)	
Treatment			
Chemotherapy	103(59.9%)	40(57.1%)	0.7
Chemotherapy and radiation	69(40.1%)	30(42.9%)	
<b>IPS risk factors</b>			
Age in years			
> 45	48(27.9%)	12(17.1%)	0.07
≤ 45	124(72.1%)	58(82.9%)	
Albumin (g/dL)(N =174)			
≥ 4	54(45%)	14(25.9%)	0.001
< 4	66(55%)	40(74.1%)	
Hemoglobin (g/dL)			
> 10.5	115(66.9%)	36(51.4%)	0.02
≤ 10.5	57(33.1%)	34(48.6%)	
White blood cell count×(10) <sup>9</sup>			
> 15	33(19.2%)	31(44.3%)	0.0001
≤15	139(80.8%)	39(55.7%)	
Absolute lymphocyte count×(10) <sup>9</sup>			
≥ 600	171(99.4%)	66(94.3%)	0.01
< 600	1(0.6%)	4(5.7%)	
Male	102(59.3%)	39(55.7%)	0.6
Stage 4	31(18%)	12(17.1%)	0.6

LMR denotes absolute lymphocyte count/absolute monocyte count at diagnosis; IPS: International Prognostic Score.

### Prognostic significance of LMR

For patients, those with LMR < 2.9 had a significantly lower survival compared with those with LMR ≥2.9 (5-year OS: 81.4% vs 91.9%,  $p = 0.03$ ; and 5-year PFS: 67.1% vs 79.1%,  $p = 0.04$ ) (Fig .1). In Univariate Analysis, Patients with an AMC- DX of 720 cells/mL or more had inferior overall survival and progression-free survival compared with patients with an AMC-DX of less than 720 cells/mL [overall survival: median 6.1 years versus 6.4 years  $P=0.03$ ]; [progression-free survival: median 4.9 years versus 5.3 years,  $P=0.03$ ]. Patients with an LMR of 2.9 or more had superior overall survival and progression-free survival compared

with patients with an LMR less than 2.9 [overall survival: median 6.4 years versus 5.9 years, 5-year overall survival rates of 91.9% versus 81.4%,  $p=0.03$ ; progression-free survival: median 5.5 years versus 4.7 years, 5-year progression-free survival rates of 79.1% versus 67.1%,  $P=0.04$ ]; Neither age nor gender of patients nor bulky mediastinal mass was predictive of overall survival or progression-free survival compared with the other prognostic factors studied (Table 3). In Multivariate Analysis, LMR remained an independent prognostic for overall survival and progression-free survival (Table 3).

**Table 3: Univariate and multivariate analysis for overall survival (OS) and progression-free survival (PFS).**

Covariate	Univariate analysis					
	OS			PFS		
	HR	95%CI	P value	HR	95%CI	P value
Age (>45years)	0.6	[0.2-1.7 ]	0.8	0.4	[0.2-1.5]	0.3
Male	0.7	[0.3-1.5]	0.3	0.6	[0.2-1.5]	0.4
WBC (> 15) ×10 <sup>9</sup>	2.5	[1.2-5.3]	0.01	2.3	[1.1-5.2]	0.01
ALC-DX cells/mL < 600	4.2	[1.1-8.9]	0.004	3.1	[0.9-6.4]	0.002
AMC-DX cells/mL ≥ 720	2.1	[0.3-8.9]	0.03	2.5	[0.9-7.1]	0.03
LMR < 2.9	2.6	[1.2-5.4]	0.001	2.4	[0.1-1.8]	0.003
Albumin (< 4) g/dL	1.3	[0.1-1.9]	0.04	1.2	[0.1-1.7]	0.01
Hemoglobin g/dL (≤ 10.5)	2.4	[1.1-4.9]	0.02	2.3	[1.1-4.9]	0.02
Bulky disease (≥ 10cm)	1.2	[0.4-3.9]	0.6	1.1	[0.3-3.5]	0.8

Stage 4	1.3	[1.2–1.8]	0.02	1.4	[0.1–1.8]	0.02
CT and RT versus CT alone	1.4	[0.1–1.8]	0.01	1.3	[0.1–1.7]	0.01
Covariate	Multivariate Analysis					
	OS			PFS		
	HR	95% CI	P value	HR	95% CI	P value
LMR < 2.9	2.3	[1.2-6.3]	0.01	2.1	[1.3– 6.2]	0.02

ALC-DX: absolute lymphocyte count at diagnosis; AMC-DX: absolute monocyte count at diagnosis; LMR: lymphocyte count/ monocyte count ratio, CT: chemotherapy; RT: radiation; WBC: white blood cell count.

**Survival based on the ratio of absolute lymphocyte count to absolute monocyte count at diagnosis by limited/advanced stage at diagnosis**

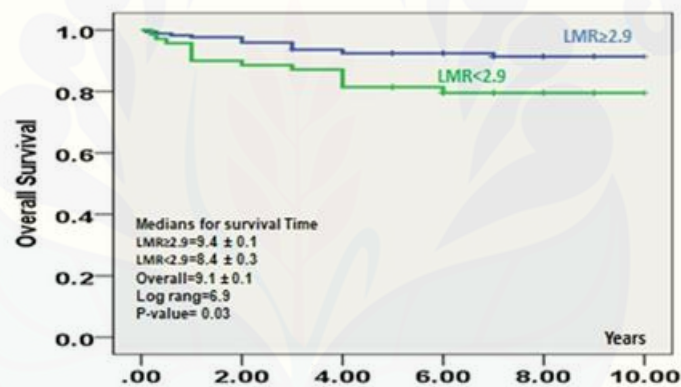
Patients with an LMR of 2.9 or more had superior clinical outcomes compared with patients with an LMR

Less than 2.9 regardless of limited stage (5-year overall survival rates of 100% versus 75%, p=0.007) or advanced stage (5-year overall survival rates of 90.3% versus 80.3%, p=0.4) (Table 4).

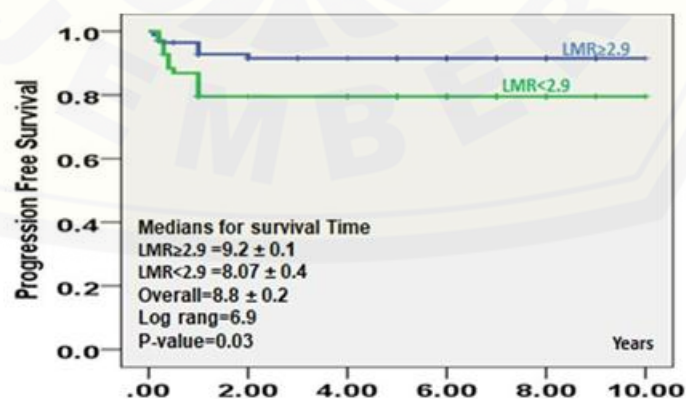
**Table 4: Clinical outcomes based on the LMR at diagnosis according to patients' stage at diagnosis.**

	Advanced stages		Limited stages	
	OS	P-value	OS	P-value
LMR ≥ 2.9	90.3%	0.04	100%	0.007
LMR < 2.9	80.3%		75%	

A



B



**Figure 1: Comparison of the survival using the cutoff value of 2.9 for LMR at diagnosis. (A): Overall survival and (B) progression-free survival.**

## DISCUSSION

Recently, the AMC and ALC/AMC ratio at diagnosis (LMR) have been used as prognostic factors to identify high-risk patients with lymphoma.<sup>[11,12,13]</sup> Although the differentiation between cut off values reported in the various studies, similar results were obtained by different working groups, indicating that monocytosis or lymphopenia at diagnosis has an adverse impact on survival in patients with HL.

The LMR representing a surrogate biomarker for the interaction between host immunity and tumor microenvironment has been reported to predict clinical outcomes, specifically PFS and OS in cHL. We, therefore, studied the LMR as representative markers of the interaction between tumor burden, host immunity, and tumor microenvironment to further stratified clinical outcomes in cHL. To support the hypothesis that the LMR can further stratified PFS and OS in cHL patients, it was necessary to demonstrate that the LMR was an independent predictor of PFS and OS. By univariate analysis, we determined that patients presenting with an AMC-DX of 720 cells/ $\mu\text{L}$  or more had an inferior survival of OS and PFS. LMR of 2.9 or more was associated with superior overall survival and progression-free survival. By multivariate analysis, LMR remained an independent prognostic factor for survival when compared to these prognostic factors. Furthermore, patients in the group with an LMR less than 2.9 tended to have adverse features, including advanced stage (i.e., tumor burden), suggesting an impact of host immunity (i.e., ALC) versus tumor microenvironment (i.e., AMC) on tumor growth control. Our results also demonstrated that a lower LMR was associated with worst prognostic factors such as a hemoglobin level of less than 10.5 g/dl, a WBC count of more than 15,000 cells/ $\text{mm}^3$ , and an albumin level of less than 4 g/dl. A limitation of the IPS scoring system is that it only applies to patients with advanced stage classical Hodgkin's lymphoma and not to those with limited stage disease. We, therefore, investigated the prognostic value of LMR to assess survival in patients with limited and advanced stage disease. The LMR was able to discriminate clinical outcomes not only in patients with limited or advanced stage disease. In our study a low LMR was associated with the OS and PFS outcomes. In comparison with global studies, Porrata *et al.* used the cutoff of 1.1, and LMR was an independent prognostic factor for OS and PFS in a series of 476 patients with classical HL.<sup>[7]</sup> In a Korean analysis of 312 patients with classical HL, the cutoff of 2.9 was used, and LMR correlated with OS, but not event-free survival.<sup>[4]</sup> In this study, LMR was also negatively, albeit moderately, correlated with TAM content, estimated by immunohistochemistry. The largest series of HL patients that has been analyzed for the prognostic impact of AMC and LMR ratio was recently reported by Tadmor *et al.*<sup>[10]</sup> Data on 1,079 patients treated with ABVD (43%) or BEACOPP-like CT (29%) were initially presented in abstract form by Sacchi *et al.*, and the cutoff of 1.5 was proposed.<sup>[10]</sup> The adverse

prognostic effect of LMR, 1.5 was independent of IPS or CT regimen used. Strength of our study, the LMR combines the clinical surrogate biomarkers for the inflammatory, pathological biomarkers – tumor-infiltrating lymphocytes and tumor-associated macrophages – which directly affect the biology of classical Hodgkin's lymphoma. Secondly, LMR is a simple, easily determined clinical biomarker that can be used to assess the clinical outcome in limited and advanced stages of classical Hodgkin's lymphoma. Thirdly, we report the clinical value of a single biomarker (LMR) to assess clinical outcomes in classical Hodgkin's lymphoma based on a widely available, inexpensive, routine clinical test: the complete blood count.

A major limitation of this study is that formal investigations of the tumor microenvironment in this population were not performed. Future researches should correlate the peripheral blood absolute lymphocyte count and monocyte count with microenvironmental data. Other limitations of this study include the retrospective nature of it and the short follow-up period of some recent cases. Further studies, including prospective clinical trials, are required to investigate the effect of the LMR on clinical outcomes, and to confirm the present findings. In conclusion, LMR is a single, low cost, predictive biomarker for clinical outcomes in classical Hodgkin's lymphoma.

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## DEMOGRAPHIC AND SOCIOECONOMIC FACTORS INFLUENCING ITNS USE AMONG THE JAGGERY AND TEA WORKERS IN THE PREVENTION OF MALARIA IN SOUTH MUGIRANGO SUB COUNTY, KISII COUNTY, KENYA

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### ABSTRACT

**Background;** This study interviewed about 209 respondents working at the Jaggery and Tea farms. More than half of respondents understudy were at risk of contracting malaria infection due to the demographic and socioeconomic factors influencing ITNs use. Published literature on demographic and socioeconomic factors that influence ITNs use among the Jaggery and tea workers in South Mugirango Sub County, Kisii County, Kenya is limited. **Purpose;** This study aims to establish the demographic and socio-economic factors influencing ITNs use among the Jaggery and tea workers. **Methods;** A descriptive cross sectional study design was used and South Mugirango was purposively selected. The study systematically and randomly selected and interviewed 209 Jaggery and tea workers on demographic and socioeconomic factors influencing ITNs use. Qualitative methods were used to investigate their demographic and socioeconomic factors on use of ITNs. Data was collected using structured questionnaire, focused group discussion and key informants interviews to obtain views. **Results;** A total of 209 Jaggery and tea workers were selected and interviewed; 116 (56%) males and 93 (44%) female. Over 100% of non users of ITNs were male aged between 18-28 years and singles with no formal education. Also 64.7% by occupation were tea workers and among the non users of ITNs who were found using them as tea carrying baskets. About 94.1% of non users lived in grass thatched houses this led to low level of ITNs use due to their low level of income. Education and gender were found to be positively related with ITNs use ( $P < 0.001$ ) respectively. Accessibility, cost and house structure were significantly related with ITNs use. **Conclusion and recommendations;** the study concludes that demographic and socioeconomic factors influence use of ITNs among the Jaggery and Tea workers. Therefore, the study recommends; (a) Policy review on housing so that the government can give subsidies to low income earners to improve their living conditions within their communities. (b) Education as one of the socio pillar should be enhanced as this will impart knowledge to improve ITNs use among the Jaggery and Tea workers of various age groups with emphasis on proper use.

**KEYWORDS:** Demographic, cost, House Structure, Insecticide Treated Nets, Infection, Malaria, Risk.

### INTRODUCTION

Globally and in Tropical Africa, malaria is the leading cause of morbidity and mortality with at least 90 percent deaths (UNICEF, 2009). Sub-Saharan Africa experiences more than three quarters of malaria deaths yearly. It is estimated that there were about 207 million cases of malaria with 627000 deaths in the year 2013 alone (WHO, 2013). Therefore, malaria continues to be a significant cause of morbidity and mortality among adults living in malaria endemic areas.

Some people develop a level of partial immunity to malaria as a result of repeated exposures. This naturally acquired partial immunity involves both cellular immune and humoral responses and appears protective against symptomatic disease, but not against malaria infection (WHO, 2008).

Almost one and half decades ago, about half of the African countries started scaling up free of charge and highly subsidized provision of mosquito nets due to

waived taxes and tariffs on netting materials and insecticides. As a result, there has been a substantial increase in mosquito net coverage in African countries (UNICEF, 2009).

In Kenya, malaria accounts for 25-40 percent of all outpatient visits at health care facilities. Up to 20 percent of all hospital admissions and 15 percent of in-patient deaths are due to malaria. About 30-40 percent of all fevers seen in health centers in Africa are due to malaria with huge seasonal variability between rainy and dry seasons. At the end of the rainy season, it is less than 10 percent and more than 80 percent as the rainy season winds up.

Therefore, on its part, Kenya Vision 2030 includes among its health sector objectives the intention to reduce the proportion of inpatient malaria fatality to 3 percent by ITNs as one of the most effective tools on malaria prevention (Republic of Kenya, 2010). Consistent use of ITNs can reduce malaria transmission by up to 90 percent (Gimning *et al.*; 2008) and overt as much as 44 percent of all causes mortality (Lengeler, 2010).

## METHODOLOGY

The researcher employed descriptive cross sectional study design whereby both qualitative and quantitative data was collected. The study area was in South Mugirango Sub County, Kisii County Kenya which was purposively selected.

A total of 209 both male and female Jaggery and Tea workers were interviewed on the use of ITNs. Ten investigators were hired and administered the questionnaire to investigate how demographic and socioeconomic factors influenced the ITNs use among the group understudy. The same questionnaire were pretested by the ten research assistants with observation checklist.

The 14.5% prevalence of malaria in the study area among the in-patient and out -patient from Kisii Referral Hospital was used to determine the sample size.

The study participants were selected using systematic sampling from a list of sugar cane growers (Jaggery) and tea workers. The desired sample size of 209 Jaggery and Tea workers was obtained by the predetermined intervals from both lists.

The Jaggery and Tea workers aged 18-49 years were interviewed while those one below and above the age bracket and none response were excluded.

Quantitative data was collected by use of the interviewer administered structured questionnaire while qualitative data was obtained by use of interview schedule from Focused Group Discussion. Key Informants interviews were conducted and this included Jaggery and Tea field officers, Public Health Officers and an Administration

Officer In-Charge of the Sub County and Village Heads. The questionnaire sought the information on how demographic and socioeconomic factors influenced ITNs use in the prevention of malaria among the Jaggery and Tea workers.

The respondents data was cleaned and coded before being analyzed using SPSS Version 20 with 95% CI and statistical level of significance set at 5% ( $P < 0.05$ ). Descriptive statistical test (means and standard deviation) were used. Chi-Square was used to determine the relationship between the variables understudy.

Ethical clearance was sought from Kenyatta University ethics research committee and research permit from National Commission for Science and Technology and Innovation (NACOSTI) prior to the commencement of the study. Informed consent and confidentiality was assured throughout the study.

## RESULTS

In determining the demographic and socioeconomic factors influencing ITNs use among the Jaggery and tea workers in the prevention of malaria in South Mugirango sub county, Kisii, Kenya. A total of 209 Jaggery and Tea workers consented to be interviewed and their data was the analyzed as can be seen in (*Table.1*) below.

### 3.1 Gender of the Jaggery and Tea workers

In terms of gender it was found out that there were more males 116 (56%) than female workers 93 (44%) in both the Jaggery and Tea industry as also can be seen from demographic and socioeconomic characteristics in (*Table1*) below.

### 3.2 Age of the Jaggery and Tea workers

The average age of the Jaggery and Tea workers respondents was 34years .Their age ranged between 18years and 50 years. Most of the Jaggery and Tea workers were between the ages 29-39 years at 85 (41%) while those aged between 18-28years were 69 (33%) with 55 (26%) aged between 40-49 years as can be seen from demographic and socioeconomic characteristics in (*Table 1*) below.

### 3.3 Marital status of the Jaggery and Tea workers

From the demographic and socio economic characteristics, 95 (45%) were married with 42 (20%) being single while 29(14%) were divorced with 23 (11%) being widowed. A bout 11(5%) had no response as well as 9 (4%) were living together in their residence without any formal arrangement.

### 3.4 Level of education of the Jaggery and Tea workers

On level of education, 88(42%) percent had secondary education while 62(30%) had college education. About 29 (14%) had primary level education. 16(7%) had vocational training, with 14(7%) without education at all as can be seen from demographic and socioeconomic characteristics (*Table 1*) below.

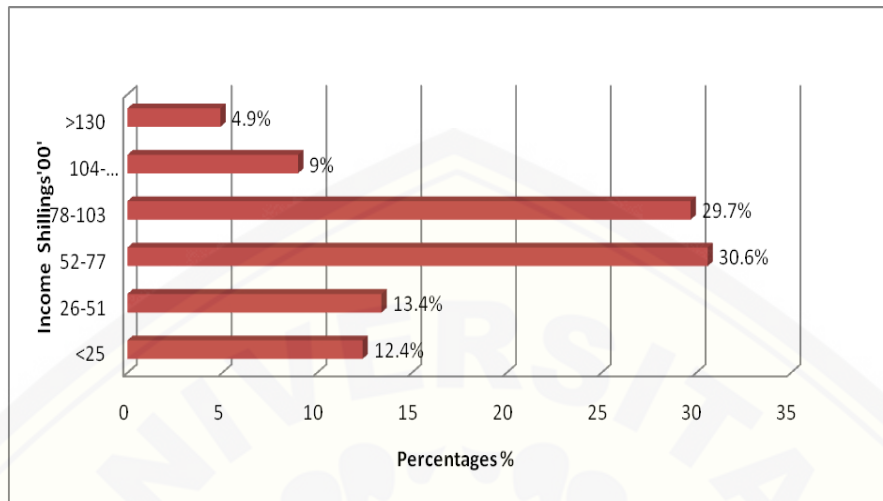


**3.5 Occupation of the Jaggery and Tea workers**

About 116 (56%) percent were tea workers by occupation while 87 (42%) percent were working in the Jaggery industry with 6 (2%) percent did small scale work.

**3.6 Income of the Jaggery and Tea workers**

About 12.4% percent earned less than Shs 2,500 while 13.4% percent earned Shs 2,600-5,100. 30.6% percent earned between Shs 5,200 -7,700, while (62)29.7% percent earned also Shs7800-10300, 19 (9%) percent earned Shs10,400-12,900, with a few 10 (4.9%) earned.



**Figure 1: Income shillings\*000 of the Jaggery and Tea worker.**

**3.7 Demographic factors among the Jaggery and Tea worker versus use of ITNs**

**Table 1: Demographic and use ITNs.**

Demographic Variables	Use of ITNs	None use of ITNs	Chi-square P<values
	Yes n (%)	No n(%)	
<b>Gender</b>			<0.001
Male	99(51.6%)	17(100%)	
Female	93(48.4%)	0(0.0%)	
<b>Age</b>			0.130
18-28	52(27.1%)	17(100%)	
29-39	85(44.3%)	0(0.0%)	
40-50	55(28.6%)	0(0.0%)	
<b>Marital status</b>			0.362
Single	25(13%)	17(100%)	
Married	95(49.5%)	0(0.0%)	
Widowed	23(12.0%)	0(0.0%)	
Divorced	29(15.9%)	0(0.0%)	
Living together/ without formal arrangement	9(4.7%)	0(0.0%)	
No response	11(5.7%)	0(0.0%)	
<b>Education</b>			<0.001
No Formal Education	0(0.0%)	14(82.4%)	
Primary level	26(13.5%)	3(17.6%)	
Secondary level	88(45.5%)	0(0.0%)	
College level	62(32.3%)	0(0.0%)	
Vocational training level	16(8.3%)	0(0.0%)	
<b>Occupation</b>			
Jaggery worker	87(45.3%)	0(0.0%)	
Tea worker	105(54.7%)	11(64.7%)	
Others (occupation)	0(0.0%)	6(35.3%)	

The above demographics and use of ITNs (Table 1) shows that (51.6%) percent of gender were male, while (48.4%) percent were female. Among the non- users of

ITNs from the group (100%) were found to be male and by use of checklist had none in their households.

Those respondents between 29-39 years were (44.3%) percent and were user of ITNs, while (45.5%) percent had attained secondary level education. About (45.3%)

percent were Jaggery workers by occupation with a few (35.3%) percent practiced other occupation.

**3.8 Economic factors among the Jaggery and Tea workers versus use of ITNs**

**Table 2: Economic factors versus use of ITNs.**

Economic Variables	Use of ITNs	Not using an ITNs	P-Value
<b>Economic factors</b>	<b>Yes (n) (%)</b>	<b>No (n) (%)</b>	
<b>Cost</b>			0.010
High cost of ITNs	144(75.0%)	17(100.0%)	
Low cost of ITNs	48(25.0%)	0(0.0%)	
<b>(ii) Accessibility</b>			<0.001
Yes (did access)	192(100%)	0(0.0%)	
No (didn't access)	0(0.0%)	17(100%)	
<b>Structure of the house</b>			<0.001
Grass thatched house	8(4.2%)	16(94.1%)	
Mud house	58(30.2%)	1(5.90%)	
Semi-permanent house	79(41.1%)	0(0.0%)	
Permanent house	47(24.5%)	0(0.0%)	
<b>Number of rooms</b>			0.520
One room	31(16.1%)	12(70.6%)	
Two rooms	64(34.9%)	4(23.5%)	
Three rooms	45(23.4%)	1(5.9%)	
Four rooms	29(15.1%)	0(0.0%)	
More than four rooms	20(10.4%)	0(0.0%)	

From the above Table2 on economic factors among the users of ITNs (75%) percent that the cost was high while over 100% of users said that they did access the ITNs though the cost was as well high. About 41.1 %percent

lived in semi permanent house structures. Only 34.9% percent were living in two roomed house with 10.4% had house structures which had more than four rooms.

**Table 3: Perceived beliefs and how malaria is transmitted.**

Perceived beliefs and how malaria is transmitted	Responses	N	Percentages %
(unprompted) causes of malaria	Through anopheles mosquito	108	53.0
	By dirty environment	26	14.0
	Through stagnant water	34	17.2
	By eating sugar cane	14	10.3
	Being rained on	26	13.1
What are ways of preventing malaria infection?	Through any net	115	56.0
	Through malaria drugs	42	25.0
	Living in clean environment	19	9.2
	Use of ITNs	17	6
	Don't know	9	4.0
Reasons for not sleeping under mosquito bed net	Cause suffocation an breathing problems	66	31.5
	Cause irritation to skin	43	20.5
	Cause dreaming	53	25.3
	No mosquito presence	21	10.3
	Don't have	18	8.6
	Forgot	8	3.6

**DISCUSSION**

Demographic and socio economic factors were investigated to determine how they influenced ITNs use among the Jaggery and Tea workers in the prevention of malaria in South Mugarango sub county, Kisii, Kenya.

This study found out that there weremore males (56%)percent than females who were (44%)percent.

Most of respondents understudy who were aged between 29-39 years were (41%) percent. On marital status only 45% percent were married and this influenced use of ITNs as they the couple could remind each other to hang

the ITNs before they slept, while 17 (100%) of the singles were found to be non-users of ITNs in this study. Age and marital status were found not to be statistically significant.

On levels of education 42% percent of the respondent had attained secondary education as well as 32.3% percent had also attended college level. This study revealed that literacy play a role as a mechanism of social transformation among the Jaggery and tea workers in relation to the use of ITNs in the prevention of malaria in South Mugarango and this concurred with a study previously documented by (Rashed *et al.*; 1999).

The findings showed that (32.3%) who attended college and 16 (8.3%) vocational training were found using ITNs than those with no education at all. However, among all the variables, only education found to influence knowledge the use of ITNs as can be seen in (Table1) above.

Therefore education and occupation were also found to be statistically significant with the  $P < 0.001$  and  $P < 0.003$  respectively. Most 88 (45.5%) of the Jaggery and tea workers had attained secondary education. On their occupation, it was revealed that 105 (54.5%) were tea workers and users of ITNs.

On income levels this study found out that most of the households accessed income with average of Shillings 103 to sustain their livelihood. Lack of financial resources was frequently mentioned.

*"I don't have enough money to buy an ITN"* One of the female key informants said. And this was a key barrier to obtaining or ownership net among the low income earners as this let them to prioritize their needs in comparison to ITNs. Gender was found to play a great role and was statistically significant  $P < 0.001$  among the ITNs users.

*"An ITN is bad as it deplete air in the room."* key informant from focused group discussion said. This is the reason for not using the ITNs.

This study found that if (Table.2) an ITNs are readily affordable, accessible and available within the house structure then utilization is paramount. Therefore, it was found out that there are other factors within the household that could influence or deter the use of ITNs such as high cost, lack of access, house structure and the number of rooms. Therefore, this study found out that enabling factors within the community, such as economic empowerment; access and availability determined ITNs use the households.

This study therefore, concurs (Mac Cormack *et al.*; 1989) which reported that households with low income would not consider purchasing any health items at the expense

of the basic needs hence the reasons why some household (Table 2) 17(8.1%) had none.

From this study (Table 2) it was revealed that house structure will always determine the ITNs use. House structure was found to be statistically significant with ITNs use with  $P < 0.001$  (41.1%) percent lived in semi-permanent structures.

The majority 70.6% of non ITNs users lived in one room and grass thatched as these were related to their level of income. It was found out that both pregnant Jaggery and tea workers in the household were given preferences to sleep under the mosquito net. This showed that there is a relationship of mosquito nets ownership in the household and malaria episodes among those who had less than two as a result of disruption of sleeping arrangements especially when they had visitors.

The findings revealed a low likelihood of the Jaggery and tea workers on use of ITNs in the prevention of malaria and this concurred with (Somi MF, *et al.*; 2007) who found a dual causation link between malaria socioeconomic in rural Tanzania.

Although the awareness level has improved over time, studies by (Osero *et al.*, 2005) and (Adeneye *et al.*, 2007) have shown that a lot of factors militate against actual ownership and correct use of ITNs. This study found out that the number of rooms were not statistically significant  $P < 0.521$  with the ITNs use.

## CONCLUSION

This study concludes that there was a relationship between the demographic and socio-economic factors and ITNs use among the Jaggery and tea workers in terms of gender, education, housing and accessibility with the  $P < 0.001$  respectively. Therefore, low levels of ITNs use were attributed by the demographic and socio economic characteristics among the Jaggery and tea workers in the prevention of malaria.

## Recommendation for further study

A study on policy reviews on housing so that the government can give subsidies to low income earners to improve their living conditions and emphasis on proper use of ITNs.

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## THE MOST FREQUENT PRESCRIBED ANTIMICROBIAL IN HOSPITALS OF NINEVEH, IRAQ – 2019

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### ABSTRACT

**Context:** Antimicrobials are one of the most successful forms of chemotherapy in the history of medicine. It saves many lives and significantly contributes to the control of infectious diseases. **Aim:** The current study is aiming for determining the most frequent prescribed antibiotics in hospitals in Nineveh governorate at the north of Iraq. **Method and Subjects:** A cross-sectional study design was adopted to analyze data that were collected from statistics which were referred formally from hospitals to the Department of Pharmacy in Nineveh Health Directorate during the period from January 1<sup>st</sup> to the end of December 31<sup>st</sup>, 2019. **Results:** The current study had found that penicillin group was the most frequent antibiotic that was prescribed to hospitalized patients (66.42%); followed by Cephalosporin Group (13.32%) and Quinolones Group. **Conclusion:** Antibiotic that are belong to penicillin, cephalosporin and quinolones groups are the most frequently prescribed to hospitalized patients in Nineveh Governorate. **Recommendation:** The use of all antibiotics in general, and penicillin group in particular is recommended to be balanced.

**KEYWORDS:** Antibiotics, consumption, cross-section, Nineveh, hospitals.

### INTRODUCTION

Antimicrobials are now considered one of the most successful forms of chemotherapy in the history of medicine. It is not necessary to reiterate here how many lives they have saved and how significantly they have contributed to the control of infectious diseases that were the leading causes of human morbidity and mortality for most of human existence.

The discovery of first three antimicrobials, Salvarsan, Prontosil, and penicillin, was exemplary, as those studies set up the paradigms for future drug discovery research. The paths, followed by other researchers, resulted in a number of new antibiotics, some of which made their way up to the patient's bedside. The period between the 1950s and 1970s was indeed the golden era of discovery of novel antibiotics classes, with no new classes discovered since then. Therefore, with the decline of the discovery rate, the mainstream approach for the development of new drugs to combat emerging and re-

emerging resistance of pathogens to antibiotics has been the modification of existing antibiotics.<sup>[1]</sup>

It is important to know that the routine measurement and display of consumption information to prescribers and policy-makers are a first step in increasing the awareness and importance of careful antibiotic use. It is then possible to attempt to define levels of optimal use. Comparative information can help to define those levels by evaluating individual consumption and proportions in the context of recognized leaders in the area. Conformity to local practice guidelines can be evaluated, and expected levels of consumption can be estimated by defining the incidence of disease requiring antimicrobial therapy. Feedback to prescribers is one potential form of intervention.<sup>[2]</sup>

The current study is aiming for determining the most frequent antibiotics that were prescribed for hospitalized patients in Nineveh at the north of Iraq.



## METHOD AND SUBJECTS

Nineveh Governorate contains 18 hospitals, half of them are locating in the center of the Province (Mosul). All hospitals are included in the study.

A cross-sectional study design was adopted in order to achieve aim of the current study. The required data were collected from the formal statistics that were regularly referred from the hospitals to the Department of Pharmacy in Nineveh Health Directorate during the period from January 1<sup>st</sup> to the end of December 31<sup>st</sup>, 2019.

After tabulation of the collected data, frequency of the antibiotics that were prescribed to the hospitalized patient during time of data collection was estimated. However, different units are used to express the prescribed antibiotics (tablets or capsules, syrup, vial, ampule).

## RESULTS

The current study had found that penicillin group was the most frequent antibiotic that was prescribed to hospitalized patients (66.42%); followed by Cephalosporin Group (13.32%) and Quinolones Group. Table (1).

**Table (1): Frequency distribution of antimicrobials according to pharmacological classification.**

Antimicrobials	Frequency	
	No.	%
Penicillin Group	1742278	66.42
Cephalosporin Group	349509	13.32
Quinolones Group: Ciprofloxacin	187290	7.14
Nitroimidazole Group: Metronidazole	135302	5.15
Aminoglycoside Group	77382	2.95
Sulfonamide Group: Methheprim Tablet (480mg)	35631	1.35
Macrolides Group	30385	1.15
Carbapenem Group: Meropenem Vial	17137	0.65
Tetracycline Group: Doxycyclin Capsule (100mg)	16300	0.62
Antiviral Group: Acyclovir	14545	0.55
Glycopeptide Group: Vancomycin Vial	10148	0.38
Imidazole Group: Miconazole Nitrate	6760	0.25
Benzimidazole Group: Albendazole Suspension (400mg/20ml)	162	0.006
<b>Total</b>	<b>2622829</b>	

Among penicillin group, Amoxicillin/Clavulanic acid tablet 625 mg was the most frequent (56.12%) as shown

by table 2. While amoxicillin capsule 500 mg represented almost the third (32.99%).

**Table (2): Frequency distribution of the penicillin antimicrobial drugs.**

Penicillin group		Frequency	
		No.	%
Amoxicillin/Clavulanic acid	Tablet 625mg	977900	56.12
	Suspension 312.5mg/5ml	30918	1.77
	<b>Total</b>	<b>1008818</b>	<b>57.89</b>
Amoxicillin	Capsule 500mg	574856	32.99
	Vial 500mg	121509	6.97
	Suspension 250mg/5ml	29054	1.66
	<b>Total</b>	<b>725419</b>	<b>41.62</b>
Ampicillin	Vial	2831	0.16
Pipracillin	Vial	4210	0.24
procaine penicillin	Vial	1000	0.05
<b>Total</b>		1742278	

Table 3 displays frequency of antibiotics that belong to the cephalosporin group. First generation cephalosporin

represented more than half (55.28%) of the group particularly cephalexin capsule 500 mg (53.58%).

Table (3): Frequency distribution of the Cephalosporin antimicrobial drugs.

Cephalosporin Group		Frequency	
		No.	%
1 <sup>st</sup> G	Cephalexin Capsule 500mg	187290	53.58
	Cephalexin Suspension 250mg/5ml	5840	1.67
	Cefazolin vial (1g)	100	0.028
	<b>Total</b>	<b>1878840</b>	<b>55.28%</b>
3 <sup>rd</sup> G	Ceftriaxon vial (1g)	70515	20.17
	Cefotaxim	66898	19.14
	Ceftazidim vial (1g)	18060	5.16
	Cefixim Capsule 400mg	760	0.22
	Suspension 100mg	46	0.01
	<b>Total</b>	<b>156279</b>	<b>44.72%</b>
<b>Total</b>		<b>349509</b>	

## DISCUSSION

Despite preventive efforts, infections will always occur, and we will always need safe and effective therapy for them. The collapse of the antibiotic research-and-development pipeline is the result of both economic and regulatory barriers. The solution is better alignment of economic and regulatory approaches to antibiotic development. For example, public-private partnerships could align the research-and-development focus of industry with unmet medical needs. Also, a new regulatory approach, such as the Limited Population Antibiotic Drug (LPAD) proposal from the Infectious Diseases Society of America, could allow drugs to be approved on the basis of small, relatively inexpensive clinical superiority trials focused on lethal infections caused by highly resistant pathogens.<sup>[3]</sup>

Now, antimicrobial resistance (AMR) compromises the effective treatment of bacterial infections and represents a global threat to public health. Antibiotic consumption is a key driver of the development and spread of AMR, and prudent antibiotic prescribing has been identified as an important strategy to curb this problem. Prudent prescribing includes avoiding unnecessary prescriptions, delaying prescriptions when possible, favoring narrow-spectrum over broad-spectrum antibiotics and optimizing treatment duration.<sup>[4]</sup>

Because of the important role of antibiotics in disease management, a study of prevalent diseases and their management practices will aid in informing practical interventions that will aim at reducing the development and spread of antibiotic resistance as a result of antibiotic use in disease management.<sup>[5]</sup>

The development of resistance to antibiotics by reducing in the affinities of their enzymatic targets occurs most rapidly for antibiotics that inactivate a single target and that are not analogs of substrate.<sup>[6]</sup>

Antibiotic resistance can be reduced by using antibiotics rationally based on guidelines of antimicrobial stewardship programs (ASPs) and various data such as pharmacokinetic (PK) and pharmacodynamics (PD)

properties of antibiotics, diagnostic testing, antimicrobial susceptibility testing (AST), clinical response, and effects on the microbiota, as well as by new antibiotic developments. The controlled use of antibiotics in food animals is another cornerstone among efforts to reduce antibiotic resistance. All major resistance-control strategies recommend education for patients, children (e.g., through schools and day care), the public, and relevant healthcare professionals (e.g., primary-care physicians, pharmacists, and medical students) regarding unique features of bacterial infections and antibiotics, prudent antibiotic prescribing as a positive construct, and personal hygiene (e.g., handwashing). The problem of antibiotic resistance can be minimized only by concerted efforts of all members of society for ensuring the continued efficiency of antibiotics.<sup>[7]</sup>

The current study concluded that Penicillin pharmacological group was the most frequent antibiotic that was prescribed to hospitalized patients in Nineveh Governorate; followed by cephalosporin group and quinolones Group.

The current study recommends to balance the use of all antibiotics in general, and penicillin group in particular; otherwise problems of developing resistance as well as antibiotics wastage might emerge.

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## ANTIBIOTICS CONSUMPTION IN IBN AL-ATHEER PEDIATRIC TEACHING HOSPITAL IN NINEVEH, IRAQ

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### ABSTRACT

**Context:** Antibiotics are among the most commonly prescribed drugs in pediatrics. They are mostly started on an empirical basis, without proof of a bacterial infection. **Aim:** The current study is aiming for enumerating antibiotics that are frequently consumed by Ibn-Alatheer pediatric teaching hospital in Mosul, Iraq. **Method and Subjects:** A cross-sectional study design was adopted. Data was collected from the formal statistics of Ibn-Alatheer Pediatric Teaching Hospital over the last year from January 1<sup>st</sup> to the December 31<sup>st</sup>, 2019. **Results:** It was found that the most frequent consumed antibiotics (56.6%) were grouped as penicillin, cephalosporin (17.1%) and aminoglycoside (10.1%). **Conclusion:** It is concluded that penicillin is the most frequent prescribed antibiotics in Ibn-Alatheer Pediatrics Teaching Hospital. **Recommendation:** The current study suggests that antibiotics are needed to be prescribed carefully for pediatrics.

**KEYWORDS:** Antibiotics, Penicillin, Nineveh, Iraq.

### INTRODUCTION

Despite the fact that a significant percentage of the population is unable to swallow tablets and capsules, these dosage forms continue to be the default standard. These oral formulations fail many patients, especially children, because of large tablet or capsule size, poor palatability, and lack of correct dosage strength. The clinical result is often lack of adherence and therapeutic failure. The American Association of Pharmaceutical Scientists formed a Pediatric Formulations Task Force, consisting of members with different areas of expertise including pediatrics, formulation development, clinical pharmacology, and regulatory science, in order to identify pediatric, manufacturing, and regulatory issues and areas of needed research and regulatory guidance. Dosage form and palatability standards for all pediatric ages, relative bioavailability requirements, and small batch manufacturing capabilities and creation of a viable economic model were identified as particular needs. This assessment is considered an important first step for a task force seeking creative approaches to providing more

appropriate oral formulations for children.<sup>[1]</sup>

Antibiotics are among the most commonly prescribed drugs in pediatrics. In most cases, antibiotics are started on an empirical basis, without proof of a bacterial infection, either before the beginning of therapy or afterwards.<sup>[2]</sup>

Epidemiological data from developed countries indicate that over a year, half of the pediatric population is prescribed medications, from a wide range of therapeutic agents, and mainly in younger children (Clavenna 2009a; Clavenna 2009b; Zhang 2013). Anti-infective drugs, especially antibiotics, remain the most frequently prescribed medication. Other commonly used medications are respiratory drugs, analgesics, psychoanaleptics, antiepileptics, or corticoids (corticosteroids). Low- and middle-income countries (LMIC) provide very limited data; the most widely used medications in children are antimalarial drugs, antibiotics and analgesics/antipyretics (Clavenna 2009a).

Health authorities and organizations now recognize that medication use in children is a worldwide burden that cannot be addressed with the available medications that are primarily designed for use in adults (WHO 2008; WHO 2012; EMA 2013; FDA 2016). Thus, there is an urgent need for the development and assessment of effective and safe medications for children (Standing 2005; Ivanovska 2014; Salunke 2016). In parallel, selecting and developing age-appropriate pediatric formulations that ensure success and safety of administration and adequate adherence is a critical objective for health authorities and pediatric researchers (Nunn 2005; EMA 2006; WHO 2008; Cram 2009; Rieder 2010; WHO 2012; EMA 2013; Batchelor 2015; Venables 2015).<sup>[3,4]</sup>

The current study is aiming for enumerating antibiotics that are frequently consumed by Ibn-Alatheer pediatric teaching hospital in Mosul, Iraq.

## METHOD AND SUBJECTS

A cross-sectional study design was adopted in order to achieve aim of the current study. The required data were collected from the formal statistics of Ibn-Alatheer Pediatric Teaching Hospital during the last year from January 1<sup>st</sup> to the December 31<sup>st</sup>, 2019. All statistics were referred to the Department of Pharmacy in Nineveh Health Directorate.

The reported antibiotics were listed according to their frequency. The studied items were expressed by different units (tablets or capsules, syrup, vial, ampule).

## RESULTS

Table 1 shows list of antibiotics that are commonly consumed in Ibn-Alatheer teaching Hospital for Pediatrics. More than half of them (56.6%) were grouped as penicillin. Almost a quarter represented by cephalosporin (17.1%) and aminoglycoside (10.1%). Antiviral agent was the least frequent at the bottom of the list (2.8%).

**Table (1): List of consumed antibiotics in Ibn-Alatheer teaching Hospital for Pediatrics.**

Antimicrobials	Frequency	
	No.	%
<b>Penicillin Group</b>	52156	56.6
<b>Cephalosporin Group</b>	15754	17.1
<b>Aminoglycoside Group</b>	9300	10.1
<b>Nitroimidazole Group</b>	4731	5.1
<b>Sulfonamide Group</b>	4580	5.0
<b>Glycopeptide Group</b>	2979	3.2
<b>Acyclovir</b>	2590	2.8
<b>Total</b>	<b>92090</b>	<b>100%</b>

Regarding penicillin group, amoxicillin was the most frequent antibiotic (82.5%). While injectable cefotrioxon represented almost half of the consumed antibiotics (49.4%). Amikacin ampule comprised 63.4% of aminoglycoside group. Table 1, 2 and 3.

**Table (2): Details of penicillin group.**

Penicillin group		Frequency	
Name	Drug Form	No.	%
Amoxicillin	Capsule 250 mg	12000	23.0
	Vial 500 mg	18900	36.2
	Capsule 500 mg	10000	19.2
	Suspension 250 mg	2136	4.1
Co-Amoxiclave	Capsule 625 mg	6000	11.5
	Suspension 312 mg/ 5 ml	3120	6.0
<b>Total</b>		<b>52156</b>	<b>100%</b>

**Table (3): Details of Cephalosporin group.**

Cephalosporin group		Frequency	
Name	Drug Form	No.	%
Cefotrioxon	Vial 1 g	7788	49.4
Ceftazidim	Vial 1 g	2400	15.3
Cefotaxim	Vial 1 g	1816	11.5
Cephalexin	Capsule 250 mg	3000	19.4
	Suspension 250 mg	750	4.6
<b>Total</b>		<b>15754</b>	<b>100%</b>

**Table (4): Details of Aminoglycoside group.**

Aminoglycoside group		Frequency	
		No.	%
Amikacin	Ampoule 100 mg	5800	62.4
	Ampoule 500 mg	100	1.0
Gentamicin	Ampoule 80 mg	3400	36.6
<b>Total</b>		<b>9300</b>	<b>100%</b>

## DISCUSSION

The present study had performed to detect the percentage of antibiotics utilized in Ibn-Alatheer pediatric teaching hospital.

Despite preventive efforts, infections will always happen, and we will always need safe and effective therapy for them. The collapse of the antibiotic research-and-development pipeline is the result of both economic and regulatory barriers. The solution is better alignment of economic and regulatory approaches to antibiotic development. For example, public-private partnerships could align the research-and-development focus of industry with unmet medical needs. In addition, a new regulatory approach, such as the Limited Population Antibiotic Drug (LPAD) proposal from the Infectious Diseases Society of America, could allow drugs to be approved on the basis of small, relatively inexpensive clinical superiority trials focused on lethal infections caused by highly resistant pathogens.<sup>[5]</sup>

Society plays an important role in use and abuse of antibiotics as well as the spread of uncritical tendencies. Due to higher number of infectious diseases in developing countries like Iraq, the use of antibiotics is widespread. However, because of the relaxed laws in Iraq and other developing countries, it is not difficult to obtain antibiotics without prescription (over the counter drugs) and hence, antibiotics abuse by public is common.<sup>[6]</sup>

Unnecessary antibiotic use, which have evaluated as a type of inappropriate antibiotic use, had defined as the presence of at least one of following conditions.<sup>[7]</sup>

- Use of antibiotic in conditions where no infectious disease has found, or a viral infection has found when clinical findings, laboratory variables (white blood cell count, neutrophil count, CRP and procalcitonin value), lung imaging, and culture results have evaluated.
- Use of prophylactic antibiotic even though no indication is present.
- Use of antibiotics for longer than necessary.

The present study concluded that more than half of consumed antibiotics in Ibn-Alatheer Pediatrics Teaching Hospital for are one of penicillins; followed by cephalosporin and aminoglycosides.

The current study suggests that antibiotics are needed to be prescribed carefully for pediatrics.

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## FEMALE GENITAL MUTILATION AND SOCIO-CULTURAL IMPLICATIONS ON BINI TRADITION

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### ABSTRACT

Female circumcision, also known as female genital mutilation [FGM] is a common practice in many countries across the globe, especially Africa. Current study investigated the social and cultural implications of FGM on the natives of Bini, Southern Nigeria. A 150 open ended questionnaire was carefully structured, validated and distributed (n = 150) to selected Bini indigenes of the target area in Oredo Local Government Area of the ancient city of Benin, Edo state of Nigeria. This prospective study was based on female children and parents who presented on account of FGM in the past. The questionnaire was designed to obtain relevant cultural and traditional norms of the Bini tribe as it relates to FGM. Sociodemographic data of sampled respondents were also collected. In the end, various sections of the questionnaire were subjected to statistical analysis, while expressing results in simple percentages to extrapolate the effect of FGM on the socio-cultural well-being of the people. Following careful observation, study found that about 74.5% of the respondents supported that till date, the Bini's support cultural norms than global best practices on FGM as stipulated by the World Health Organizations (WHO). Whereas, about 55.7% of the subjects opposed to this. Study also observed that the social implication of FGM on the girl child within captured area is evident in their sexual life as about 40.6% of the respondents posited that the average Benin girl who underwent FGM is likely to lost control of their libido with time; even in their matrimony, while 29.2% however opposed to this. Planned health education campaigns are recommended to elude the drawbacks of FGM and hazards of continuation of this practice in current communities that practice FGM.

**KEYWORDS:** Female Genital Mutilation, Benin, Socio-Cultural, Tradition.

### INTRODUCTION

Also known as female genital mutilation [FGM], Female circumcision or cutting [FC]; FGM is a common practice in several countries across the globe, especially Africa.<sup>[1,2]</sup> The World Health Organization (WHO) defines it as a procedure by which the female external genitalia is partially or totally removed with excruciating pain and injury to the female genital organs, either for cultural or non-therapeutic reasons.<sup>[3]</sup> There are four major types of FGM. While Type I (Clitoridectomy) involves the partial or total removal of the clitoris; an erectile and hypersensitive part of the female genitals and prepuce, the surrounding skin fold in some cases; Type II procedure Excise partially or totally, the clitoris and labia minora, with or without the majora.<sup>[1,3]</sup> Type III (most severe) on the other hand Infibulates and narrows the vaginal opening through a covering seal by cutting

and repositioning the inner or outer labia, with or without removing the clitoris.

In African mythology, FGM practices are deeply rooted in gender disproportion, cultural exclusiveness, as well as in the beliefs and practices of purity, restraint, aesthetics, class and reputation. It acts as a testament for the control of women's libido and sexual desires, promoting fidelity and chastity, and is often encouraged by both women and men.<sup>[3,4]</sup>

The cultural and traditional elements of FGM reportedly vary across ethnic enclaves,<sup>[5]</sup> with procedures reportedly observed across ages of six and eight, and a few cultures preferring it at birth, menarche, or before marriage.<sup>[5]</sup> FGM is often time undergone alone, with the aid of special instruments.<sup>[6]</sup> The procedure is almost always performed in ceremonial manners with music notes,

food, and gift items as the process unfolds. Till recent times, FGM is still in active practice across six states of the federal republic of Nigeria with relatively stable prevalence rates over time.<sup>[7,8]</sup>

In Edo state for instance; where FGM and related practices was banned in October 1999, traditional sceptics have however condemned the ban, with some applauding it as a good step in the right direction. To this point, there exist a lacuna in an all-inclusive knowledge base on the socio-cultural response on FGM practicing communities in Nigeria and Edo State in particular, even with the recent legislations (Nigeria’s 2015 VAPP Act) that calls for the elimination of FGM practices by 2030, with no rigorous review and intervention models within the country.<sup>[9]</sup> Current study was therefore devised to provide a unique opportunity for spawning such vital information on the effect of FGM on socio-cultural activities of Edo state and Nigeria in general.

**AIM OF STUDY**

This study aimed at examining the socio-cultural implications of FGM on the norms and values of Bini residents in Oredo Local Government Area of Edo State, Nigeria. Specifically, the study;

1. Determined if FGM still exists and is currently being practiced in Edo State
2. Evaluated the social and cultural impact of FGM on the girls in Ordo Local Government Area of Edo State.
3. Determined the difference(s) between cultural beliefs and FGM and their Elicit importance to the Bini culture.

**MATERIALS AND METHOD**

**Research Design**

This study adopted the survey type of research design as it is exploratory in nature and consist of data gathering from a large number or respondents, strategically investigating and conceiving answers to research questions or problems.

**RESULTS**

**Table I: Biodata of respondents.**

Variables	Attributes	Frequency	Percentage
<b>Age</b>	30 – 40	122	57.5
	40 – 50	42	19.8
	50 – 60	28	13.2
	60 – 70	18	8.5
	70 and above	2	0.9
<b>Religion</b>	Christian	148	69.8
	Muslim	26	12.3
	Traditional	36	17.0
	Others	2	0.9
<b>Educational qualification</b>	SSCE and below	56	26.4
	OND	18	8.5
	HND	28	13.2
	B.Sc.	84	39.6

**Study Population**

The population for this study comprises of Bini residents in Oredo Local Government Area of Edo State, literate and non – literates who are conversant with the cultural practices and norms of the ancient Benin kingdom as it relates to FGM.

**Sample Size**

A total of one hundred and fifty (150) participants (sample) were drawn from the population of Bini indigenes who were resident in Oredo Local Government Area of Edo State; the study area. This sample was drawn to reflect the various segment of the population without any form of bias.

**Sampling Technique**

Using the simple random sampling technique, this study selected a part of a population for the purpose of this Research, this method was adopted due to its relative ease and affordability, providing quick opportunity to pick from the entire population of study without any form of bias.

**Method of Data Collection**

Study adopted both primary and secondary methods of data collection. Basically, the primary method consists of the use of well-structured and validated questionnaire and in-depth interview. The gaps which existed after the administration of the questionnaires were filled with interview conducted during the study. Only personals with deep understanding of Bini traditions, who are possibly custodians of the Bini culture were interviewed. The secondary sources of data collection include Journal, books and articles / publications.

**Analytical Approach**

Obtained collected from respondents were subjected through statistical measures of central tendencies and average values (means) obtained after proper sorting. Data was then represented in frequency distribution table, analysed, interpreted and presented using simple percentage.

	M.Sc.	20	9.4
	Ph.D.	6	2.8
<b>Tribe</b>	Benin	112	52.8
	Esan	42	19.8
	Owan	24	11.3
	Etsako	16	7.5
	Others	18	8.5
<b>Residential area</b>	GRA	14	6.6
	Ikpoba Okha	2	0.9
	Ologbo	4	1.9
	Oredo	182	85.8
	Ughelli	10	4.7

**Table II: Implications of FGM on Culture.**

		Frequency	Percentage
Do you believe in FGM	Yes	92	43.4
	No	120	56.6
Do you know the importance of FGM on the Benin culture	Yes	114	53.8
	No	98	46.2
Do you believe that the people of Benin respect their culture more than the practice of FGM	Yes	160	75.5
	No	52	24.5
What is the relationship between FGM and the Benin culture	No response	122	57.5
	Circumcision	24	11.3
	Identity	6	2.8
	No Relationship	42	19.8
	To Control Prostitution	18	8.5
Despite the importance of FGM, do the Benin still practice FGM	Yes	120	56.6
	No	92	43.4

**Table III: Influence of Benin Culture on FGM Practice.**

Variables	Attributes	Frequency	Percentage
To what extent are the Benin ready to practice FGM against their culture	A large extent	138	65.1
	Very large extent	74	34.9
	Extremely large extent	0	0.0
Do all Benin believe in their culture	Yes	76	35.8
	No	34	16.0
	Not fully	102	48.1
Do all Benin give their cooperation/consent during the practice of FGM	Yes	34	16.0
	No	178	84.0
	Not fully	0	0.0
Are the Benin ready to forgo their culture and obey the practice FGM	Yes	50	23.6
	No	162	76.4
Do the Benin strongly belief in their cultural value	Yes	170	80.2
	No	42	19.8
Despite the importance of FGM, do the Benin still want to obey the FGM or obeying their culture	Yes	116	54.7
	No	96	45.3

**Table IV: Values of Bini People on FGM.**

	Yes	No
Do the Benin Value their culture more than the practice of FGM	158(74.5)	54(25.5)
Do the Benin still practice FGM	118(55.7)	94(44.3)
Do the Benin respect and obey their traditional ruler rather than the WHO law?	146(68.9)	66(31.1)

**Table V: Social Implication of FGM on the Girl Child.**



	Yes	No
Do the Benin that girls who are circumcised are likely to be a prostitute	86(40.6)	126(59.4)
Do you believe that girls who are not circumcised enjoy sex	94(44.3)	118(55.7)
Do you believe that girls who are circumcised enjoy sex	62(29.2)	150(70.8)
Do you believe that girls who were not circumcise stay more in their matrimonial home	60(28.3)	152(71.7)
Do girls from Benin culture have any choice of being circumcised	112(52.8)	100(47.2)
Do the Benin parents believe more in their culture rather than the World Health Organization about FGM	134(63.2)	78(36.8)
Do girls who are not circumcised command respects in the society	90(42.5)	122(57.5)
As a girl, have you been circumcised	74(34.9)	138(65.1)

## DISCUSSION

As a common practice in several African countries, the introduction of female genital mutilation [FGM] has spark divergent debates to the creams of religious and socio-economic practitioners across the globe. To the World Health Organization (WHO), be it for cultural, ethno-religious or non-therapeutic reasons, FGM is a painstaking procedure that involves partial and/or total removal of the external female genitalia with perturbed conscious injury to the female genital organs.<sup>[3]</sup> It (FGM) is traditionally practiced with partial or total incision or excision of the female external genitalia for a non-therapeutic reason, usually without their consent. FGM is common in Africa with varying prevalence in different countries, though the incidence is reducing due to human rights issues and tremendous advocacy for its elimination by non-governmental organizations, it is however underreported in many African countries especially where it has been declared illegal.

FGM is often performed by a nonmedical practitioner with the aim of fulfilling religious or cultural rites and sometimes for economic benefits with the resultant acute, intermediate and late complications.<sup>[6,7]</sup> It is sometimes performed by medical practitioners when it is speciously believed that its medicalization reduces the complications associated with the practice. The sensitivity of FGM is amplified when compared to male circumcision and voluntary alterations of the female external genitalia like piercing and tattooing as similar practices. The magnitude of the physical and psychosocial consequences of FGM outweighs the presumed benefits of the procedures highlighting the need for improvement of the multiple preventive measures by all the stakeholders and in all the sectors. To this point, current study was undertaken to examine the impact of FGM on the cultural norms and values of the Bini people of Oredo Local Government Area of Edo State, Nigeria.

This study drew a total of two hundred (200) participants to reflect the various segment of the population in Oredo Local Government Area of Edo sate, Nigeria. These subjects were randomly group with the adoption of both primary and secondary methods of data collection using the questionnaire and in-depth interview.

From our socio-demographics, a total of one hundred and twenty-two 122 (57.5%) of sampled respondents were of

the age range of 30-40 years, with 42 (19.8%), 28 (13.2%), 18 (8.5%) and 2 (0.9%) being within age brackets of 41-50, 51-60, 61-70 and 71+ years respectively (table I). on religious believes, a total of 148 (69.8%) and 26 (12.3%) of sampled subjects were Christians and Muslims respectively, while African Traditional Religionists accounted for about 36 (17.0%) of the total sample (table I). Also, a close look at the result reveals a 56 (26.4%), 18 (8.5%), 28 (13.2%), 84 (39.6%), 20 (9.4%) and 6 (2.8%) qualification levels of SSCE, OND, HND, B.Sc., M.Sc. and Ph.D. degrees respectively for sampled subjects; while 112 (52.8%), 42(19.8%), 24 (11.3%), 16 (7.5%) and 18 (8.5%) of participants were Benin, Esan, Owan, Etsako and Other tribes respectively. Also, about 14 (6.6%) of the participants lived in GRA, whereas, 2(0.9%) lived in Ikpoba Okha, 4(1.9%) in Ologbo and environ, with majority 182(85.8%) in Oredo and 10(4.7%) were indigenes of Ugheli, Delta State.

Several reports have it that FGM is performed at varying age groups, from the first week of life, during infancy, before puberty, before the first childbirth and other periods in the woman's life, depending on the location and major reason underlying the practice across Africa.<sup>[10]</sup> It is usually performed individually but can be done in groups of girls or women. In Africa, specific rates from studies done by the United Nations shows it to be more in children.<sup>[11]</sup> The body further projects that over the next decade 30 million girls less than 15 years old are at risk of FGM. Within each country, there are wide differences in the types of procedure and prevalence of practice as the state specific figures reveal for the states in Nigeria.<sup>[12]</sup> These figures contrast with those obtained in 2013 for the same geopolitical zones of the country but by the fourth Nigeria Demographic and Health Survey.<sup>[10]</sup>

The cultural and traditional components of FGM vary between ethnic enclaves.<sup>[12]</sup> The procedure is routinely carried out between the ages of six and eight with a few cultures preferring to cut at birth, menarche, or before marriage.<sup>[9]</sup> Mutilation is more often undergone alone, but can occur in groups, using same instruments on more than 40 women.<sup>[13]</sup>

A closer look at Table II shows the obtained responses on the importance of FGM on the culture of the people. From the table, a total of 92 (43.4%) of the responses

believed in FGM as against the 120 (56.6%) responses that opposed to it. Of these responses, about 114 (53.8%) appeared to be very knowledgeable on the importance of FGM to the Benin culture as against the 98 (46.2%) that were not conversant with it. From our result, a great percentage of respondents (160 of 75.5%) supported that the people of ancient Benin kingdom strongly believe and honour their culture on the cultural practices and norms as it relates to FGM, while a lesser number of them (52 of 24.5%) opposed to this view. This is indicative that FGM remains an important aspect of the culture of these people till recent times.

Previous reports on the prevalence of the various types of FGM varies geographically across the African continent, with Type I reportedly mostly practiced in Ethiopia, Eritrea and Kenya; while Type II appeared prevalent in regions of West Africa such as Benin, Sierra Leone, Gambia, Guinea and Nigeria.<sup>[5]</sup> Also, according to UNICEF's global databases of 2016, the practice of FGM on girls up to fourteen years old is most prevalent in Gambia (56% of the age group), Mauritania (54%) and Indonesia (49%).<sup>[14]</sup> among 15 to 49-year-old females, FGM is mostly heavily practiced in Somalia (98%), Guinea (97%) and Djibouti (93%).<sup>[15]</sup> Midwives or trained circumcisers travel across several villages, conducting the surgery without anesthesia, antibiotics or sterile equipment.<sup>5</sup> Although the majority of women in many of these countries now believe the practice should be ended, some still believe in the tradition. Further complicating efforts for its global eradication, the majority of girls and women in Guinea (76%), Mali (73%), Sierra Leone (69%), Somalia (65%) and Egypt (54%) still support the tradition.<sup>[16]</sup> These reports are partly in concordance with the findings of this study.

The complexity of FGM in its relation to urban and immigrant health is comprised of a combination of concerns that center on gender equality, religious freedom, cultural traditions, and societal norms.<sup>[17]</sup> Therefore, maintaining this tradition remains of utmost importance to many individuals whose region once practiced it. These issues form a dynamic that thrives within immigrant communities that make it increasingly difficult to eradicate the procedure.<sup>[17]</sup>

Table III shows the extent to which the Binis are ready to obey their culture rather than FGM practice. From the responses, it is seen that majority 138 (65.1%) of Benin's are more likely to comply to the FGM practices than their culture, with 74(34.9%) responses to a very large extent. It was also noticed that 76(35.8%) of the Benin's believe in their culture, 34(16%), while 102 (48.1%) were not fully reported. It was gathered that 50(23.6%) of Benin's are ready to forgo their culture and obey the practice of FGM, majority 162(76.4%) disagreed. Again, a huge number of respondents 170(80.2%) posited that the Benin's strongly believe in their cultural value, while 42(19.8%) disagreed. It was reported by majority 116(54.7%) that despite the importance of FGM, Benin's

still want to obey the FGM than their culture. Whereas, 96(45.3%) disagreed on this. Furthermore, respondents indicated that the reduction of female sexuality (61.4%) followed by tradition and customs of the Binin (14.9%) were the reasons for practicing FGM. Outcome of this study disagree with that of previous reports by Fold'es *et al.*, (2009), who conducted a similar study among Germans from 1998 to 2009.

FGM is performed in developing countries with the most occurrences reported in sub-Saharan Africa, the Middle East, and Asia. These countries have many FGM victims, as the procedure produces a three-pronged platform that makes eradication difficult. FGM has deep sociological roots that create societal norms in order for families to be accepted by the communities. The social conventions place pressure on parents to perform FGM on their daughters in order to prepare them for marriage and adulthood. Its cultural significance leads to the notion that it maintains girls' chastity, preserves fertility, improves hygiene, and enhances sexual pleasure for men.

FGM is utilized as an initiation rite of passage to womanhood and aims to ensure premarital virginity and marital fidelity by reducing her desire for extramarital sexual acts. When the vaginal opening is altered to create a smaller orifice, the fear of opening it further discourages extramarital sexual intercourse.<sup>[18]</sup> Parents and religious leaders enforce circumcision throughout their communities in order to ensure the next generations of children maintain tradition. The combination of these aforementioned factors creates a dynamic that renders FGM a public health concern that requires cultural competence to address.<sup>[13]</sup>

Table V of current study shows the social implication of FGM on the girl child. From the table, it is reported by 86(40/6%) of the respondents that Benin girls who are circumcised are likely to be a prostitute, 94 (44.3%) reported they believe that girls who are not circumcised enjoy sex, while about 62 (29.2%) reported their believe that girls who are circumcised enjoy sex, about 60(28.3%) however reported that girls who were not circumcised stay more in their matrimonial home, 112(52.8%) reported that girls from Benin culture have choice of being circumcised, 134(63.2%) reported that Benin parents believe more in their culture rather than the WHO about FGM, 90(42.5%) reported that girls who are not circumcised command respects in the society, 74(34.9%) reported they have been circumcised.

Current study has revealed a significant association between FGM and female sexual function, where reduction of all aspects was obtained (namely desire, arousal, lubrication, orgasm, satisfaction and pain). Here, the total score of female sexual function for cases was significantly lower than their control of libido, implicative of more sexual drive. An Egyptian report of 2001 had proven that women with FGM have higher rates of dyspareunia with lack of sexual drive, explaining



a possible predisposition to fibrosis and rigid scar tissue occasioned by narrowing of the vaginal orifice and muscular spasm to cause painful intercourse.<sup>[5]</sup> These physical factors will predispose to psychological one, where the painful experience will result into loss of sexual desire and satisfaction. Report from this study is in line with that of El-Defrawi *et al.*, (2001).

## CONCLUSION

Female circumcision is practiced in many regions throughout Africa, Asia, and the Middle East. Studies have however reported that the highest prevalence rates are found within the Horn of Africa. From current study, FGM has been associated with medical, sociocultural, economic and educational consequences in the ancient city of Benin, Edo State of Nigeria. Elimination of FGM is therefore proven to be possible through directing resources in an efficient manner, targeted towards intervention programs on cultural and ethnical proponents. Thus, future research should explore the effects of intervention strategies to prevent FGM among the Binis, and Africans by extension.

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## DENGUE FEVER RISK ASSESSMENT BASED ON BEHAVIOUR PREVENTION ON FOUR SUB DISTRICTS IN JEMBER DISTRICT

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### ABSTRACT

Dengue fever is one of the main problems of public health in the world. Dengue Fever has reached a hundred countries from Afrika up to Western Pacific. Indonesia was the first rank of dengue cases for the Asia Region in 2010. Jember District is one of the highest bestower dengue cases with changes risk areas. A surveillance system can be applied as a new solution tool that is used to monitor area conditions for dengue cases based on prevention as a factor that influenced dengue fever accidents. The purpose of this study is to assess dengue fever risk based on behaviour prevention. This research method is quantitative research, with a crosssectional design. Four sub-districts that become research area. This research population is all of the householder on 4 sub-districts in Jember District, and the sample is 100 householders in 4 sub-district. The research tool are documentation, questioner, and observation sheet. The data analysis are univariate analysis to multivariate analysis. Based on research results, only environmental factor which not influence dengue case. The most influential factor for dengue incidences in Jember District is the health behavior for the prevention. The Risk assessment showed that Pakusari subdistrict with score 44 and Mumbulsari subdistrict with score 42 are in the medium risk, meanwhile Pantl subdistrict with score 56 and Arjasa subdistrict with score 48 are in the low risk.

**KEYWORD:** dengue fever, risk assesment, health behavior prevention, surveillance.

### INTRODUCTION

Dengue Hemorrhagic Fever (DHF) is one of the main public health problems in the world. This disease is a major disease that affects morbidity and mortality, especially on children.<sup>[1]</sup> There were only nine countries that experienced dengue outbreaks before 1970. The development of this disease vector *Aedes species mosquitoes* now have reached 100 countries from Africa, America, the eastern part of Mediaterania, Southeast Asia, to the western Pacific with 390 million cases in the year of 2013.<sup>[2]</sup>

Southeast Asia is an optimum location for breeding of *Aedes Aegypti* mosquitoes and also a DHF endemic area. Where there is a surge in cases of dengue outbreaks in Southeast Asia and the West Pacific.<sup>[3]</sup> Western part of the Pacific and Southeast Asia accounted for the largest number of dengue outbreak cases with a total of 60 cases in 2010 (53.57%) from a total of 112 outbreak cases throughout the world.<sup>[4]</sup> Southeast Asia has also become a region with the largest DHF incidence above 50-100

million in the last ten years.<sup>[5]</sup> The countries in Southeast Asian regions with dengue endemic categories are Cambodia, Malaysia, Philippines, Singapore, Vietnam, and Indonesia with a growing number of cases over the past 10 years. Indonesia was the first rank of dengue cases for the Asia Region in 2010.<sup>[6]</sup> The DHF cases in Indonesia continue to experience fluctuations until now.

Based on the Ministry of Health data for the 2016<sup>[7]</sup>, it is known that the number of dengue cases in 2015 in Indonesia reached 126,675 cases. Dengue incidences increased to 204,171 cases in 2016, and it decreased to 68,407 cases in 2017. *Case Fatality Rate* (CFR) of dengue fever cases was 0.97% in 2015, this figure indicates a decrease in CFR since the beginning of the disease spread by 41.4%.<sup>[8]</sup> CFR refers to the percentage of people who die from a particular disease. East Java Province is one of the biggest contributors to dengue incidence in.<sup>[9]</sup> The East Java's DHF *Incidence Rates* (IR) has reached 64.8 (or 15.3 above the national target of <49.5) in 2016. The high number of IR will affect the increment of the number for dengue cases, and it

happens with the increase of 4,246 IR cases (20%) in 2016. Jember District was determined as one of the districts with the largest number of dengue cases for East Java in 2015.

Based on preliminary study results to the Health office of Jember District, it can be noted that the rural areas in Jember district are now significantly increased dengue cases in 2019. Panti sub-district was the tenth rank district for the most dengue fever incidence in Jember district with 42 cases in 2019 and Pakusari sub-district which has an increment dengue fever case about 3 times from the previous year. Arjasa sub-district still has fluctuations dengue fever cases and Mumbulsari sub-district became the sub-district with the highest increased dengue case about 6 times increased dengue case more than the previous year in 2019. The three sub-districts (Pakusari, Arjasa, Panti) are rural areas, while Mumbulsari sub-district is a semi-urban area.

The new pattern for the spread of dengue cases in Jember District is influenced by various factors. Factors that can influence this change as population growth, urbanization, behavior changes, ineffective vector control, and bad water management.<sup>[10]</sup> Where human behavior is influenced by age, level of education, and geographical factors.

As for several ways that can be used to prevent the spreading of vectors, namely through healthy behavior in the form of not providing stagnant water, closing septic tanks, using insecticides, using pants and clothes.<sup>[11]</sup> This effort is a form of preventing the distribution of vectors, so it is expected to minimize new cases of dengue. Aside from promoting healthy behavior, four other methods that can be carried out, namely diagnosis and case management, *surveillance* integrated and preparedness for epidemics, development of disease vaccines, and implementation of results.<sup>[5]</sup>

The preparation of a surveillance system is a form of early detection effort in its implementation can also be used to know the problem management of DHF disease. It is one of the methods of prevention and control of Disease DHF.<sup>[5]</sup> The output data from surveillance is recommendation for policy maker to make solution program. Based on these problems and findings, researchers feel the need to examine the DHF surveillance system disease based on the shift in distribution of DHF disease and the concept of disease prevention behavior. The benefit for this research can give actual data about DHF condition in Jember District. Researchers will conduct research on "Dengue fever risk assessment based on behaviour prevention on four sub districts in Jember district".

## MATERIAL AND METHOD

This research type is quantitative research. While this research approach is analytic observational. When viewed based on time, the design of this study is

*crosssectional*. Based on the results of *clustering*, there are 4 Sub-districts in Jember district which become research areas. The population in this study is all household heads in four sub-districts Jember district in 2020 about 64,132 households. The sample used by researchers is individuals as constituent groups in several areas about 100 people. The sample criteria for this study are as follows.

- a. Head family or other family members (preferably mother or wife).
- b. Living in the research area for at least one year
- c. More than 17 years old
- d. Willing to be a research respondent.

The sampling technique in this study is using a *multistage random sampling technique*. This method is a combination of several sampling techniques as *cluster sampling*, *simple random sampling*, and *proportionate random sampling*. The techniques used to collect data in this research are interviews, observations, and documentation. Research instruments are the form of questionnaires and observation sheets. The collected data will be processed and then analyzed (univariate, bivariate, and multivariate) using the SPSS computer program.

The risk assessment analysis is a total score that showed sub-district DHF risk status. The total score is divided by a quartile cut of points as controlled risk, low risk, moderate risk, and high risk levels. The category and interval results are as 1) high risk when the range of total score between 18-31, 2) medium risk when the total score between 32-45, 3) low risk when the total score between 46-59, and 4) controlled risk when the total score between 60-72.

## RESULT AND DISCUSSION

The sample in this study is people from 4 Districts in Jember District (Arjasa Sub District, Kaliwates Sub District, Mumbulsari Sub District, and Pakusari Sub District). The selection of sub-districts is based on the results of *clustering* for each category *cluster* with several assessment indicators. Indicators for determining *cluster* values are rainfall, population density, altitude, urban or rural status of an area. The total respondents in this study are 100 respondents which 70 people are women with the majority aged 31-45 years around 54.3%. Male respondents are about 30 people with the majority aged 46-60 years around 43.3%. Respondents with more than 60 years of age have the lowest percentage of participation as respondents, about 3 people (3%).

Respondents characteristics can be categorized based on occupation, as the results there are no male respondents who do not work. Male respondents generally work as farmers and entrepreneurs around 36.67% and 40%. The majority of female respondents work as housewives as many as 34 people (49%), and 8 people (11.4%) do not work.

Eight peoples (8%) who did not work have education exactly not graduating from junior high school. There are no respondents (0%) did not work or work as farmers

who have graduated from a high school and university level. The majority of respondents work as entrepreneurs 26% and farmers 23%.

**Table 1: Respondent demographic characteristics.**

No	Characteristics	Category	N	
			n	%
1	Sex	a. Male	30	30
		b. Female	70	70
2	Age	a. 18-30 years	24	24
		b. 31-45 years	45	45
		c. 46-60 years	28	28
		d. >60 years	3	3
3	Occupation	a. Unemployment	8	8
		b. Worker	6	6
		c. Entrepreneur	26	26
		d. Farmer	23	23
		e. Others	37	37
4	Education	a. No Education	17	17
		b. Primary	37	37
		c. Secondary	27	27
		d. Higher Secondary	12	12
		e. University	7	7

The bivariate test is using Chi-square test, the results showed that the health promotion strategy has a relationship to predisposing factors related to dengue fever prevention behavior (DHF) as shown in table 2.

Where the determination All variables are related to other variables, if the calculated  $P < P\text{-value}$  (0.05) or  $H_0$  is rejected.

**Table 2: Correlation between health education with predisposition, reinforcing and enabling factors.**

No	Category	p-value	p-score	Conclusion
1	Predisposition	0,000	0,05	$H_0$ rejected
2	Reinforcing	0,000	0,05	$H_0$ rejected
3	Enabling	0,012	0,05	$H_0$ rejected

The results of table 2 showed that the predisposing factor is knowledge that has a relationship with the existence of health education related to the prevention of DHF. Other predisposing factors, attitudes, and *self-efficacy* are also related to the presence of health education related to dengue prevention. The p-value of the three indicators is  $p = 0,000$  or  $<0.05$ , which indicates that the existence of health education is related to the knowledge, attitudes and *self-efficacy* related to the behavior prevention of DHF.

The relationship test between the two variables uses the *Chi-Square* tet as shown in table 2 as an example. The relationship between the existence of health education with reinforcing factors such as the role of families dan community leaders in supporting dengue prevention behaviors. Where the *p-value* of the indicator is 0,000 or  $<0.05$  which indicates that the existence of health education is related to the role of family and community leaders in supporting dengue prevention behavior.

The *odds ratio* value of these two factors amplifier (the role of family and community leaders to support dengue

prevention behaviors) are 56.4 and 37.6. This score showed that the existence of routine health education to the community regarding the dengue prevention behavior has a potential of 56.4 times for respondents to increase the role of families in supporting dengue prevention behavior.

Table 2 showed that the *p-value* = 0.012 or  $<0.05$  which indicates that the existence of health education is related to the availability of facilities and infrastructure to support DHF prevention behaviors. While the *odds ratio* value is 3.64, which means that the existence of routine health education for the community regarding the dengue prevention has a potential of 3.64 times for residents to obtain and provide facilities and infrastructure related to dengue prevention behavior. Infrastructure means in question is the provision of abate, routine fogging, health promotion media, and other information facilities that can increase public understanding.

Predisposing factors in this research were assessed based on three indicators (knowledge, attitudes, and *self-efficacy*). The test result showed that there is a



relationship between predisposing factors with dengue fever prevention behavior. Here is a test result relations

between the two variables, as shown in Table 3.

**Table 3: Correlation between predisposition, reinforcing, and enabling factor with health behavior prevention.**

No	Category	p-value	p-score	Conclusion
1	Predisposition	0,000	0,05	H0 rejected
2	Reinforcing	0,000	0,05	H0 rejected
3	Enabling	0,000	0,05	H0 rejected

The relationship of dengue prevention behavior with the dengue incidence showed that there is a relationship between the two variables with a value of  $p = 0,000$  or  $<0,05$ . The  $p\text{-value} <0,05$ , results in the meaning that H0

is rejected as shown in table 4. Whereas the *odds ratio* value is 35.48. This result indicates that mosquito nests worker is a variable that can affect the dengue fever incidence directly with that value.

**Table 4: Correlation between mosquito eradication practices with DHF incidences.**

Category	DHF Incidences				Total
	N	%	N	%	
Less	21	95,5	29	37,2	50
Good	1	4,5	49	62,8	50
Total	22	100	78	100	100

The environmental variables have no relationship with the dengue fever incidence. The environment variable itself is the condition of the environment around the community which includes social, economic, physical,

and biological aspects. The result is shown in table 5 for example, an indicator for the number of families has  $p\text{-value} = 0,878$ .

**Table 5: Correlation between environmental conditions with DHF incidences.**

Amount of Family	DHF Incidences				Total
	Amount	%	None	%	
>4 peoples	6	27,3	20	25,6	26
1-4 peoples	16	72,7	58	74,4	74
Total	22	100	78	100	100

The several variables that have been described, only environmental variables that have no relationship with the dengue fever. The most influential factor for the dengue fever incidence is the eradication practice of mosquito nets variables. Where the value of  $p = 0,005$  or  $<0,05$ . The  $p\text{-value}$  for eradication practices of mosquito nests variable is the smallest or the only one whose value is  $<0,05$ .

Risk assesment will create risk status against dengue disease whcih obtained from the calculation results of several proposed research variables. Where the total sub-variables used to perform the mapping are 9 sub-variables. The status of the four sub-district risk assesment is as follows.

**Table 6: The DHF Risk status of four sub-districts.**

No	Category	Total score	Conclusion
1	Panti	56	Low dengue risk status
2	Arjasa	48	Low dengue risk status
3	Mumbulsari	44	Medium dengue risk status
4	Pakusari	42	Medium dengue risk status

The health promotion strategy is assessed based on the presence or absence of periodic counseling to the community, while the predisposing factor is assessed by three aspects namely knowledge, attitudes and *self efficacy*. Health education is a means to change people's behavior through providing information.<sup>[12]</sup> Health education is also a form of health promotion strategy as a form of independent intervention that plays a role in

helping individuals, families, groups and the community in dealing with their health problems. In the case of dengue fever, the incidence of the disease is generally caused by human health behavioral factors. Providing health information is important, one of which is through counseling.<sup>[13]</sup>

The existence of health promotion is related to the level

of knowledge of citizens, attitudes, and *self-efficacy*. Other research also states the same thing, that the lack of public knowledge is caused by the lack of community development activities or health promotion carried out on society.<sup>[14]</sup> In addition to influencing knowledge, community development activities also affect people's attitudes towards dengue fever.

Attitude is a collection of symptoms in response to stimuli, so attitudes involve thoughts, feelings, attention, and psychiatric symptoms.<sup>[15]</sup> The existence of health promotion interventions as a stimulus can be responded well by respondents, increasing attitudes towards behavior.<sup>[16]</sup> The results of other studies that are in line, states there are changes in attitude before and after the provision of health promotion interventions. The attitude value after the majority of health education provision increased due to respondents being able to understand health intervention material.<sup>[17]</sup>

The third indicator which also relates to the existence of community development activities is *self-efficacy*. An individual's belief that can do a behavior, can be improved by conducting health education. The aim is to form an interest in healthy behavior to prevent disease and add to it as a source of literacy, to adopt the behavior.<sup>[18]</sup>

The family has many roles in influencing the behavior of family members, including biological functions, economic functions, educational functions, social functions, protection functions, recreational functions, and religious functions.<sup>[19]</sup> In carrying out its function in the form of providing education related to behavior, family members need a source of health information. Information exposure has an important role in influencing disease prevention behavior, information facilities such as radio TV, and social media can reach various.<sup>[20]</sup> Health information can also be provided through health education methods with the target being community leaders and families who play a role in preventive behavior.<sup>[21]</sup> Families with adequate information sources can guide other family members to conduct dengue prevention behaviors. The higher the insight, will have an impact on attitudes.<sup>[22]</sup>

The second indicator of the reinforcement variable is related to the role of community leaders. Health promotion strategies through community development have a relationship with the positive role of community leaders. This relationship can arise if community leaders understand the importance of implementing healthy behaviors. The community leaders have to understand the importance of the application of dengue prevention behavior or it cannot work. Thus efforts are needed to provide health information to community leaders. Where a character has a big influence in moving the wider community because the general public is more easily accept what is explained by the prominent figure.<sup>[23]</sup>

The facilities and infrastructure in this research are related to the completeness or readiness of the community in providing media to prevent the occurrence of dengue fever. The facilities and infrastructure are the availability of abate, information media, and *fogging* programs. Community readiness for providing health information is important. Health education is also a form of health promotion strategy as a form of independent intervention that plays a role in helping individuals, families, groups, and the community in dealing with their health problems. People can adopt healthy behaviors such as *fogging* with good information.

Fumigation is very effective in breaking the chain of mosquitoes transmission, including those that are active, die instantly when in contact with the particles. *The existence of a routine fogging* can help the community carry out prevention efforts. The efforts to make people aware of the importance of *routine fogging* is to provide information about disease prevention behavior, through media such as radio TV, and social media to reach various.<sup>[20]</sup> Besides, it can also be done by holding regular health education.

Knowledge and attitude can influence behavior, according to previous research. Where knowledge and positive attitudes will gain positive behaviors towards preventive behavior. Not always this relationship is directly proportional, there is still the potential that this relationship is missing. There are three components of behavior change knowledge, attitudes, and behavior. It is difficult to say that knowledge is a major factor in shaping human behavior.

Self-efficacy as a belief in one's own ability to deal with and solve problems effectively. Self-efficacy also means self-confidence themselves able to succeed and succeed. Individuals with high self-efficacy are committed to solving the problem and will not give up when finding that the strategy being used is not successful. *Efficacy* also helps determine the extent of the effort to be deployed by people in an activity, how long they will persevere when face obstacles, and how tenacious they will face that situation no *Self-efficacy* can also be used as a tool or indicator to limit a good health behavior or not.

Someone has a family with a positive attitude towards behavior prevention, it will show good disease prevention behavior as well. These results are also like previous research, which states that a positive family attitude can help other family members to behave positively towards a behavior. Environmental support especially family and community leaders can be the main variable influencing health behavior compared to knowledge and attitude.<sup>[24]</sup>

Community leaders as role models or *role persons* play a role in changing public health behaviors to be more positive. Community leaders also play a role in early

detection of dengue fever based on the results of health education, so that immediately gets the appropriate treatment.<sup>[25]</sup> This indicates that the handling of dengue fever is not only based on the health department but also requires an active role.<sup>[23]</sup>

Strengthening factors (facilities and targets) have an important role in the behavior of DHF reinforcement in Jember Regency. Although *fogging and the use of abate* are not the main factors that make individuals to form healthy behaviors, both can still be used to break the chain of disease transmission. Information exposure has an important role in influencing disease prevention behavior, information facilities such as radio TV, and social media can reach various.<sup>[20]</sup>

Health information can also be provided through health education methods with the target being community leaders and families who play a role in preventive behavior.<sup>[21]</sup> Health information is inseparable from health education media. Media education or health information acts as a tool for the health education process that aims to facilitate the reception of health messages. With adequate facilities and infrastructure, it can help the community to form healthy behaviors.

The eradication practice of mosquito nests through the movement of draining, closing, and burying has a role in reducing the number of dengue incidence. Previous research also stated that there was a significant influence between 3M Plus behavior on the occurrence of Dengue Hemorrhagic Fever in Purwoharjo District, Banyuwangi Regency.<sup>[26]</sup> This prevention and control effort is one form of action to break the chain of transmission by eradicating the transmission of mosquito larvae. The lack of public attention about this draining, closing, and burying behavior so that from year to year increases the incidence of dengue fever increasingly.<sup>[27]</sup>

The findings of the relationship for the environment to the dengue fever incidence, differ from previous studies. Where the more the number of family members, the better the dengue behavior prevention that the family has. More and more families can play a role in maintaining house hygiene and sharing information related to behavior.<sup>[28]</sup>

These results are consistent with the findings of previous studies which also stated that dengue behavior prevention through mosquito nests worker practices has an important role to prevent the dengue incidence. Human behavior plays an important role in eradicating mosquito breeding grounds or in preventing mosquitoes from spreading, one way is to close the shelter.<sup>[29]</sup> This is due to the lack of vaccines or specific drugs for dengue disease so that the activities of supervision and eradication of mosquito nests have an important role in preventing events.<sup>[30]</sup>

Table 6 showed that the four sub-districts are in two risk categories (low dengue risk and medium dengue risk). Panti and Arjasa sub-district are in low dengue risk, Mumbulsari and Pakusari sub-district are in medium risk. Based on the results of clustering determination for all sub-districts in Jember Regency, it can be known that Panti sub-district is in cluster 1 and Arjasa sub-district is in cluster 2. While Pakusari sub-district is in cluster 3 and Mumbulsari sub-district is in cluster 4. The higher the cluster level, indicating the higher level of regional risk against dengue disease.

Where the higher the level of clustering districts, the higher the risk of dengue disease. This is derived from the results of the study, which shows things are in line. Panti sub-district has the highest final score, which is 58 which belongs to the category of low risk areas. Mumbulsari sub-district, which is included in cluster 4, has the lowest value of 42.

## CONCLUSION

Based on the results of this study, it can be concluded that the most influential factor in the dengue hemorrhagic fever (DHF) incidence on Jember Regency is dengue prevention behavior through the practice of eradicating mosquito nests. The dengue risk status for four sub-districts are in low risk and medium risk. Where the higher the level of clustering a sub-districts, the higher dengue disease risk in that sub-district. The dengue prevention behavior itself is influenced by the level of knowledge, attitudes, *self-efficacy*, the role of families, community leaders, the presence of facilities, and infrastructure which are all related to health promotion through health education activities or community development.

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## PROGNOSTIC FACTORS OF ACUTE RENAL FAILURE IN PATIENTS ADMITTED TO INTENSIVE CARE UNIT

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### ABSTRACT

**Background:** Acute renal failure (ARF) has been recognized as common condition in patients admitted to intensive care unit (ICU) and it is associated with increased risk of morbidity and mortality. **Objective:** the present study aims to determine incidence, risk factors, and outcome of acute renal failure in patients admitted to ICU. **Materials and Methods:** This is prospective, observational study conducted in ICU in Tishreen University Hospital-Lattakia -Syria from November 2018 to December 2019. Patients aged 18 to 70 years were screened for ARF according to (RIFLE) criteria. **Results:** During study period, of 152 patients, 49 (32.2%) developed ARF. Independent predictors of ARF were age older of 65 year (OR=3.8 [1.9 – 7.8], p:0.008), presence of infection on admission (OR=3.3 [2.1–8.9], p:0.002), history of diabetes mellitus (OR=2.4 [1.1–4.9], p:0.001), MAP<65 (OR=4.1 [1.4–12.2], p:0.003) as well as hypertension (OR=5.4 [2.4 –11.8], p:0.001). The average length of stay in ICU for patients with ARF was longer than those without ARF (17.6 vs 10.5, p:0.002) with high rate of mortality (45% vs 22.3%, p:0.02). **Conclusion:** Acute renal failure in critically ill patients is associated with worsening prognosis, so identification risk factors of ARF and initiate preventive measures should be part of the management.

**KEYWORDS:** Acute renal failure, intensive care.

### INTRODUCTION

Acute renal failure (ARF) is defined as sudden decrease in kidney function resulting in failure of kidney to eliminate nitrogenous waste products and maintain homeostasis of water and electrolytes.<sup>[1]</sup> The two major causes of ARF that occurs in hospital are prerenal diseases and acute tubular necrosis (ATN).<sup>[2]</sup>

ARF in intensive care unit (ICU) is common and is associated with significant morbidity and mortality that increase with progress degree of renal dysfunction.<sup>[3]</sup> The incidence in ICU is increasing and reach up to 67%, variability of incidence is depending on population analyzed and criteria employed in definition ARF.<sup>[4]</sup> The common causes of ARF in ICU are sepsis, cardiac surgery, malignancy, and acute liver failure.<sup>[5]</sup> Early diagnosis of ARF and prompt management is essential to reduce mortality that can reach up to 50%.<sup>[6,7]</sup> The absence of local studies prompted us to carry out this research to identify risk factors associated with ARF.

### MATERIALS AND METHODS

#### Study design and data collection

We prospectively studied patients aged 18 to 70 years admitted to the ICU in Tishreen University Hospital – Lattakia-Syria from November 2018 to December 2019. Patients with one of the following: evidence of preexisting CKD stage III or IV, need for renal replacement therapy, and those who had renal transplantation were excluded.

Demographic data including age, sex and related to comorbidities were recorded. All patients were screened for ARF by using serum creatinine, urea, sodium, in addition to urine output measurement. The outcomes at discharge including mortality were also recorded.

#### Definitions

**Acute renal failure:** We used RIFLE criteria for diagnosis acute renal failure in ICU. RIFLE criteria defines failure as a three- fold increase of serum creatinine or serum creatinine >4 mg/dl or decrease in GFR of >75%.<sup>[8]</sup>

**Mean arterial Pressure(MAP):** is defined as the average pressure in patient's arteries during cardiac cycle, normal range is(65-110 mmHg).<sup>[9]</sup>

**Outcome:** Recovery was recorded once creatinine improved to known baseline. Chronic kidney disease defined as renal function had not recovered during 3 months. Statistical Analysis Statistical analysis was performed by using IBM SPSS version20. Basic Descriptive statistics included means, standard deviations(SD), Frequency and percentages.

Differences of distribution examined using chi- square test or Fisher exact test if it need. Risk factors were evaluated in univariate analysis, and in multivariate analysis by a multiple logistic stepwise regression procedure. Variables with p less than 0.05 were included in the model. Odd ratios were estimated from b

coefficients obtained, with respective 95% confidence intervals(CI 95%).

## RESULTS

A total of 152 patients were admitted to our ICU from November 2018 to December 2019, 49 patients (32.2%) developed ARF during their stay in ICU. The baseline characteristics of patients are as given in table(1).

Patients who developed ARF were older(median age 69 vs 55 years, p:0.002),with significant difference between both sexes(p:0.01).They are more likely to have infection on admission(28.6% vs 10.7%, p:0.02).

Diabetes mellitus, hypertension, and renal disease were more common in patients with ARF (p<0.001).

**Table 1: Demographic characteristics of the study population by comparison of ARF and non-ARF groups.**

Variables	ARF- patients n=49(32.2%)	Non-ARF patients n=103(67.8%)	p-value
Age(year)	69 [34 - 70]	55 [18 - 70]	0.002
<u>Sex</u>			
Male	21(42.9%)	66(64.1%)	0.01
Female	28(57.1%)	37(35.9%)	
<u>Causes of admission</u>			
Pulmonary	5(10.2%)	11(10.7%)	0.9
Cardiac disease	2(4.1%)	12(11.7%)	0.3
Cancer Infection	2(4.1%)	8(7.8%)	0.1
Neurological	14(28.6%)	11(10.7%)	0.02
Renal disease	16(32.7%)	42(40.8%)	0.1
Gastrointestinal	8(16.3%)	6(5.8%)	0.04
Others	2(4.1%)	4(3.9%)	0.4
	0(0%)	8(7.8%)	0.09
<u>Co=morbidities</u>			
Diabetes mellitus	22(44.9%)	26(25.2%)	0.01
Hypertension	38(77.6%)	40(38.8%)	0.0001
Hyperuricemia	0(0%)	4(3.9%)	0.1
Systemic diseases	3(6.1%)	1(1%)	0.06
Renal diseases	6(12.2%)	2(1.9%)	0.008
Others	18(36.7%)	36(35%)	0.8
MAP	77.02±21.8[37 -113]	91.6±17.6 [40-147]	0.001
<u>Laboratory findings</u>			
Urea	82.7±48.7	53.6±46.3	0.001
Cr	2.5±1.9	1.3±1.8	0.001
Na	138.6±5.7	136.7±4.1	0.03
Length of ICU stay(days)	17.6[2 - 130]	10.5[1 - 45]	0.02
<u>Outcome</u>			
Recovery	30(61.2%)	88(85.4%)	0.03
Chronic disease	6(12.2%)	0(0%)	0.008
Hospital mortality	22(44.9%)	23(22.3%)	0.02

Stay in the ICU was longer in patients with ARF (17.6 vs10.5 day in patients without ARF, p:0.02), and mortality rate was higher in patients with ARF(44.9% vs22.3%, p:0.02) .

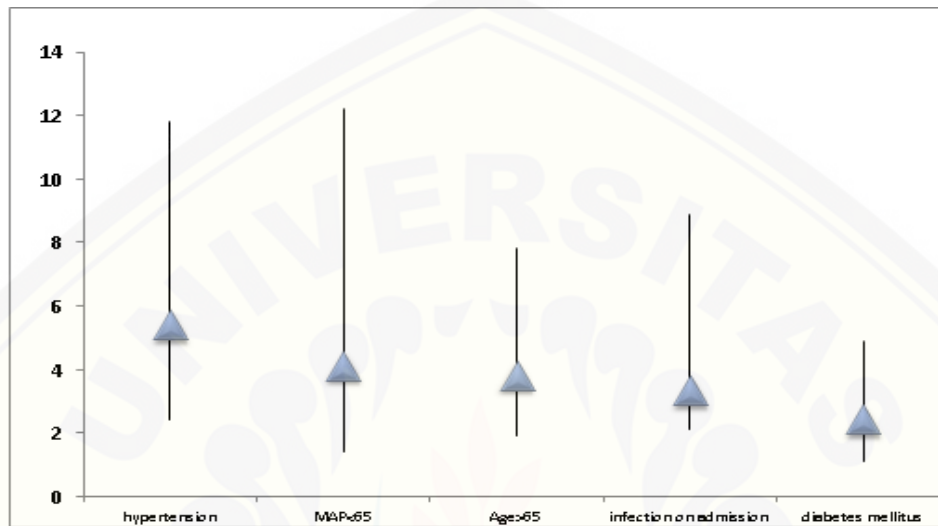


**Table 2: Risk factors for developing ARF in study population by multivariate logistic regression.**

Factor	OR(95% CI)	p-value
Age>65	3.8 [1.9 – 7.8]	0.008
Hypertension	5.4 [2.4 – 11.8]	0.0001
MAP<65	4.1 [1.4 – 12.2]	0.003
Infection at admission	3.3 [2.1 – 8.9]	0.002
Diabetes mellitus	2.4 [1.1 – 4.9]	0.001

Significant independent risk factors for developing ARF were: Age>65, infection on admission, history of

diabetes mellitus, hypertension and MAP<65 Fig.1.



**Figure 1: Risk factors for developing ARF in study population.**

**DISCUSSION**

This prospective study demonstrated incidence, characteristics, and predictive risk factors of ARF in patients aged 18-70 years admitted to ICU. The overall incidence of ARF (32.2%) in our study was comparable with previous studies. Vincent *et al* reported that the incidence of ARF in ICU was 24.7%<sup>[10]</sup>, Zahra *et al* also found that incidence of ARF in ICU was 31.1% in Iran.<sup>[11]</sup> In contrast to that, Vohra *et al* found that incidence of ARF in ICU in India was low(3.8%)<sup>[12]</sup>, and this may be explained by the difference of criteria used for definition of ARF in the different studies.

ARF was more frequently in patients with infection on admission and co-morbid conditions such as diabetes mellitus and hypertension, these findings agree with results of other studies. Herrera *et al* found that ARF was more frequently in patients with diabetes mellitus, high blood pressure, and sepsis on admission.<sup>[13]</sup> Sherif *et al.*, 2017 also found that patients with ARF had co-morbidities such as diabetes mellitus and CVD, in addition to that sepsis was more common in those patients.<sup>[14]</sup>

In the present study, the most important risk factors for ARF were: advanced age, presence of infection on admission, hypertension, MAP<65, and diabetes mellitus, and those have been reported as risk factors in other studies (Vincent *et al.*, 2000) and(Ryan *et al.*,

2019).<sup>[15]</sup>

Mortality rate was higher in patients with ARF than those without ARF(45% vs 22%), and this is comparable with other studies. Vincent *et al* found that ICU mortality was 43% in patients with ARF.

To the best of our knowledge, this is the first study investigate epidemiology, and prognostic factors for ARF in patients admitted to ICU in Syria.

**CONCLUSION**

ARF is a common complication in patients admitted to ICU and is associated with substantial morbidity, mortality in addition to high medical costs, so that early diagnosis is essential to improve prognosis.

**List of abbreviations**

ARF: acute renal failure, ICU: intensive care unit, MAP: Mean arterial pressure, RIFLE: Risk, Injury, Failure, Loss, End-stage Renal Disease, CVD: cardiovascular diseases.

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## ETNOCARING: RECOVERY METHOD FOR CHILD FEVER SEIZURES BASED ON BAJO TRIBE TRADITION IN THE NORTH BUTON, INDONESIA

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### ABSTRACT

**Introduction:** Children who experience febrile seizures are very important to be given proper treatment from the beginning to after the seizure period. The success of recovering from a child's febrile seizure will determine the degree of health and quality of life in the future. The Bajo tribe has its method of recovery which is still being carried out and is believed to be able to overcome the health problems of children with fever seizures. **Purpose:** to find out the method of restoring child febrile seizures based on the traditions of the Bajo Tribe in the North Buton. **Method:** The research design used was qualitative: ethnography. The number of participants was 16 shamans from the Bajo Tribe in the North Buton and 4 women as triangulation participants. The sampling technique used was snowball sampling. The data analysis used was thematic. **Result:** The findings in this study are described in the theme of herb therapy and seawater splash therapy. **Conclusion:** The method of restoring pediatric febrile seizures based on the North Buton tradition consists of herb therapy and seawater splash therapy.

**KEYWORDS:** Recovery, seizures, fever, tradition, Bajo.

### INTRODUCTION

Seizures are intermittent clinical manifestations that are very characteristic and can include disturbances in consciousness, behavior, emotions, motor, sensory, and autonomic caused by the release of electric charges in brain neurons.<sup>[1]</sup> Fever seizures are a health problem that threatens the lives of children if not treated properly.<sup>[2]</sup>

The incidence of febrile seizures in the world such as America and western Europe has increased every year by 2 to 4% (Presto et al., 2020). In Indonesia, the incidence of febrile seizures that occur in children aged 6 months to 3 years is 2-5% and 30% of them will experience recurrent febrile seizures.<sup>[3]</sup> The incidence of febrile seizures in North Buton Regency, Southeast Sulawesi province in 2018 was 68 cases and 18% of them were recorded as having died.<sup>[4,5]</sup>

Febrile seizures are caused by several things such as fever, effects of toxic products rather than microorganisms, allergic responses or general abnormalities due to infection, changes in fluid and electrolyte balance, and viral encephalitis.<sup>[6]</sup> Fever seizures also have risk factors, namely genetic factors and age factors.<sup>[7]</sup>

Management of febrile seizures can be done pharmacologically and non pharmacologically.<sup>[8]</sup> The non-pharmacological treatment of pediatric febrile seizures is grouped into two groups, namely treatment during treatment and recovery.<sup>[2]</sup> Recovery methods that can be done non-pharmacologically are: warm compresses, wearing thin clothes, monitoring temperature regularly, and increasing oral fluid intake when the child has a fever, giving herbal ingredients such as ginger juice when the child is no longer having seizures, and so on.<sup>[8]</sup>

Recovery of children with febrile seizures is also very important to do properly.<sup>[2]</sup> Good recovery will be able to restore the child's body system to work properly, such as when the child has not had a febrile seizure.<sup>[9]</sup> Vice versa, inadequate recovery can also affect the disability or the inability of the child's body systems to work and normally as before experiencing a febrile seizure.<sup>[10]</sup>

Currently, there are still many people in several areas who are recovering from child fever seizures based on their traditions, such as using traditional healers.<sup>[11]</sup> This has become a cultural habit and is carried out from generation to generation.<sup>[12,13]</sup> Many factors cause people to maintain this culture, including the level of trust in health workers, education level, economic level, and



access to health facilities.<sup>[8,11]</sup> Besides, the superiority of services provided by traditional healers when dealing with child febrile seizures such as providing maximum support to the family when a child has a febrile seizure, making direct visits to the home to provide services, and providing additional therapy after the child has had a febrile seizure, also influences the community in maintaining care and recovery. febrile seizures according to tradition.<sup>[1,13]</sup>

The Bajo Tribe in the North Buton is one of the tribes in Indonesia, precisely in North Buton Regency, Southeast Sulawesi province. Until now, this tribe still upholds the traditions and culture in every activity of its life, including the recovery of child fever seizures.<sup>[4,14,15]</sup> The results of interviews with 4 mothers from the North Buton Bajo tribe stated that every time the child had a febrile seizure, they always used the help of a shaman, where the form of therapy given was warm compress therapy and bites of cloth bites when the child had a fever and seizures, while after the child did not seizures and fever begin to fall for some remedial therapy.

The description of the method of care and recovery for the Bajo tribe is local cultural wisdom that is very important to be preserved and scientifically proven as a treatment for febrile seizures in children, so that it can save children's lives.<sup>[16,17]</sup>

## MATERIALS AND METHOD

### Desain

The research design used in this study was qualitative: Ethnography.

### Setting

The research was conducted in Indonesia, to be precise in Bajo Village, North Buton Regency, Southeast of Sulawesi. The research was conducted from 22 July 2020 to 18 October 2020.

### Research subjects

The number of participants in this study was 20 people consisting of 16 traditional healers from the Bajo Tribe in the North Buton and 4 women as triangulation participants, which was determined by the snowball sampling technique.

### Data analysis

Data analysis used in this research is thematic analysis with the stages of data reduction, data presentation, and verification or concluding.

## RESULT

The results of the study consisted of three main themes of recovery methods in children's fever seizures based on the traditions of the North Bajo Buton Tribe, namely herb therapy, abstinence, and seawater splash therapy.

### 1. Herb therapy

Herb therapy themes were identified in the category of composition and giving method.

a. The composition category is described by the keywords honey, ginger, and water through the verbatim snippet as follows:

"... A concoction of honey and ginger is given after the fever drops and the seizures are gone..."(P1,P2,P5,P6,P10)

"...this honey ginger herb must be mixed with plain water, but not much..."(p3)

"... But the honey must be real honey, not the ones in the shops ..." (P4)

"... Just two spoons of honey then mix it with half a glass of boiled ginger water ..." (P7)

"... Boil about two ginger seeds in two glasses of aqua until the remaining water is one glass of aqua ..." (P8)

"... Just boil two ginger until the water remains just one glass ..." (P9)

"... Honey is one or two tablespoons mixed in half a glass of ginger water ..." (P11)

"... This mixture of ginger and sugar water is only given if the child has had a fever and has not had seizures ..." (P12)

"... This herb ginger honey has been passed down from generation to generation, always given (P13)

"... Don't make lots of boiled ginger water ..." (P14)

"... This honey is great for the child recovery, but the real thing ..." (P15)

"... If in the past the honey was just squeezed from the wasp nest but now it's hard ..." (P16)

The participant statement is strengthened by the following triangulation participant statement:

"... After the fever drops and the seizures are gone, usually therapy is continued with a concoction consisting of honey and ginger boiled water ..." (PT1)

"... Healer (shaman) usually recommends consuming a mixture of honey and ginger for recovery ..." (PT2)

"... The stew of ginger water and honey is a healing therapy after my child had a fever and seizures healed.." (PT3)

"... The honey we use is real honey, not honey as advertised on television ..." (PT4)

b. The categories of giving methods are described by the keywords mix, boil, drink, morning, and evening through the verbatim snippet as follows:

"... Boil two or three pieces of ginger for 10 to 15 minutes ...." (P1)

"... If I drink water to boil about 2 glasses ..." (P2)

"... I use ginger in 2 cups of drinking water, boil it up to the remaining 1 cup ..." (P3)

"... Usually boil the ginger only for 15 minutes ..." (P4, P5)

"... I usually pick out the fresh ginger first, I clean it and open the skin then boil it ..." (P6)

"... Ginger cooking water mixed with honey ..." (P7, P8, P12, P13)

"... If I give two tablespoons of the honey mixture with half a glass of boiled ginger water ..." (P9)  
 "... Give the child the honey herb ginger every morning and night ..." (P10)  
 "... The honey ginger herb is drunk morning and night ..." (P11, P14, P15, P16)

The participant statement is strengthened by the following triangulation participant statement:

"... Healer (shaman) always boils ginger, then mixes honey with it for my child's recovery ..." (PT1)  
 "... My child's honey ginger herb always drinks after the fever drops ..." (PT2)  
 "... If he has already drunk the honey ginger mixture from the parents (shaman) my child will immediately be healthy ..." (PT3)  
 "... A concoction of ginger and honey is usually given every morning and evening, but if you don't have seizures ..." (PT4)

## 2. Seawater splash therapy

The theme of seawater splash therapy was identified in the category of time, duration, and procedure.

a. The time category is described by the keyword after and directly through the verbatim snippet as follows:

"... After the child's fever and seizures have disappeared, the children still have to be treated by putting them in seawater ..." (P1)  
 "... If the fever comes down, we immediately put it in seawater ..." (P2)  
 "... This seawater splash is done after the fever has dropped so that the child's temperature will quickly return to normal ..." (P3)  
 "... Seawater splash therapy is carried out after the child's fever has decreased (P4, P5, P8, P9, P10, P13)  
 "... After having a fever, continue by splashing seawater, so the child is immersed in seawater ..." (P6)  
 "... But you have to be careful, children are thrown into seawater after the fever drops or it doesn't get too hot anymore ..." (P7)  
 "... If I have to also continue to be immersed in water, it's a child, after the heat is not too high ..." (P11)  
 "... My grandmother's grandmother, if a child who had a fever was not too hot, immediately put it in seawater ..."  
 "... Oh no-no, after I checked the heat went down, I put the child in the sea ..." (P14)  
 "... Immediately continue with the sea splash therapy, if the fever has dropped ..." (P15, P16)

The participant statement is strengthened by the following triangulation participant statement:

"... My child was dropped into the sea, usually the second day after the heat fell ..." (PT1)  
 "... Healer (shaman) always immediately throws my child in the sea when the fever has dropped ..." (PT2)  
 "... usually the sea splash therapy, ordered by the parents (shaman), is done after my child's fever has decreased ..." (PT3)

"... I've only been treated for sea immersion once, yes he (shaman) immediately dumped my child in the sea, after the heat fell and prayed first ..." (PT4)

b. The duration category is described by the keyword day, week & times via the verbatim snippet as follows:

"... So my child put it three times in a row ..." (P1)  
 "... When doing seawater splash therapy, I usually do it in the afternoon ..." (P2)  
 "... Do the seawater splash therapy once a day ..." (P3, P4, P5, P6, P7, P8, P12, P16)  
 "... I threw myself in the sea, but not for long and only once a day ..." (P9)  
 "... But this splash therapy is usually only for 1 week ..." (P10)  
 "... Just did it for 1 week ..." (P11, P13, P14)  
 "... I put my child in the sea every day, but in the afternoon, it continues until one week ..." (P15)

The participant statement is strengthened by the following triangulation participant statement:

"... Healer (shaman) throws my child out every evening ..." (PT1, PT2)  
 "... usually for one week ..." (PT3)  
 "... So I was put in the sea once a day ..." (PT4)

c. The procedure categories are described by the open, splash, input & Lift keyword via the verbatim snippet as follows:

"... If you want to throw a child into the sea, first open the clothes and then splash them ..." (P1)  
 "... hold the child's armpits, then put it in the sea, don't take long, then pick it up and drop it again, repeat three times ..." (P2)  
 "... After the child has been immersed, throw it in and throw it again 3 times ..." (P3, P4, P5, P6, P8, P11, P12)  
 "... The principle is that you just lift it 3 times ..." (P4, P9)  
 "... This is how you input it at sea, let it sit for a while and then you lift it again, after that, you put it back in the sea, repeat but just three times, don't take long ..." (P10)  
 "... Plunge and then lift three times ..." (P13, P14, P16)  
 "... Pour it slowly e, until the neck is submerged in seawater, then lift it and repeat three times ..." (P16)

The participant statement is strengthened by the following triangulation participant statement:

"... My son took off his shirt, then put it in seawater and lifted it, then put it in again ..." (PT1)  
 "... The act of splashing and then repeated 3 times ..." (PT2, PT3, PT4).

## DISCUSSION

### 1. Herb therapy

The herb used by the Bajo tribe of North Buton Regency as a healing therapy for children with fever seizures is a mixture of honey ginger. This concoction consists of 3 tablespoons of honey mixed into ½ cup of the ginger cooking water. Ginger water is obtained from boiling 3 pieces of ginger into 2 drinking glasses that are boiled

until the remaining 1 cup of boiled ginger water or boiling for 10-15 minutes. The herb ginger honey is given to children who have fever seizures with a frequency of drinking 2 times a day, namely in the morning and at night.

Ginger is used as an herbal medicinal ingredient because it contains essential oils with active chemical compounds, such as zingiber, camphor, lemonin, borneol, shogaol, cineol, fellandren, zingiberol, gingerol, and zingeron which are efficacious in preventing and treating various diseases including rheumatism, influenza, asthma, colds, and sore throat.<sup>[18]</sup> Ginger also contains gingerol which can help increase intestinal motility and acts as an antipyretic agent, so it is very good for the recovery of children who have fever seizures.<sup>[18,19]</sup>

Honey contains compounds that are like chemical compounds that include various chemical groups, such as monoterpenes, C13-norisoprenoid, sesquiterpenes, benzene derivatives, esters, fatty acids, ketones, and aldehydes.<sup>[20]</sup>

Honey is also composed of glucose, protein, organic acids, minerals, and vitamins. Some of the vitamins contained in honey are thiamine (B1), riboflavin (B2), nicotinic acid (B3), pantothenic acid (B5), pyridoxine (B6), biotin. (B8 or H), folic acid (B9), and vitamin C (21). These vitamins are very good for restoring fitness, increasing appetite, and increasing endurance.<sup>[22]</sup> Giving honey to children who have fever seizures can be a non-pharmacological recovery therapy that can restore the child's good physical condition, as well as the adequate immune system.<sup>[23,24]</sup>

The combination of honey and ginger, like the traditional ingredients of the Bajo tribe of North Buton is a very good herbal blend to increase endurance and restore children who experience a fever.

## 2. Sea Water Splash Therapy

Another method of recovery that is carried out according to the traditions of the Bajo Tribe in handling child fever seizures is the seawater splash therapy. This therapy is carried out after the child's fever has decreased and the seizures have disappeared. Seawater splash therapy is carried out for one week with a frequency of 1 time a day, namely every afternoon. The way the Bajo tribe performs this therapy by removing the child's clothes, then holding both hands on the armpits, after that the child is put into the sea and held for about 5 minutes, then lifted again and the procedure is repeated 3 times.

Seawater contains chemical elements such as Chlorine (Cl) 55%, Sodium (Na) 31%, Magnesium (Mg), Calcium (Ca), Sulfur (S), and Potassium (K), Bromium (Br), Carbon (C), Strontium (Sr), Barium (Ba), Silicon (Si), and Fluorium (F) (Prastuti, 2017). The content of seawater also consists of various gases such as oxygen

(O<sub>2</sub>) and carbonic acid gas (CO<sub>2</sub>), and water has very high levels of essential minerals.<sup>[25,26]</sup>

These contents, especially essential minerals, can minimize the occurrence of damage to human muscles, thereby increasing human resistance to physical activity and restoring muscle flexibility.<sup>[25]</sup> According to the American Academy of Pediatrics, seizures in children with fever will force the muscles to contract above their capacity so that it has the potential for muscle stiffness and damage.<sup>[23]</sup> The principle of restoring and maintaining muscle flexibility by utilizing the levels of essential minerals in seawater is the right technique to correct the condition of a child's muscles after experiencing seizures during fever.<sup>[23,25]</sup> This is in accordance with the tradition of restoring child fever seizures that have been carried out by the Bajo Tribe of North Buton Regency.

## CONCLUSION

Handling of febrile seizures in children according to the tradition of the Bajo tribe is done by using herb therapy and seawater splash therapy.

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## RENAL MANIFESTATIONS OF SICKLE CELL DISEASE

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### ABSTRACT

**Background:** Patients with sickle cell disease (SCD) are at increased risk of serious morbidity and mortality. Renal abnormalities in SCD are well known but renal involvement in Syrian patients with SCD has not been studied. **Aim:** We sought to identify the renal manifestations of sickle cell anemia among patients attending Tishreen University Hospital in Lattakia. **Materials and Methods:** This descriptive observational study included 76 patients (42 males, 34 females) diagnosed with sickle cell anemia confirmed by hemoglobin electrophoresis, and followed at Tishreen University Hospital in Lattakia, during the period between 2019 - 2020. The glomerular filtration rate was estimated (eGFR) using the 'modification of diet in renal disease' (MDRD) formula. All patients underwent evaluation by urine examination to detect hematuria, and 24- hour urine collection to measure to quantitate proteinuria. We constructed a multivariate logistic regression model to assess the association between hydroxyurea and proteinuria. **Results:** The renal manifestations of sickle cell anemia were as follows: glomerular hyperfiltration (9.2%), impaired renal function (31.6%), proteinuria (39.5%), and hematuria (19.7%). Patients with impaired renal function had a greater mean age and a higher prevalence of proteinuria compared with patients with normal renal function. A statistically significant inverse linear relationship was found between age and eGFR values ( $r = -0.547$ ,  $p < 0.001$ ). The mean age of patients with proteinuria was greater compared to patients without proteinuria ( $P < 0.05$ ). Use of hydroxyurea is associated with a lower prevalence of proteinuria in patients with sickle cell anemia. The mean eGFR in patients treated with hydroxyurea was significantly greater compared to patients not treated with hydroxyurea ( $P < 0.05$ ). **Conclusion:** Renal abnormalities are present in a significant number of Syrian patients with SCD and proteinuria is the most common abnormality. Hydroxyurea use may prevent development of overt nephropathy or the progression of sickle cell disease nephropathy to end- stage renal disease.

**KEYWORDS:** Sickle cell disease, Renal manifestation, Hydroxyurea.

### INTRODUCTION

Sickle cell hemoglobinopathies are a group of genetic disorders that result from a single base pair DNA mutation in the globin gene, which leads to the formation of an abnormal hemoglobin tetramer, hemoglobin S.<sup>[1]</sup>

When the S-globin gene is inherited in a homozygous pattern (SS disease), it results in a severe disease, with profound anemia and multiple organ involvement, including cerebrovascular events, acute vaso- occlusive episodes, retinopathy, acute chest syndrome, and renal damage.<sup>[2]</sup>

The term sickle cell nephropathy encompasses all the

structural and functional abnormalities of the kidney seen in sickle cell disease (SCD).<sup>[3]</sup> It is primarily a consequence of glomerular hypertrophy and resultant focal segmental glomerulosclerosis.<sup>[4]</sup>

Chronic sickling underlies several mechanisms for end-organ damage including kidney disease. The process of kidney damage is mediated by adherence of the polymerized sickle cell hemoglobin to the erythrocyte membrane. This alters the blood rheology and leads to binding of sickle cell to the endothelium, thereby causing microvascular injury which eventually leads to vaso-occlusion and ischemia ultimately culminating in end-organ damage.<sup>[5-7]</sup>

In the kidneys this leads to worsening of medullary hypoxia and hypertonicity leading to loss of vasa recta and resulting in a defect in the concentrating capacity with consequent isosthenuria.<sup>[8]</sup> The medullary hypoxia has been found to lead to edema, focal scarring, and interstitial fibrosis resulting in tubular atrophy.<sup>[9]</sup> Interstitial fibrosis and scarring would naturally lead to progression of chronic kidney disease (CKD). Renal hemodynamics in SCD reveals increases in renal blood flow leading to hyperfiltration and glomerular hypertrophy. As the disease progresses, impairment of glomerular permselectivity develops with increased ultrafiltration coefficient, worsening glomerular hyperfiltration, and consequent proteinuria.<sup>[9,10]</sup> Prolonged glomerular hyperfiltration may cause further glomerular injury resulting in focal segmental glomerulosclerosis which is commonly seen in adults with SCD.<sup>[11,12]</sup> Further progression of the disease leads to ischemia and fibrosis with obliteration of glomeruli which would manifest as progressive renal insufficiency ultimately leading to reduced ultrafiltration capacity, renal plasma flow and resulting in end-stage renal disease.<sup>[9,13,14]</sup>

## MATERIALS AND METHODS

Adult patients with SCD followed up at the hematology and nephrology outpatient clinic, Tishreen University Hospital, Lattakia, were prospectively studied.

### Inclusion criteria included

- Age of 18 years or older
- Documented homozygous or heterozygous SCD confirmed by hemoglobin electrophoresis.

Patients with sickle cell trait, diabetes mellitus, pregnant females, patients with acute pain episodes during the two weeks prior to the assessment, suspected urinary tract infection or renal stones, and patients who refused to participate in the study were excluded.

All patients gave informed consent. A total of 76 patients with SCD were studied. All patients had blood extraction for blood urea nitrogen (BUN), serum creatinine, complete blood count (CBC), Na and K determination. The estimated glomerular filtration rate was calculated at admission using the MDRD equation.<sup>[15]</sup>

$eGFR [mL /min/1.73 m^2] = 186 \times (\text{Serum creatinine} - 1.1054) (\text{mg} / \text{dL}) \times (\text{age} - 0.203) (\text{years old}) \times 0.742$  (if woman).

In addition, all patients had 24-hour urine collection to quantify proteinuria. 24-hour urine were collected from 8 AM to 8 AM next day according to the standard protocol. Protein concentration was measured with an automatic Mindray BS-380 device via the SYRBIO® Pyrogallol method. At a temperature of 37 degrees Celsius and expressed as grams / 24 hours". Proteinuria was defined as the excretion of more than 0.150 g/24 hours.

Urine samples were collected in the morning (not

necessarily the first sample in the morning). Urine samples were tested for the presence of blood, protein, hemoglobin and other abnormalities. Hematuria was defined as the presence of 3 red cells in the field (high magnification).

According to the National Kidney Foundation recommendations,<sup>[16]</sup> patients were divided into six groups:

- Hyperfiltration (eGFR  $\geq$  140 mL /min/1.73 m<sup>2</sup>).
- Normal renal function (eGFR 90-139 mL /min/1.73 m<sup>2</sup>).
- Mild renal insufficiency (eGFR 60-89 mL /min/1.73 m<sup>2</sup>).
- Moderate renal insufficiency (eGFR 30-59 mL /min/1.73 m<sup>2</sup>).
- Severe renal insufficiency (eGFR 15-29 mL /min/1.73 m<sup>2</sup>).
- Renal failure (eGFR < 15 mL /min/1.73 m<sup>2</sup>).

Then we conducted a statistical analysis after dividing the patients into two groups:

- 1- Normal renal function: eGFR  $\geq$  90 mL/min/1.73 m<sup>2</sup>
- 2- Renal impairment: eGFR < 90 mL/min/1.73 m<sup>2</sup>

### Statistical analysis

The analysis was performed using the Statistical Package for Social Sciences (SPSS) (version 20) (IBM Corporation, Armonk, New York, USA) and Excel 2010 program. A predictive value less than 0.05 was considered statistically significant. Continuous data were expressed as minimum, maximum, median and range while categorical data were expressed as percentages. Clinical parameters were compared between groups using the Mann-Whitney U test for non-parametric data. Chi-square (X<sup>2</sup>) was used as appropriate to assess the relationship between categorical variables. In addition, Spearman's correlation was used to assess the association between variables.

## RESULTS

### Patients' characteristics

Our study included 76 sickle cell anemia patients, males were 42 patients (55.3%) and females were 34 patients (44.7%). The mean age of patients was 25  $\pm$  12.5 years in a range of 18-61 years. The largest proportion of research patients were in the 20-29 age group. The distribution of additional baseline characteristics is presented in (Table 1).



**Table 1: Demographic and clinical characteristics of patients.**

Characteristics	Number	Percent
<b>Age (years)</b>		
<20	9	11.8%
20 – 29	36	47.4%
30 – 39	19	25%
40 – 49	5	6.6%
50 – 59	5	6.6%
≥ 60	2	2.6%
<b>Gender</b>		
Male	42	55.3%
Female	34	44.7%
<b>hydroxyurea therapy</b>		
Yes	20	26.3%
No	56	73.7%

**Table 2: Hematological and biochemical indices of patients.**

Indices	Median	Range
WBC (10 <sup>9</sup> /L)	10.8	7.3 – 13.5
Hgb (g/dl)	7.5	6.7 – 8.9
Plt (10 <sup>9</sup> /L)	193	15 – 970
Serum Cr (mg/dl)	0.6	0.4 – 9.3
Urea (mg/dl)	16.8	8 – 228
eGFR (ml/m/1.73m <sup>2</sup> )	129.1	50.8 – 240
NA (mEq/L)	135	125 – 141
K (mEq/L)	4.4	3.2 – 5.2
24h urine volume (ml)	3577	1400 – 9000
24h urine protein (g/day)	0.15	0.04 – 13.4

The median and range of hematological and biochemical indices of patients is presented in (Table 2).

Table 3: Shows the distribution of kidney function according to eGFR.

**Table 3: The distribution of kidney function according to eGFR.**

eGFR (ml/m/1.73m <sup>2</sup> )	Number	Percent
≥ 140 (Hyperfiltration)	7	9.2%
139 – 90 (Normal renal function)	45	59.2%
89 – 60 (Mild renal insufficiency)	11	14.5%
59 – 30 (Moderate renal insufficiency)	6	7.9%
29 – 15 (Severe renal insufficiency)	4	5.3%
<15 (Renal failure)	3	3.9%

Median protein excretion in 24-hours for the patient cohort was abnormal (0.15 g/day, range 0.04-13.4). Proteinuria was found in 30 patients (39.5%). Majority of the patients with protein in the urine had mild proteinuria

while five patients (6.6%) had nephrotic range proteinuria (> 3 g/day). Hematuria was found in 15 patients (19.7%). Table 4 shows the renal manifestations of sickle cell anemia in study population.

**Table 4: Renal manifestations of sickle cell anemia in study population.**

Renal manifestations	Number	Percent
Proteinuria	30	39.5%
Hematuria	15	19.7%
Hyperfiltration (eGFR ≥ 140 mL/min/1.73 m <sup>2</sup> )	7	9.2%
Renal impairment (eGFR < 90 mL/min/1.73 m <sup>2</sup> )	24	31.6%

**Patients’ characteristics according to kidney function**

Table 5 shows comparison of the demographic, clinical, hematological and biochemical characteristics between patients with normal renal function (eGFR ≥ 90 mL/min/1.73 m<sup>2</sup>) and patients with renal impairment (eGFR < 90 mL/min/1.73 m<sup>2</sup>)

**Table 5: Comparison of the demographic, clinical, hematological and biochemical characteristics between patients with normal renal function and patients with renal impairment.**

Characteristics	eGFR		Test	P-value
	< 90	≥ 90		
Gender				
Male	13 (54.2%)	29 (55.8%)	0.017**	0.89
Female	11 (45.8%)	23 (44.2%)		
Age	29.7 ± 10.7	23.3 ± 13	2.116*	0.0376
Age groups				

< 20	2 (22.2%)	7 (77.8%)	0.414**	0.519
20 – 29	9 (25%)	27 (75%)	0.457**	0.499
30 – 39	5 (26.3%)	14 (73.7%)	0.325**	0.568
40 – 49	2 (40%)	3 (60%)	0.176**	0.674
50 – 59	4 (80%)	1 (20%)	5.8**	0.015
≥ 60	2 (100%)	0 (0%)	4.45**	0.034
<b>Proteinuria</b>				
Yes	14 (58.3%)	16 (30.7%)	5.222**	0.022
No	10 (41.7%)	36 (69.3%)		
<b>Hematuria</b>				
Yes	6 (25%)	9 (17.3%)	0.613**	0.433
No	18 (75%)	43 (82.7%)		
<b>Biochemical indices</b>				
WBC (109/L)	10.7 ± 3.8	11 ± 3.07	0.366*	0.714
Hgb (g/dl)	7.80 ± 2.1	7.3 ± 2.2	0.934*	0.353
Plt (109/L)	195 ± 90	210 ± 112	0.575*	0.566
Serum Cr (mg/dl)	1.9 ± 0.8	0.6 ± 0.1	11.61*	<0.0001
Urea (mg/dl)	24 ± 5.4	13.6 ± 4.1	9.27*	<0.0001
eGFR (ml/m/1.73m2)	54 ± 8	135 ± 3	64.2*	<0.0001
NA (mEq/L)	133±2.4	135.7 ± 10	1.3*	0.197
K (mEq/L)	4.7 ± 1	4.2 ± 1.2	1.77*	0.08
<b>Blood pressure</b>				
SBP	125 ± 13	124 ± 10	0.367*	0.714
DBP	67 ± 4	64 ± 10	1.414*	0.161

\* Mann-Whitney U test

\*\*Chi-square (X2) test

We studied the linear correlation between age and eGFR values (figure1), There is a significant inverse correlation between age and eGFR values, eGFR values decrease with aging (r= -0.547, P<0.001).

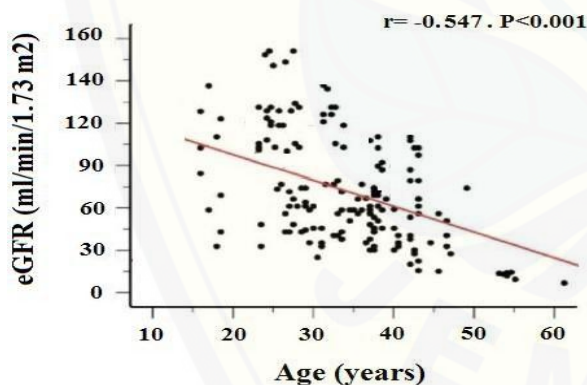


Figure 1: Correlation between eGFR and age in our study.

**Patients’ characteristics according to proteinuria**

Table 6 Shows comparison between patients with and without proteinuria.

Table 6: Comparison between patients with and without proteinuria

Characteristics	Proteinuria		Test	P-value
	Yes	No		
Age (years)	28.4 ± 11	23.5 ± 10	2.007	0.048
eGFR (ml/m/1.73m2)	98 ± 20	133.5 ± 15	8.82	<0.0001

**Patients’ characteristics according to hydroxyurea therapy**

The number of patients treated with hydroxyurea in the study was 20 patients (26.3%). Proteinuria was found in

25% of them, and in 44.6% of those not treated with hydroxyurea. Table 7 illustrates the relationship between proteinuria and eGFR and hydroxyurea therapy and in patients with sickle cell anemia in the study.

**Table 7: The Relationship between proteinuria and Egfr and hydroxyurea therapy.**

Characteristics	hydroxyurea therapy		Test	P-value
	Yes	No		
Proteinuria				
Yes	5 (25%)	25 (44.6%)	4.308**	0.037
No	15 (75%)	30 (55.4%)		
eGFR (ml/m/1.73m2)	136 ± 27	122 ± 23	2.23*	0.0287

\* Mann-Whitney U test \*\*Chi-square (X2) test

**DISCUSSION**

Sickle cell disease is one of the most common severe single-gene genetic disorder in the world. Despite simple molecular causation, sickle cell disease is a multi-organ disease with episodes of acute disease and progressive organic injury. Renal impairment in the settings of sickle cell disease includes many glomerular and tubular disorders and is associated with increased mortality if left untreated. Kidney disease begins in childhood and progresses with age. Our study was aimed to determine the renal manifestations of sickle cell anemia in patients attending Tishreen University Hospital in Lattakia. The study included 76 patients (42 males, 34 females) diagnosed with sickle cell anemia confirmed by hemoglobin electrophoresis. Patients ages ranged between 18-61 years with a mean age of 25 years. 54 patients (71%) had fewer than 3 episodes of sickle cell crises per year, 15 patients (19.5%) had 3-5 episodes per year, and 7 patients (9.2%) had more than 5 episodes per year was.

Advances in the medical care of patients with Sickle cell anemia has made it possible for this individual to live longer and as such, they are confronted with long-term complications of the condition such as chronic kidney disease.<sup>[17]</sup> Therefore, it is not surprising that the mean age of patients in our study was 25 years. Aleem et al,<sup>[18]</sup> reported a mean age of 23 years, Arogundade et al,<sup>[19]</sup> reported a mean age of 23 years, Bukar et al,<sup>[20]</sup> reported a mean age of 27 years, Drawz et al,<sup>[21]</sup> reported a mean age of 36.6 years.

The mean estimated GFR calculated according to the MDRD equation was: 129.1 ± 36 mL/min/1.73 m2. Glomerular hyperfiltration (defined as eGFR ≥ 140 mL/min/1.73 m2) was found in 7 patients (9.2%), and renal impairment (defined as eGFR < 90 mL/min/1.73 m2) in 24 patients (31.6%). Proteinuria was found in 39.5% of patients, and hematuria in 19.7%.

Bhaskar et al,<sup>[22]</sup> found a hyperfiltration rate of 9.9%. Bukar et al,<sup>[20]</sup> found a hyperfiltration rate of 26.8%. In the study by Ephraim et al,<sup>[23]</sup> hyperfiltration rate was 68.4% in children and 31.2% in adults.

Glomerular changes in SCD occur early in the first decade of life even though SCD patients remain asymptomatic. These are characterized by high renal blood flow, hyperfiltration and hypertrophy. Current data suggest that infants with SCD develop a hyperfiltration phase, which

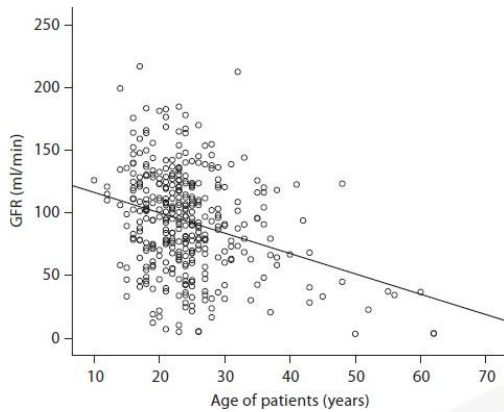
plateaus during early childhood. As early as the first year, renal enlargement is observed in correlation to hyperfiltration. Hyperfiltration is a well-known phenomenon in SCD even though the pathogenesis and pathophysiology is less well understood. As a result of hyperperfusion, increased amount of fluids is presented to the proximal tubule triggering more tubular reabsorption of sodium and water in order to restore glomerulotubular balance. Increased proximal tubular sodium reabsorption is associated with high metabolism and adaptive cellular response leading to overall renal enlargement. This complex phenomenon might be relevant to the glomerular hypertrophy that occurs in SCD.<sup>[24]</sup>

Our study demonstrated that 24 patients (31.6%) had renal impairment (defined as eGFR < 90 mL/min/1.73 m2). Renal impairment rates in previous studies was 38.9% (Bukar et al),<sup>[20]</sup> 20.6% (Bhaskar et al),<sup>[22]</sup> 55.2% (Guasch et al),<sup>[25]</sup> 31.6% in children and 68.4% in adults (Ephraim et al).<sup>[23]</sup>

When the factors associated with impaired renal function were studied, no significant difference was found according to gender (P=0.89). Patients with renal impairment were older compared to patients with normal renal function (P= 0.0376). When studying the correlation between age and eGFR values, a statistically significant inverse correlation was found (r= -0.547, p <0.001). Patients with renal impairment had more proteinuria (58.3%) compared to patients with normal renal function (30.7%) (P=0.022). Hematuria was present in 25% of patients with renal impairment and in 17.3% of patients with normal renal function, the difference was not statistically significant (P> 0.05). Patients with renal impairment had a significantly higher concentrations of serum creatinine and urea and a significantly lower rate of glomerular filtration. No significant differences in the mean systolic or diastolic pressure was found between the two groups.

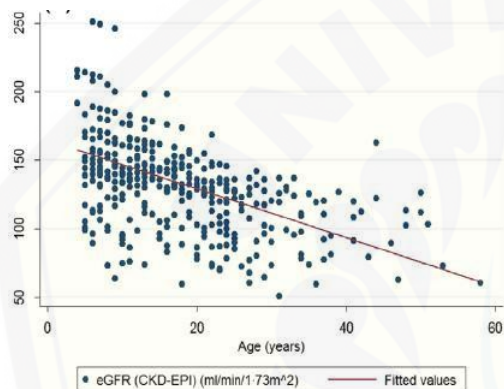
Our results are consistent with the study of Arogundade et al.<sup>[19]</sup> which showed that eGFR decreases with age, with a linear correlation (r = -0.245, P <0.001) (Figure 2).





**Figure 2: Correlation between eGFR and age (Arogundade et al).<sup>[19]</sup>**

Geard et al.<sup>[26]</sup> also showed that eGFR decreases with age with a linear correlation ( $r = -0.55, P < 0.001$ ) Figure (3).



**Figure 3: Correlation between eGFR and age (Geard et al).<sup>[26]</sup>**

Proteinuria was found in 39.5% of the patients in our study. The mean age of patients with proteinuria was greater than patients without proteinuria ( $P = 0.048$ ). Patients with proteinuria had a significantly lower eGFR compared to patients without proteinuria ( $P < 0.0001$ ).

Proteinuria is more sensitive than elevated serum creatinine as a marker for detecting glomerular injury, and it has been reported as an early manifestation of sickle-cell nephropathy. In our study, proteinuria was found in 30.7% of patients with normal renal function, and in 58.3% of patients with renal impairment. Aleem et al.<sup>[18]</sup> reported that proteinuria was found in 41% of patients with sickle cell anemia. Guasch et al.<sup>[25]</sup> found that proteinuria was present in 37.1% of patients. It is known that proteinuria in sickle cell anemia is age dependent. The prevalence of proteinuria in the first three decades of life is up to 27% increasing to 68% in older SCD patients.<sup>[27]</sup>

Hematuria was found in 19.7% of the patients in our study. Some studies reported higher prevalence rates, Bukar et al.<sup>[20]</sup> reported the prevalence of hematuria in 33.1%. Aleem et al.<sup>[18]</sup> found that hematuria was present in 8.5% of patients. Haematuria is among the most common renal manifestations of SCD, and can present as

microscopic or macroscopic haematuria; the latter can be lifethreatening.<sup>[28]</sup> Haematuria reflects capillary congestion, especially in the medullary vessels, with extravasation of RBCs into the tubular lumen. Congestion and rupture of the submucosal capillaries in the renal pelvis can also be responsible for haematuria, these vessels branch from the efferent arterioles of the juxtamedullary nephrons, from which the vasa recta also arise. Blockage of the vasa recta can divert blood flow to capillaries that supply the mucosa of the renal pelvis and to the peritubular capillaries of the juxtamedullary nephrons. Haematuria emanates more frequently from the left kidney than the right because of the so-called nutcracker phenomenon imposed upon the left renal vein as it passes between the aorta and the superior mesenteric artery, this phenomenon leads to compression of the vein.

In our study, treatment with hydroxyurea was associated with a lower prevalence of proteinuria. The mean eGFR in patients treated with hydroxyurea was significantly greater compared to patients not treated ( $P = 0.0287$ ). Laurin et al.<sup>[29]</sup> showed that the use of hydroxyurea was associated with a lower prevalence of albuminuria (34.7% vs 55.4%). The use of hydroxyurea was also associated with a higher eGFR (151 versus 128 ml/min/1.73 m<sup>2</sup>). In another study Geraldo B. Silva Junior et al.<sup>[30]</sup> showed that the use of hydroxyurea was associated with a lower prevalence of proteinuria, but no significant difference was found in eGFR between hydroxyurea treated and untreated patients (112 versus 105 ml/min/1.73 m<sup>2</sup>) ( $p = 0.504$ ).

**CONCLUSIONS**

1. The most common renal manifestations of sickle cell anemia are: Glomerular hyperfiltration (9.2%), impaired renal function (31.6%), proteinuria (39.5%), and hematuria (19.7%)
2. Patients with renal impairment are older than patients with normal renal function. There is a significant inverse correlation between age and eGFR ( $r = -0.547, p < 0.001$ ).
3. The prevalence of proteinuria among patients with impaired renal function (58.3%) is significantly higher compared to patients with normal renal function (30.7%) ( $P = 0.022$ ).
4. The mean age of patients with proteinuria was greater than patients without proteinuria ( $P = 0.048$ ). Patients with proteinuria had a significantly lower eGFR compared to patients without proteinuria.
5. Treatment with hydroxyurea was associated with a lower prevalence of proteinuria. The mean eGFR in patients treated with hydroxyurea was significantly greater compared to patients not treated.

**Recommendations**

1. Renal complications associated with sickle cell anemia are common and progressive. Therefore, we emphasize the recommendations regarding periodic follow-up for patients.
2. Conducting more studies on the factors predicting the

development of these complications by following-up the patients for long periods of time.

3. Conducting more studies on the effect of drug interactions on the progression of sickle cell nephropathy.
4. Hydroxyurea is recommended to relieve kidney disease.

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## DEVELOPMENT AND VALIDATION OF STABILITY INDICATING RP-HPLC METHOD FOR THE SIMULTANEOUS ESTIMATION OF DAUNORUBICIN AND CYTARABINE IN BULK AND PHARMACEUTICAL DOSAGE FORMS

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### ABSTRACT

This present work describes a new validated Reverse Phase High Performance Liquid Chromatography (HPLC) method for the simultaneous determination of anti-cancer drugs, Daunorubicin and Cytarabine. A simultaneous determination method saves cost and time as both drugs can be injected into a single HPLC system without the need to change or re-equilibrate with a new mobile phase. The objective of the study is to develop a simultaneous estimation of two anti-cancer drugs in Pharmaceutical Dosage forms. The mobile phase consists of a mixture (50:50 v/v) of 0.1% Octane sulphonic acid: acetonitrile at a flow rate of 1 ml/min, with a PDA detector at 238 nm. Separation was achieved on a Xbridge C18 (150 x 4.6mm) maintained at 30°C temperature in a column oven. The method was linear between 22µg/ml – 110µg/ml for Daunorubicin and 50µg/ml - 250µg/ml for Cytarabine. The limit of detection was 2.98µg/ml for Daunorubicin, and 3.00µg/ml for Cytarabine and the limit of quantification was 10.00µg/mL for Daunorubicin and 9.98µg/mL for Cytarabine. The developed RP-HPLC method achieved good precision and accuracy. The developed and validated method was suitable to be used for routine analysis of Daunorubicin and Cytarabine.

**KEYWORDS:** Daunorubicin, Cytarabine, RP-HPLC, ICH-guidelines, Method development and Validation.

### INTRODUCTION

Daunorubicin is also known as Daunomycin, is a chemotherapy medication used to treat cancer (Fig.1). Specifically, it is used for acute myeloid leukemia (AML), acute lymphocytic leukemia (ALL), chronic myelogenous leukemia (CML), and Kaposi's sarcoma. It is used by injection into a vein. Cytarabine (cytosine arabinoside, 1-b-D-arabinofuranosyl cytosine, ara-C) is a pyrimidine nucleoside analog which is predominantly used against acute myelogenous leukemia and non-Hodgkin's lymphoma (Fig. 2).

Daunorubicin and Cytarabine (I.V injection) is a liposomal combination of that is FDA approved for the treatment of adults with newly-diagnosed therapy-related acute myeloid leukemia (t-AML) or AML with myelodysplasia-related changes (AML-MRC).<sup>[1-3]</sup>

Daunorubicin interacts with DNA by intercalation and inhibition of macromolecular biosynthesis. This inhibits

the progression of the enzyme topoisomerase II, which relaxes supercoils in DNA for transcription. Daunorubicin stabilizes the topoisomerase II complex after it has broken the DNA chain for replication, preventing the DNA double helix from being resealed and thereby stopping the process of replication. Cytarabine is a cell cycle phase-specific anti-neoplastic agent, affecting cells only during the S-phase of cell division. Cytarabine acts primarily through inhibition of DNA polymerase.

Literature review reveals estimation of by RP-HPLC.<sup>[4-6]</sup> and by Spectroscopy method,<sup>[7]</sup> individually. In combination, Daunorubicin and Cytarabine only one method was published,<sup>[8]</sup> but yet there is a need to develop new stability indicating RP-HPLC method with more sensitivity, accuracy and precision.

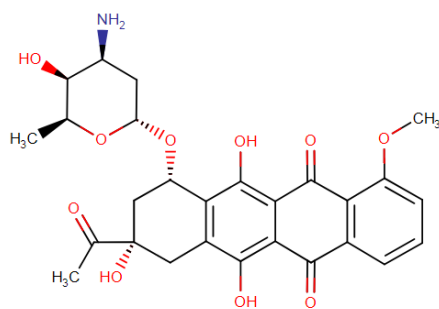


Fig. 1: structure of daunorubicin

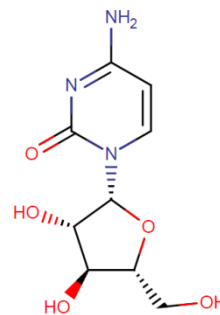


Fig. 2: Structure of cytarabine

## MATERIALS AND METHODS

**Chemicals and Reagents:** Both Daunorubicin and Cytarabine (API) were obtained as a gift sample from Pharmatrain Pvt. Ltd., Hyderabad, India. The marketed formulation in the brand name Vyoxeos (Dauno-29 mg & Cyta-65 mg) procured from the local pharmacy. All the chemicals and reagents used in this work were HPLC grade water, acetonitrile, methanol, potassium dihydrogen orthophosphate buffer, orthophosphoric acid was obtained from Merck.

**Instrumentation:** A HPLC system with waters 2695 separation module provided with an UV detector, autosampler injection with Empower-2 software. Electronic balance, ultrasonicator, hot air oven and pH meter were used.

**Chromatographic Conditions:** The chromatographic separations achieved on a Xbridge C18 column (150 × 4.6 mm, 5 μm particle size) as a stationary phase. The mobile phase was composed of 50:50 v/v of 0.1% Octane sulphonic acid pH 3 and acetonitrile at a flow rate of 1.0 ml/min and injection volume is 20 μl. The column oven temperature was maintained at 30 °C, and the drugs were detected at 238 nm.

### Preparation of 0.1% Octane sulphonic acid

Transferred about 1gm of Octane sulphonic acid into 1000 ml of HPLC water and pH was adjusted up to 3.0. Final solution was filtered through 0.44 μm whatmann membrane filter and sonicated it for 10 mins.

### Preparation of mobile phase

Transferred 500 ml (50%) of above buffer and 500 ml (50%) of HPLC grade Acetonitrile were mixed and degassed in an ultrasonic water bath for 10 minutes and then filtered through 0.45 μ filter under vacuum filtration.

### Diluent Preparation

The Mobile phase was used as a diluent.

### Mixed Standard Solution

Accurately weighed quantity of 100 mg of Cytarabine and 44 mg of Daunorubicin working standard were transferred into a 100 ml clean dry volumetric flask, sufficient amount of solvent was added and sonicated to

dissolve it completely and made volume up to the mark with the same solvent. (Stock solution). Further pipetted out 1.5 ml of the above stock solutions into a 10ml volumetric flask and diluted up to the mark with diluent.

### Sample Solution

Accurately weighed powder equivalent to 100 mg of Cytarabine and 44 mg Daunorubicin sample was transferred into a 100 ml clean dry volumetric flask dissolved with diluent and sonicated and made volume up to the mark with the same solvent. Then it is filtered through 0.45-micron injection filter. Further pipette out 1.5ml and dilute to 100 ml with same solvent.

### Procedure

20 μl of the standard, sample were injected into the chromatographic system and measured the areas for Cytarabine and Daunorubicin peaks and calculate the % assay by using the formulae.

**Validation of the RP-HPLC Method:** The proposed RP-HPLC method was validated as per ICH guidelines.<sup>[9-12]</sup>

**System Suitability Parameters:** The system suitability parameters were determined by preparing standard solutions of Daunorubicin (50 μg/mL) and Cytarabine (22 μg/mL), and the solutions were injected six times and the parameters like retention time, peak tailing, resolution and USP plate count were determined.

**Specificity:** As per ICH guidelines "Specificity" can be defined as the ability of the method to specifically separate the particular API or analyte in the presence of other components.

**Linearity:** The stock solution of Daunorubicin and Cytarabine was prepared by using diluent. From that, various working standard solutions were prepared in the range of 22μg/ml to 110μg/ml, 50μg/ml to 250μg/ml and injected into the HPLC system. The calibration plot (peak area vs. concentration) was generated by replicate analysis (n=5) at all concentration levels. The linear relationship was evaluated using the least square method within Microsoft excel program.

**Accuracy:** The accuracy method was carried out using one set of different standard addition methods at different concentration levels 50%, 100% and 150% and then comparing the theoretical value and found value.

**Precision:** The precision of the method was ascertained from the peak area obtained by actual determination of six replicates of a fixed amount of the drug (50 µg/mL Daunorubicine, 22 µg/mL Cytarabine). The precision of the assay also determined in terms of intraday and interday variation in the peak area of a set of drug solutions on three different days. The peak area of a set of drug solutions was calculated in terms of relative standard deviation (RSD).

**Detection Limit and Quantification Limit:** Detection limit and quantification limit established based on the calibration curve parameters, according to the following formulas.

LOD = 3.3 SD/slope and LOQ = 10 SD/slope

or

Detection limit =  $3.3\sigma/s$ , Quantification limit =  $10\sigma/s$ ,

Where  $\sigma$  is the standard deviation of Y-intercept of the regression line and S is the slope of the curve.

**Robustness:** The Robustness of the proposed method carried out by small but deliberate changes in method parameters such as flow rate ( $\pm 0.1$ ), column temperature ( $\pm 5$ ), mobile phase ratio ( $\pm 5\%$ ). The percentage recovery and RSD of peak area were evaluated.

**Forced Degradation Tests:** The stability indicating of the method can be demonstrated by applying stress conditions.<sup>[13,14]</sup> using acid, alkaline, peroxide, thermal, UV, water degradations. The sample was exposed to these conditions the main peak of the both drugs were studied for peak purity, that indicating the method effectively separated the degradation products from the pure active ingredient.

**Acid Degradation Studies:** To 1 ml of Daunorubicin and Cytarabine stock, 1 ml of 2N HCl was added and refluxed for 30 min at 60 °C. The resultant solution was neutralized with 1 ml 2N NaOH and made up to final volume to obtain (50 µg/mL and 22 µg/mL) solution. Cool the solution to room temperature and filtered with 0.22 µm membrane filter. A sample of 10 µl was injected into the HPLC system, and the chromatograms were recorded to assess the stability of the sample.

**Alkali Degradation Studies:** To 1 ml of stock solution of Daunorubicin and Cytarabine 1 ml of 2N sodium hydroxide was added and refluxed for 30 min at 60 °C. The resultant solution was neutralized with 1 ml 2N HCl and made up to final volume to obtain (50 µg/mL and 22 µg/mL) solution. Cool the solution to room temperature and filtered with 0.22 µm membrane filter. The sample of 10 µl was injected into the system, and the

chromatograms were recorded to an assessment of sample stability.

**Peroxide Degradation Studies:** To 1 ml of stock solution of Daunorubicin and Cytarabine 1 ml of 20% hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) was added separately. The solution was kept for 30 min at 60°C.

For HPLC study, the resultant solution was diluted to obtain (50 µg/mL and 22 µg/mL) solution. Cool the solution to room temperature and filtered with 0.22 µm membrane filter. A sample of 10 µl solution was injected into the system, and the chromatograms were recorded to assess the stability of the sample.

**Thermal Degradation Studies:** The 1 ml of standard drug solution was placed in the oven at 105 °C for 6 h to study dry heat degradation. For HPLC study, the resultant solution was made up to final volume to obtain (50 µg/mL and 22 µg/mL) solution.

Cool the solution to room temperature and filtered through a 0.22 µm membrane filter. A sample of 10 µl solution was injected into the system, and the chromatograms were recorded for the assessment of sample stability.

**Photo Degradation Studies:** The photostability of the drug was studied by exposing the stock solution to UV light for 7 days or 200 Watt-hours/m<sup>2</sup> in photostability chamber. For HPLC study, the resultant solution was diluted to obtain (50 µg/mL and 22 µg/mL) solution and filtered with 0.22 µm membrane filter. A sample of 10 µl solution was injected into the system, and the chromatograms were recorded for the assessment of sample stability.

## RESULTS AND DISCUSSION

Method validation was performed according to ICH Q2 guidelines. In the blank chromatogram, there were no peaks observed at the retention times of Daunorubicine and Cytarabine.

**System Suitability:** System suitability was performed to evaluate the parameters like tailing factor, theoretical plates, resolution and % RSD for replicate injections. The results were within limits and were given in Table 1 and shown in Fig. 3.

**Specificity:** Retention times of Daunorubicin and Cytarabine were 4.144 min and 2.461 min for standard and 4.144 min and 2.461 min for sample respectively. Which were shown in Fig. 4, 5, 6.

We did not find any interfering peaks in blank at retention times of these drugs in this method. So, this method was said to be specific.



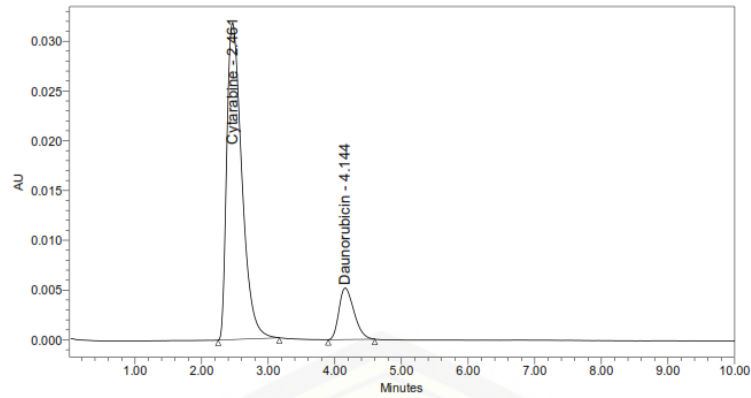


Figure 3: Chromatogram for system suitability.

Table 1: Results of system suitability parameters.

S. No.	Name	RT (min)	Area ( $\mu V$ )	Height ( $\mu V$ )	USP resolution	USP tailing	USP plate count
1	Cytarabine	2.461	494276	32593		1.40	5397.09
2	Daunorubicin	4.144	76298	5263	4.09	1.32	6776.27

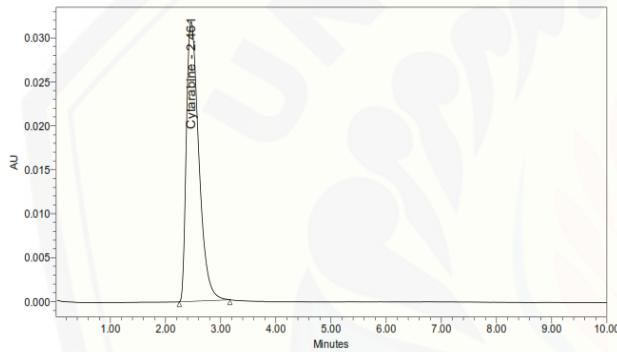


Figure 4: Chromatogram for Cytarabine.

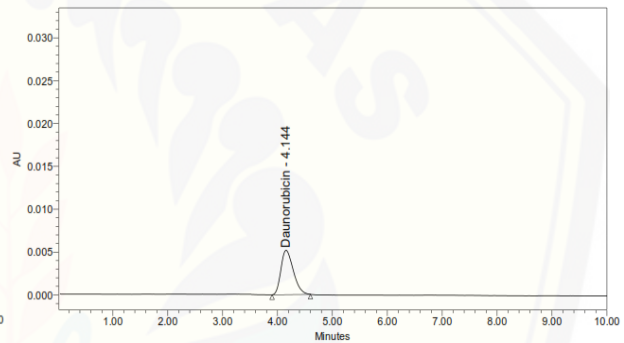


Figure 5: Chromatogram for Daunorubicin.

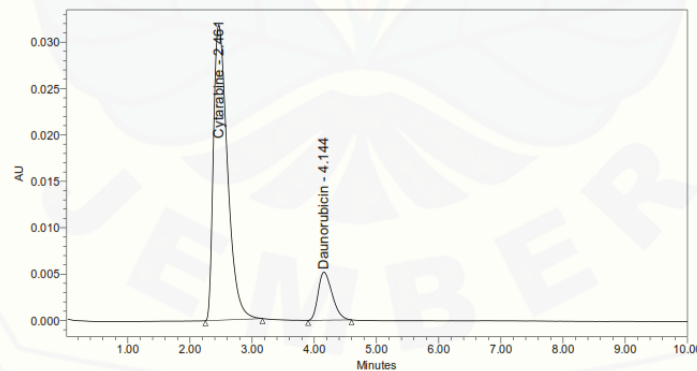


Figure 6: Chromatogram for Cytarabine and Daunorubicin.

**Linearity:** The linearity of the measurement was evaluated by analyzing different concentrations (50% to 250%) of the standard solutions of Daunorubicin and Cytarabine. The calibration curve was constructed by plotting concentration against mean peak area, and the regression equation was computed. The coefficient of correlation ( $R^2$ ) for Daunorubicin and Cytarabine were 0.999. The summary of the parameters is given in Table 2 and shown in Fig. 7, 8.

Table 2: Area of different concentration of Cytarabine and Daunorubicin.

S. No.	Cytarabine		Daunorubicin	
	Concentration (µg/ml)	Area	Concentration (µg/ml)	Area
1	50	167253	22	26286
2	100	331583	44	51274
3	150	489537	66	76528
4	200	663425	88	104363
5	250	830462	110	130287

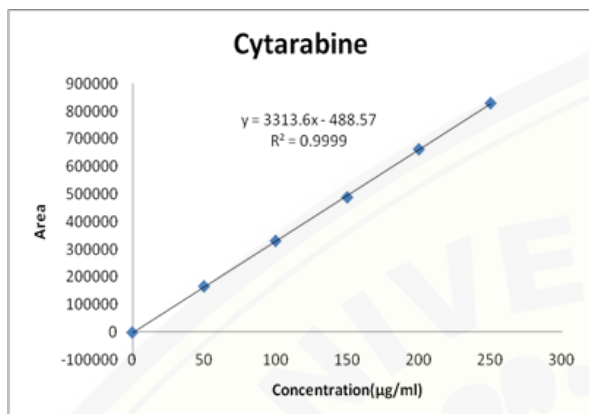


Figure 7: Calibration graph for Cytarabine.

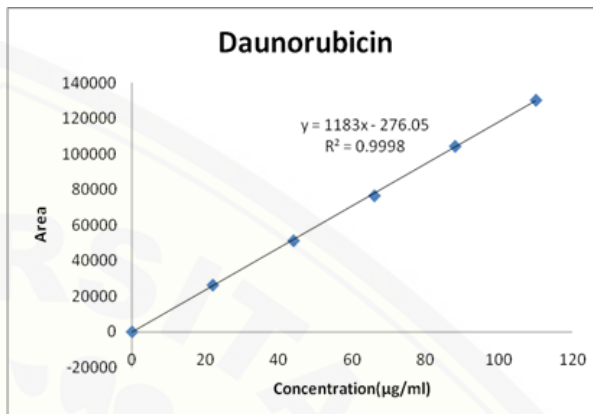


Figure 8: Calibration graph for Daunorubicin.

**Accuracy:** To determine the accuracy of the proposed method, recovery studies were conducted at three different levels, 50, 100 and 150% and were calculated.

Accuracy was calculated as the percentage of recovery, and the results were shown in Table 3,4.

Table 3: Accuracy (recovery) data for Cytarabine.

%Concentration (at specification Level)	Area	Concentration of pre analysed sample (µg)	Amount Added (µg)	Amount Found (µg)	% Recovery	Mean Recovery
50%	248273.7	100	50	50.13	100.25	100.42
100%	497256.3	100	100	100.40	100.40	
150%	747586.3	100	150	150.94	100.63	

Table 4: Accuracy (recovery) data for Daunorubicin.

% Concentration (at specification Level)	Concentration of pre analysed sample (µg)	Area	Amount Added (µg)	Amount Found (µg)	% Recovery	Mean Recovery
50%	44	38450.7	22	22.16	100.74	100.55
100%	44	76713.3	44	44.11	100.26	
150%	44	115511.0	66	66.42	100.64	

**Precision:** Precision was carried out in terms of system precision, repeatability, and intermediate accuracy. These are assessed by using six replicates at a concentration of 50 µg/mL of Daunorubicin and 22

µg/mL of Cytarabine. The data was given in Table 5 & 6. The % RSD was found to be <2, indicating the repeatability of the method is good.

Table 5: Results of Precision for Cytarabine & Daunorubicin.

Injection	Peak Area for Cytarabine	Peak Area for Daunorubicin
Injection-1	493762	76493
Injection-2	496733	76325
Injection-3	495728	76408
Injection-4	497362	76384
Injection-5	497582	76354
Injection-6	497526	76423

Average	496448.8	76397.8
Standard Deviation	1489.8	58.7
%RSD	0.3	0.1

**Table 6: Results of Intermediate precision for Cytarabine and Daunorubicin.**

Injection	Peak Area for Cytarabine	Peak Area for Daunorubicin
Injection-1	497387	76345
Injection-2	496638	76487
Injection-3	497243	76847
Injection-4	496739	76534
Injection-5	498863	76948
Injection-6	493647	76354
Average	496752.8	76585.8
Standard Deviation	1717.8	254.4
%RSD	0.3	0.3

**LOD and LOQ:** Estimation of the limit of detection (LOD) and limit of quantification (LOQ) considered the acceptable signal-to-noise ratios 3: 1 and 10: 1, respectively. LOD and LOQ of Daunorubicin and

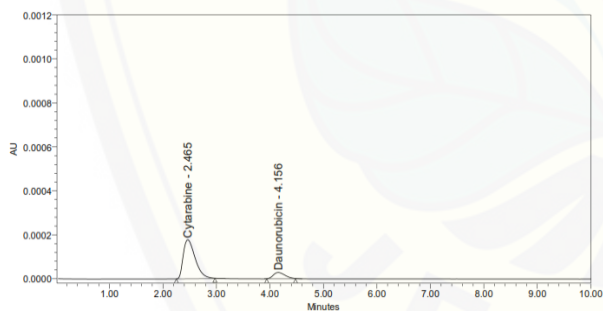
Cytarabine were determined 2.465µg/mL, 4.156µg/mL and 2.461 µg/mL, 4.144 µg/mL respectively. Which were given in Table 7, 8 and shown in Fig. 9 and 10.

**Table 7: Results of LOD.**

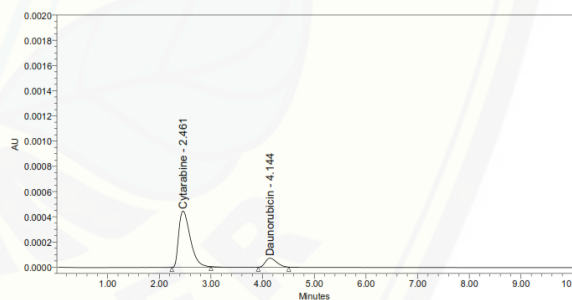
Drug name	Baseline noise (µV)	Signal obtained (µV)	S/N ratio
Cytarabine	58	174	3.00
Daunorubicin	58	173	2.98

**Table 8: Results of LOQ.**

Drug name	Baseline noise (µV)	Signal obtained (µV)	S/N ratio
Cytarabine	58	579	9.98
Daunorubicin	58	578	10.00



**Figure 9: Chromatogram showing LOD.**



**Figure 10: Chromatogram of showing LOQ.**

**Robustness:** The robustness of the method was evaluated by the method conditions such as, flow rate (± 0.1) and the column temperature (±5 °C), solvent composition (± 5%) were altered, and the influence of

these changes on the assay, peak tailing, number of theoretical plates and peak area were evaluated. The % RSD of peak areas was found to be well within the limit of 2.0%, and results were shown in Table 9-12.

**Table 9: Results for variation in flow for Cytarabine.**

S. No	Flow Rate (ml/min)	System Suitability Results	
		USP Tailing	USP Plate Count
1	0.9	1.40	5286.39
2	1.0	1.40	5397.09
3	1.1	1.40	5354.87



**Table 10: Results for variation in flow for Daunorubicin.**

S. No	Flow Rate (ml/min)	System Suitability Results		
		USP Resolution	USP Tailing	USP Plate Count
1	0.9	4.21	1.34	6687.39
2	1.0	4.09	1.32	6776.27
3	1.1	3.98	1.32	6753.29

**Table 11: Results for variation in mobile phase composition for Cytarabine.**

S. No	Change in Organic Composition in the Mobile Phase	System Suitability Results	
		USP Tailing	USP Plate Count
1	10% less	1.40	5487.33
2	*Actual	1.40	5397.09
3	10% more	1.40	5398.49

**Table 12: Results for variation in mobile phase composition for Daunorubicin.**

S. No	Change in Organic Composition in the Mobile Phase	System Suitability Results		
		USP Resolution	USP Tailing	USP Plate Count
1	10% less	4.18	1.32	6573.97
2	*Actual	4.09	1.32	6776.27
3	10% more	3.91	1.31	6877.56

**Table 13: Results of Assay for Cytarabine and Daunorubicin.**

	Label Claim (mg)	% Assay
Cytarabine	100	100.48
Daunorubicin	44	100.76

**Degradation Studies:** Since no interference of blank and degradants, the HPLC results showed that the three active ingredients Daunorubicin and Cytarabine purity angle was less than the purity threshold and hence the proposed method was the specific and revealed its stability-indicating power. The results were summarized in Table 14.

The drug Daunorubicin and Cytarabine were found to be more degraded when exposed to peroxide and acidic conditions and least degraded when exposed to necessary, thermal and photolysis degradation.

**Table 14: Results for Stability of Cytarabine and Daunorubicin.**

Sample Name	Cytarabine		Daunorubicin	
	Area	% Degraded	Area	% Degraded
Standard	494304		76362.7	
Acid	486373	1.60	73452	3.81
Base	473456	4.22	73173	4.18
Peroxide	478476	3.20	72794	4.67
Thermal	471874	4.54	72364	5.24
Photo	476773	3.55	73956	3.15

## CONCLUSION

A simple, specific and reliable reverse phase HPLC method was developed for the estimation of Daunorubicin and Cytarabine in their pharmaceutical dosage form. The method was validated over a concentration range 7.25 µg/mL and 50.0 µg/mL for Daunorubicin and 8.2 µg/mL and 66 µg/mL for Cytarabine. The two compounds were subjected to forced degradation applying several stress conditions. The proposed method successfully separated the two compounds with degradants. The proposed method was specific and stability-indicating. Hence the developed

method can be adapted to regular quality control analysis.

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## EVALUATION OF ANTI-OBESITY PROPERTIES OF AYURVEDIC INTERVENTION VACHA KUTAKI YOGA- “AN OBSERVATIONAL STUDY”

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### ABSTRACT

Obesity has become an increasing global health problem among all socio-economic groups and leading to various complications like diabetes, cardio vascular diseases and osteoarthritis knee which are responsible for morbidity & mortality. Ayurvedic approach to pathogenesis of *medoroga* or *sthaulya* can provide solution in managing rising cases of obesity among population by using various preparations. *Vacha kutaki yoga* is one of such Ayurvedic preparations. An observational study was design with the aim to assess the clinical efficacy and safety of *Vacha kutaki yoga* in the management of obesity through clinical symptoms, Body Mass Index (BMI), measurement of abdomen, chest, thigh, arm circumference and laboratory investigation on 100 patients of obesity (*medoroga* or *sthaulya*). *Vacha kutaki yoga* 1 gm (two capsules of 500 mg) thrice daily with lukewarm water for 12 weeks were used in all study participants. Clinical symptoms, BMI and circumference of body parts reduced significantly from baseline to the end of the treatment in completed 84 subjects aged between 12-60 years of both sexes. This study demonstrated the effectiveness of *Vacha kutaki yoga* in the management of obesity (*medoroga* or *sthaulya*).

**KEYWORDS:** Ayurvedic medicine, *Acorus calamus*, *Medoroga*, Obesity, *Picrorrhiza kurroo*.

### INTRODUCTION

Obesity is spreading globally; it is not limited to developed countries. It has emerged worldwide health problem in all socio-economic society. It is a harmful condition in which excess body fat has accumulated to an extent resulting a negative effect on health.<sup>[1]</sup> World Health Organization (WHO) had alarmed and reported that 13% of the world's adult population (11% of men and 15% of women) were obese in 2016. It is estimated 40 million children under the age of 5 years were overweight or obese up to 2018. It is an epidemic condition in United States and some European countries. Numerous studies clearly showed an increase in mortality rate associated with Body Mass Index (BMI) of at least 30 kg/m<sup>2</sup>. Individual with a BMI of at least 30 kg/m<sup>2</sup> have a 50-100% increased risk compared with individuals with BMI 20-25 kg/m<sup>2</sup>, due to Cardio vascular disease. Raised BMI is a major risk factor for non-communicable diseases such as cardiovascular diseases, which were the leading cause of death in 2012, diabetes mellitus, osteoarthritis, some cancers. Childhood obesity is associated with a higher chance of

obesity, premature death and disability in adulthood but in addition to increased future risks, breathing difficulties, increased risk of fractures, hypertension, and early markers of cardiovascular disease (CVD), insulin resistance and psychological effects in obese children.<sup>[2]</sup> In 1997, The WHO expert consultation on obesity warned of an escalating epidemic of obesity that would put the populations of most countries at risk of developing non-communicable diseases (NCDs).<sup>[3]</sup> Basically, obesity and the risk of associated diseases to be associated with life style, changes in dietary pattern, physical activity levels, malfunctioning of the thyroid, suprarenal, pituitary and testis. Excess intake of high calorific diets are the major auxiliary causes. In Ayurveda, *Acharya charak* has classified the drugs capable of removing fat under the group *Lekhaniya mahakashaya*. These drugs have been attributed the properties of correcting the malfunctioning of the glands in the modern sense as well as playing a substantial role in the cure of obesity due to auxiliary causes.<sup>[4]</sup> Present work was conducted on *Vacha kutaki yoga*, a combination of two medicinal plants, *Vacha* (*Acorus calamus* Linn.) and *Kutaki* (*Picrorrhiza kuroo* Royle ex



Benth.) having antiobesity properties as mentioned in Ayurvedic classical texts.<sup>[5]</sup> Although some studies resulted in initial weight loss but most of the obese patients eventually regained their weight and therefore an effective means to sustain weight loss is still a major challenge, therefore, a study was conducted by selected formulation *Vacha kutaki* which reported having antiobesity activity by using *dipana* (enhancing metabolic fire), *pachan* (enhancing digestion) and *lekhan* (therapeutic scrapping) properties.

## MATERIALS AND METHODS

This is an observational study based on day to day clinical practice on 100 patients of age 12-60 years with complaints of *Kshudha vriddhi*, *Trishna vriddhi*, *Atinidra*, *Swedadhikya*, *Daurgandhya*, *Aalasaya*, *Angamarda*, *Kshudraswasa*, *Gaurav*, *Daurbalya*, *Sandhisula*, *Sarvangshoola*; raised abdomen, arm, thigh, chest circumference etc. the study was conducted at outpatient department of Central Ayurveda Research Institute, Mumbai in accordance with Schedule Y of Drugs and Cosmetics Act, India and Indian Council of Medical Research (ICMR) ethical guidelines for biomedical research on human participants, adopted from World Medical Association (WMA)-Declaration of Helsinki.

### Trial interventions

*Vacha kutaki yoga* {Combination of equal quantity of *Vacha* (*Acorus calamus* Linn.) and *Kutaki* (*Picrorrhiza kuroo* Royle ex Benth.)} 1 gm (two capsules of 500 mg) thrice daily with lukewarm water were given to the participants for a period of twelve weeks. The trial drug was manufactured by a Good manufacturing practice certified company.

### Inclusion criteria

Subjects of either sex, age between 12-60 years, having symptoms of obesity (*medoroga* or *sthaulya*) and those who are not taking any oral conventional drug were willing able to participate in the study for 12 weeks were included in the study.

### Exclusion criteria

The subjects suffering from the complications of obesity like Diabetes, hypopituitarism, muscular hypertrophy, Cushing syndrome and other endocrinology disorders, past history of atrial fibrillation, acute coronary syndrome, myocardial infarction, stroke or severe arrhythmia in the last six months. Further, uncontrolled hypertension ( $\geq 160/100$  mm of Hg), prolonged ( $\geq 6$  weeks) medication with corticosteroids, antidepressants, anticholinergics, severe renal or hepatic disorders, pregnant and lactating woman were also excluded from the study.

### Withdrawal criteria

The subjects were free to withdrawn from the trial at any time without the permission of investigator or any reason. Further, the investigator could discontinue the

subject if he / she develop any adverse effect or there is non-compliance of the treatment regimen (minimum eighty percentage compliance was essential to continue in the study). In these cases, the actions were taken to know the reason for the withdrawal and recorded in the case report form.

### Outcomes

Primary outcome measure of study was to evaluate efficacy of Ayurvedic formulation *Vacha kutaki yoga* in the subjects suffering from Obesity (*medoroga* or *sthaulya*) by assessing changes in BMI. The secondary outcome measures were to evaluate the changes in obesity symptoms score, raised abdominal, arm, thigh, chest circumference and pathological investigations like serum cholesterol and serum triglycerides.

### Study procedures

On screening visit, subject's voluntary written informed consent was taken. General and systemic examinations as well as bio-chemical investigation, clinical assessment as per obesity symptoms using the subject's answers were graded on a quantitative scale (0=none, 1=mild, 2=moderate, 3=severe and 4=extreme) were assessed and then he/she was registered for the trial. Total 100 subjects who fulfilled the inclusion and exclusion criteria were enrolled in the study. All enrolled subjects *Vacha kutaki* powder 1 gm (two capsules of 500 mg) thrice daily with lukewarm water for 12 weeks were used in the study. Recruited subjects were advised to carry on their daily activities and exercises that they had been doing before the enrollment and also advised to continue the same till the end of study period. Obesity clinical symptoms were assessed using the subject's answers were graded on a quantitative scale (0=none, 1=mild, 2=moderate, 3=severe and 4=extreme) at baseline and end of the 84<sup>th</sup> day. Safety laboratory assessments were also done at end of the intervention period. Patients compliance was monitored by keeping a regular follow up of the patients by personal contact, telephonic communication. Subjects were advised to return empty containers of trial medicines on every follow-up visit in order to check the drug compliance. Subjects visited for follow-up visits on day 14, day 28, day 42, day 56, day 70, and day 84. On each follow-up visit, patient's general and systemic physical examination was done. Assessment of the clinical symptoms of obesity by using VAS score. Pathological investigations such as serum cholesterol and serum triglycerides were performed at baseline and at the end of 84<sup>th</sup> day. Adverse event or Adverse Drug Reaction observed during treatment period if any, were documented and its appropriate and timely management were done and recorded in the CRFs.

### Statistical analysis

The analysis of the data using statistical software SPSS 15.0 data describing quantitative measures are expressed as median or mean  $\pm$  SD or SE or the mean with range. Qualitative variables are presented as counts and percentage.

## RESULTS

This study was conducted on 100 subjects. Out of these, 84 were completed the study and 16 were dropped out due to loss to follow up. The demographic data of 84 subjects are in [Table-1]. Mean body weight is 79.15 kg, height 1.63 meter. No significant changes were observed at the end of treatment from baseline in any of the vital signs i.e. pulse rate, body temperature, respiratory rate, systolic and diastolic blood pressure.

### Treatment outcomes

At baseline visit mean BMI was 29.65 kg/m<sup>2</sup>, which was significantly reduced to 28.63 kg/m<sup>2</sup> after 84 days of treatment with these medicines [Graph 1]. At baseline visit, mean circumference of abdomen was 91.43 centimeters (cms), which was significantly, reduced to 86.40 cms after 84 days of treatment with these medicines [Graph 2]. At baseline visit mean circumference of chest was 87.14 cms, which was also significantly reduced to 85.13 cms after 84 days of treatment with these medicines [Graph 2]. At baseline visit mean circumference of thigh was 45.95 cms, which was also significantly reduced to 44.24 cms after 84 days of treatment with these medicines [Graph 2]. At baseline

visit mean circumference of triceps was 28.75 cms, which was also significantly reduced to 27.79 cms after 84 days of treatment with these medicines [Graph 2]. At baseline visit, the mean obesity clinical symptoms score was 58.36, which was significantly reduced 32.00 after 84 days of treatment with these medicines [Graph 3]. The percentage of relief on chief complaints like *Kshudha vridhi* (polyphagia) was 40.92%, *Trishna vridhi* (polydipsia) 43.96%, *Swetadhikya* (excessive sweating) 43.80%, *Daurgandhya* (foul smell in body) 50.19%, *Ati nidra* (excessive sleep) 43.92%, *Hridhrava* (palpitation) 47.20%, *Kshudra swasa* (Dyspnea on exertion) 50.00%, *Angamarda* (Fatigue) 35.51%, *Gaurava* (feeling of heaviness) 47.64%, *Alasya* (laziness) 46.30%, *Daurbalya* (weakness) 48.85%, *Sandhisula* (joints pain) 40.51%, *Sarvangashool* (body ache) 42.32%, *Pipilaka sancharvat vedana* (tingling sensation) 50.47%, *Mutra krichhata* (difficulty in urination) 48.35%, Constipation 41.57% and *Shaitya* (feeling of coldness) 45.31% was observed in the trial participants. Pathological investigation such as serum cholesterol and serum triglycerides were changed significantly [Table-3].

**Table-1: Demographic profile and baseline characteristics of study subjects (n = 84).**

Variables	N (%)
<b>Age (in years)</b>	
12-20	04 (04.77)
21-30	15 (17.86)
31-40	28 (33.34)
41-50	27 (32.15)
51-60	10 (11.91)
<b>Gender</b>	
Male	08 (09.53)
Female	76 (90.48)
<b>Marital status</b>	
Married	68 (80.96)
<b>Educational status</b>	
Illiterate	12 (14.19)
Read & write	72 (85.72)
<b>Habitat</b>	
Urban	64 (76.19)
Rural	20 (23.81)
<b>Economic Status</b>	
Above poverty Line	49 (58.34)
Below poverty line	35 (41.67)
<b>Occupation</b>	
Desk Work	18 (21.43)
Field work	22 (26.19)
House Wife	44 (52.38)
<b>Dietary Habits</b>	
Veg	26 (30.96)
Non-Veg	58 (69.05)
<b>Built wise</b>	
Heavy	60(71.60)
Medium	24(28.40)
<i>Sharirika prakriti</i>	

<i>Pitta-Kaphaja</i>	56 (66.66)
<i>Vata-Pittaja</i>	06 (7.14)
<i>Vata-Kaphaja</i>	22(26.19)

**Table 2: Effect of treatment on circumference of body parts in the subjects of obesity (n=84).**

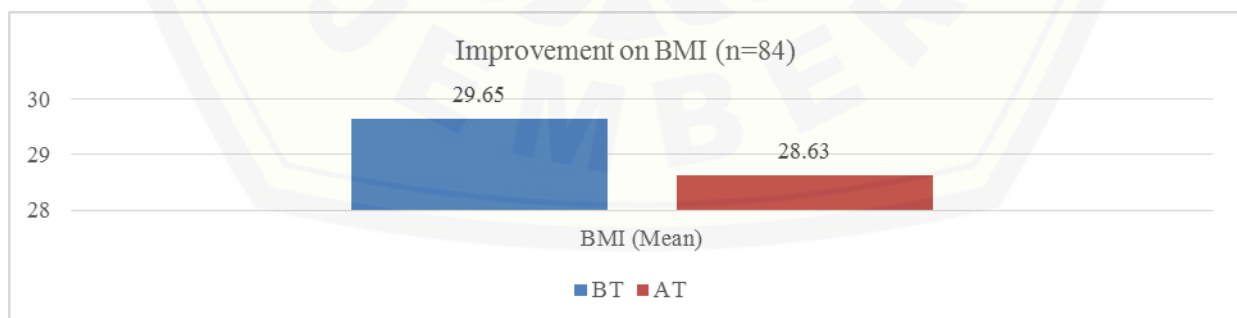
Region of the body (in Centimeter)	Start of the treatment (Mean)	End of the treatment (Mean)	Percentage of relief
Abdomen	91.43	86.40	5.50
Chest	87.14	85.13	2.30
Thigh	45.95	44.24	3.72
Triceps	28.75	27.79	3.33

**Table 3: Effect of treatment on chief complaints in the subjects of obesity (n=84).**

Clinical Symptoms	Start of the treatment (Mean)	End of the treatment (Mean)	Percentage of relief
<i>Kshudha vridhi</i> (Polyphagia)	3.47	2.05	40.92
<i>Trishna vridhi</i> (Polydypsia)	3.98	2.23	43.96
<i>Swetadhikya</i> (Excessive sweating)	4.84	2.72	43.80
<i>Daurgandhya</i> (Foul smell in body)	2.55	1.27	50.19
<i>Ati nidra</i> (Excessive sleep)	4.03	2.26	43.92
<i>Hridrava</i> (Palpitation)	3.75	1.98	47.20
<i>Kshudra swasa</i> (Dyspnea on exertion)	4.58	2.29	50.00
<i>Angamarda</i> (Fatigue)	2.14	1.38	35.51
<i>Gaurava</i> (Feeling of heaviness)	5.10	2.67	47.64
<i>Alasya</i> (Laziness)	4.19	2.25	46.30
<i>Daurbalya</i> (Weakness)	3.48	1.78	48.85
<i>Sandhisula</i> (Joints pain)	4.69	2.79	40.51
<i>Sarvangashool</i> (Body ache)	4.30	2.48	42.32
<i>Pipilaka sancharvat vedana</i> (Tingling sensation)	3.17	1.57	50.47
<i>Mutrakrichhata</i> (Difficulty in urination)	0.91	0.47	48.35
<i>Koshtabadhata</i> (Constipation)	1.90	1.11	41.57
<i>Shaitya</i> (Feeling of coldness)	1.28	0.70	45.31

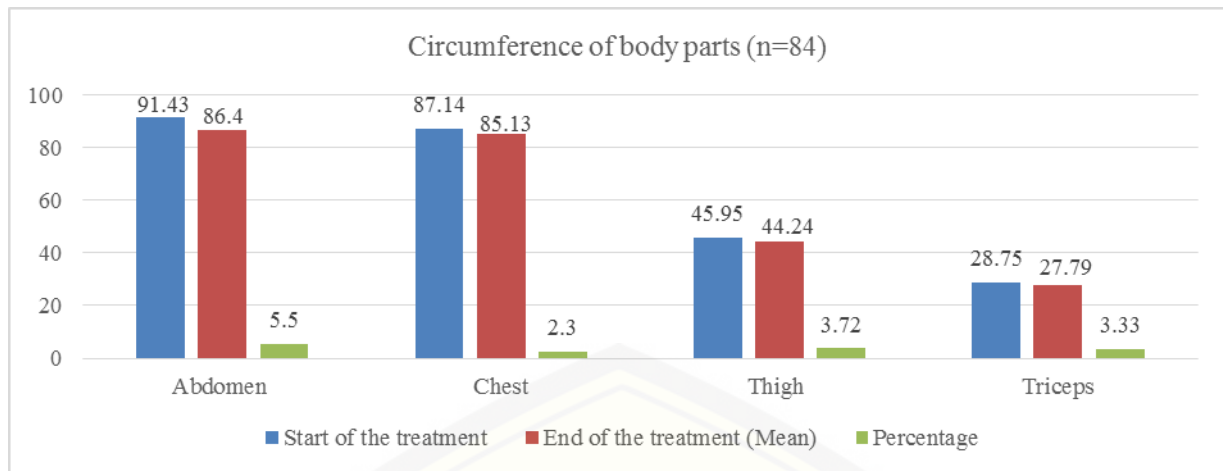
**Table 4: Assessment of pathological and bio-chemical investigation (n=84).**

Laboratory Parameters	Start of the treatment (Mean)	End of the treatment (Mean)	Percentage of Relief
Serum cholesterol (mg/dl)	318.33	226.85	28.73
Serum triglycerides (mg/dl)	163.18	140.40	08.06

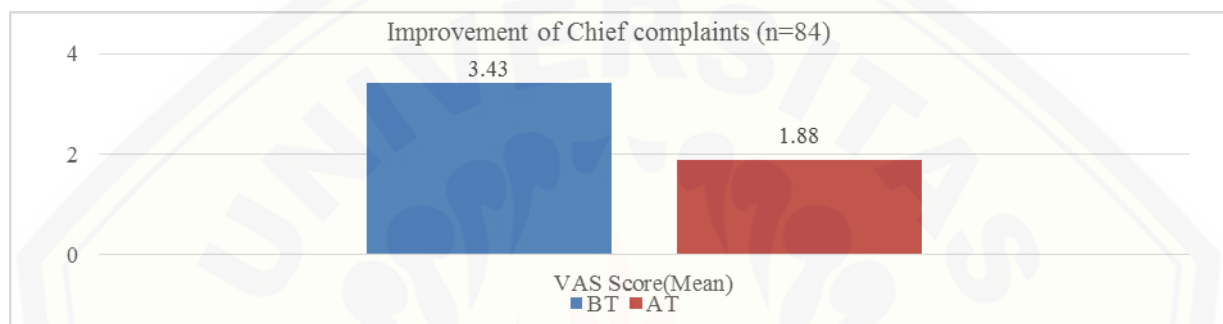


**Graph 1: Effect of treatment on BMI in the subjects of obesity (n=84).**





Graph 2: Effect of treatment on circumference of body parts in the subjects of obesity (n=84).



Graph 3: Effect of treatment on chief complaints in the subjects of obesity (n=84).

## DISCUSSION

Obesity is mentioned in Ayurvedic classics as *Medoroga* or *sthaulya* and it is as old as the history of mankind. Description of *Medoroga* remains a tremendous scope of research in the field of obesity. *Acharya charak* described that continuous intake of causative factors aggravate *kapha dosha* and *mala dhatus* due to similar properties resultant its *meda* obstruct the *srotas* and produce the obesity. He has also described *Sthaulya* is the most hazardous amongst all in *Ashtauninditeeya* chapter in their text.<sup>[6]</sup>

According to modern medicine, Obesity increases the probability of various diseases and conditions, mostly CVD, diabetes mellitus, osteoarthritis knee, obstructive sleep apnea, certain types of cancer and depression.<sup>[7]</sup> The metabolism and endocrine glands is the functioning to create the obesity. It is a collection of disorders characterized by defective regulation of carbohydrate, lipids and protein metabolism. The most common cause of obesity is excess calorie intake coupled with physical inactivity. On the basis of studies, dysfunction of the leptin systems plays a role in human obesity. Basically, it is generated by a combination of excessive food intake, lack of physical activity, and genetic susceptibility. A limited cases are caused by genes, endocrine disorders, medications, or mental disorder.<sup>[8]</sup> The view that obese people eat little yet gain weight due to a slow metabolism is not medically supported.<sup>[9]</sup> Usually, the obese people have a greater

energy expenditure than their normal counterparts due to the energy required to maintain an increased body mass.<sup>[10]</sup>

In Ayurveda, the first line of management in *Sthaulya* or *Medoroga* is *Nidana parivarjanam* (avoidance of causative factors). *Vata-kapha shamak* and *lekhan* drugs mentioned for the management of obesity.<sup>[11]</sup> *Vacha* and *kutaki* mobilized *medodhatu* from the body after *dhatupaka*. *Medodhatu* was converted in to *mala* (faeces) and *mutra* (urine) by *pachan* of *meda*. Increase in *mala* and *mutra* volume resulted in *srotosuddhi* (purification of channels) and *laghutwa* (lightness) in the body. These drugs have *deepen* (appetizer), *pachan* (digestive), *lekhan* (scraping) properties. Ayurveda has also suggested the treatment of *sthaulya roga* by drugs having *Apatarpana* and *lekhan karma* properties.<sup>[12]</sup> Efficacy of the trial drug was due to the combined effect of *medodhatu*, *amadosha*, *dhatagni* and *koshthagni*. The ingredients of *Vacha* (*Acorus calamaus Linn*) have *katu*, *tikta rasa*; *laghu*, *sara*, *tikshna guna*; *ushna veerya*; *katu vipaka*; *kaphavata shamaka*, *Akash-Vayu-Agni mahabhoot pradhan* properties.<sup>[13]</sup> These properties work against *kapha*, and resultant is reduced fat. *Kutaki* (*Picrorrhiza kurroo*) havings *katu*, *tikta rasa*, *laghu*, *ruksha guna*, *sheeta virya*, *katu vipaka* and *kapha pitta shamaka* properties.<sup>[14, 15]</sup> It is effective for dissolving the excess fat which was accumulate around the liver and gastro intestinal tract.<sup>[16]</sup> Both the ingredients of *Vacha kutaki yoga* are the member of *Lekhniya mahakashaya* (a

group of scraping drugs), which was specially designed for *lekhan karma* (scraping properties).<sup>[17]</sup> *Lekhan* property (scraping) is useful in removing any blockage in micro vessels as well as macro vessels. There were some limitations in this study as no comparator group was taken to compare the efficacy of trial drug. In future study, these points will be taken in to account.

## CONCLUSION

The present study data shows that *vacha kutaki yoga* provided significant relief in obesity (*medoroga* or *stahulya*) in both the sexes. The study reveals that the selected management is potential to reduce symptoms of obesity (*medoroga* or *stahulya*) with added advantage of being free from adverse reaction.

## ACKNOWLEDGEMENTS

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## A STUDY TO EVALUATE THE EFFECT OF CARDIAC REHABILITATION PROGRAM ON HEALTH STATUS AND TREATMENT COMPLIANCE AMONGST POST MYOCARDIAL INFARCTION PATIENTS IN A CARDIAC CENTRE

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### ABSTRACT

Efforts are constantly being made, mostly aimed at improving behavioral patterns and poor lifestyle habits. As for all cardiovascular diseases, it is recognized that the cardiac rehabilitation program is the principal method of lifestyle modification to minimize and avoid the recurrence of heart attacks. After the completion of the cardiac rehabilitation program, it revealed that its effect on health status was statistically effective in terms of BMI and blood pressure, and treatment compliance in terms of medication, diet, exercise and follow-up compliance. Substantial decline in hospitalization was observed after completion of cardiac rehabilitation program. Among two dependent variables, health status was found to be statistically non-significant in terms of blood pressure and BMI and treatment compliance in terms of medication, diet, exercise and follow-up, indicating that there is no association between them.

**KEYWORDS:** Cardiac rehabilitation program, Health status, Treatment compliance.

### INTRODUCTION

Heart diseases have become the primal cause of mortality worldwide. With expansive changes in day to day lifestyle, cardiac problems are on the rise. Cardiovascular diseases, particularly, coronary heart disease (CHD) has acquired near to epidemic proportions globally. Detection, diagnosis and systematic treatment is essential to curb the growing death rates by CHD. CHD displays deviation from normal functioning of heart. People with CHD have a reduced supply of oxygen to all the vital organs of the body which eventually causes organ failure. Conditions like atherosclerosis enhance the effect of these cardiac dysfunctions which in due course may cause severe problems like angina and acute myocardial infarction. Myocardial infarction has now become a widespread health problem, which is consuming lives at a global scale.<sup>[1]</sup>

Myocardial infarction (MI) has turned out to be a life threatening disease, influencing the physiological and mental well-being of an individual. The term together means tissue death (infarction) caused in the heart muscles (myocardium). MI is a type acute coronary syndrome, which displays an instantaneous or short term

change in rate of blood flow to the heart.<sup>[2]</sup> This disease causes an overtime myocardial cell necrosis due to considerable and sustained state of ischemia.

The high subsequent morbidity and mortality, as well as the significant physio-psychological adverse impact of the disease have led to a call for the universal provision of rehabilitative and preventive strategies for all patients with CHD. (WHO, 1993) Cardiac secondary prevention refers to the prevention of major morbid and fatal events, such as the recurrence of angina pectoris, MI, or sudden death among patients with clinically apparent CHD, through risk factor identification and modification. Cardiac rehabilitation, as defined by the WHO (1993), is “the sum of activities required to influence favorably the underlying cause of cardiac disease, as well as to ensure the patient the best possible physical, mental and social conditions so that they may, by their own efforts, preserve or resume when lost, as normal a place as possible in the life of the community”.

“Cardiac rehabilitation (and secondary prevention) services are comprehensive, long term programs involving medical evaluation, prescribed exercise, cardiac risk factor modification, education, and counseling. These programs are formulated to limit the



physiological and psychological effects of cardiac illness, reduce the risk for sudden death or re-infarction, control cardiac symptoms, stabilize or reverse the atherosclerotic process and enhance the psychosocial and vocational status of selected patients.<sup>»[3]</sup>

An exercise forms a core component of cardiac rehabilitation program. However, recent practice guidelines also recommend for the incorporation and optimization of various other components which must be a part of the comprehensive rehabilitation programs. Together, these components would help individuals to

The diagrammatic representation is



X stands for cardiac rehabilitation program which includes health record of patient, the maintenance of medication chart for 4 weeks taught by the researcher, diet chart as advised and exercises as demonstrated and advised.

O<sub>1</sub> stands for first follow up after one week of discharge which includes measuring health status, treatment compliance and number of hospitalizations.

O<sub>2</sub> stands for second follow up after four weeks of discharge which includes measuring health status, treatment compliance and number of hospitalizations.

**Statement of the Problem**

A study to evaluate the effect of cardiac rehabilitation program on health status and treatment compliance amongst post myocardial infarction patients in a cardiac centre.

**Aim of the Study**

To evaluate the effect of cardiac rehabilitation program on health status and treatment compliance amongst post myocardial infarction patients in a cardiac centre.

**Research Question**

What is the effect of cardiac rehabilitation program on health status and treatment compliance among post myocardial infarction patients?

**Objectives of the Study**

1. To assess the effect of cardiac rehabilitation program on health status in terms of BMI and blood pressure amongst post MI patients.
2. To assess the effect of cardiac rehabilitation program on treatment compliance in terms of medication, diet, exercise and follow up amongst post MI patients.
3. To explore the effect of cardiac rehabilitation program on cardiac related hospitalization.

foster healthy behaviors and eventual compliance to these behaviors would promote a healthy and active lifestyle.<sup>[3]</sup>

**MATERIALS AND METHODS**

**Research Design**

The selection of research design depends upon the purpose of the study, research approach and variables to be studied. The design selected for this study is pre experimental one group post test only design.

**Operational Definitions**

- **Cardiac Rehabilitation Program:** Cardiac rehabilitation is a designed medically supervised program to improve cardiovascular health, in this study cardiac rehabilitation program refers to the maintenance of medication card, following prescribed diet chart and performing exercises are instructed.

- **Health Status:** In this study the measures of health status include BMI and blood pressure.

$$\text{BMI: } \frac{\text{Weight in Kg}}{\text{Height in m}^2}$$

- **Body Mass Index (BMI)**
- **Blood Pressure (BP):** The force of circulating blood on the walls of the arteries. It is being taken by two measurements, systolic is measured when the heart beats and pressure is at the highest and diastolic is measured between heart beats when it is at its lowest.
- **Treatment Compliance:** In this study the measures of treatment compliance includes medication, diet, exercise and follow up compliance of selected sample.
- **Post Myocardial Infarction:** Myocardial Infarction is the sudden onset of chest pain due to lack of blood supply to myocardium. In this study those patients who were diagnosed with first episode of MI (Both STEMI and NSTEMI) are considered.
- **Patient:** In this study patients are the population who are admitted to the hospital with complaints of chest pain/ discomfort and diagnosed as the first episode of myocardial infarction.

**Variables of the Study**

Dependent variable- BMI, Blood pressure, number of missed doses of medication, follow ups, hospitalization after discharge and treatment compliance includes diet and exercises as per instructions.

Independent variable- Age, Gender, Marital Status, Employment status, Education level, Bad habit and Treatment advised.

### Assumptions

The study is based on the assumption that

1. Patients who undergo effective cardiac rehabilitation program will have better health status and treatment compliance.
2. Learning is an integral part of human nature.

### Conceptual Framework

The conceptual framework used for the study was based on Donabedian model.

### Setting of the Study

The study was conducted at National Heart Institute, New Delhi. This institute is a 104 bedded state of the art cardiac specialized hospital. It is well equipped with 6 ICUs and a cath lab unit offering cardiac procedures including percutaneous transluminal coronary angioplasty (PTCA), angiography. National Heart Institute conducts an average of 25-30 number of PTCA's in a month and the same patient are then followed up.

### Sample and Sampling Technique

#### Population

The target population of this study was those patient who had been diagnosed with myocardial infarction and had undergone cardiac rehabilitation program and had come for their first and second follow up after one week and one month of their discharge from National Heart Institute, New Delhi.

#### Sampling Technique

The purposive sampling technique was used for the present study.

#### Inclusion Criteria

The patients who will be;

1. Diagnosed as myocardial infarction.
2. Patients willing to participate in the study at the time of discharge.
3. Patients available at the time of data collection.

#### Exclusion Criteria

The patients who will be;

1. Patients with multiple episodes of MI.
2. Patients outside state territory Delhi NCR.

#### Sampling Size

Sample size for the present study was 65 myocardial infarction patients from National Heart Institute, New Delhi.

#### Ethical consideration

1. Formal scientific advisory, research and ethical committee clearance certificate was obtained from All India Heart Foundation (AIHF) of East of Kailash, New Delhi.
2. Formal permission was obtained from Vice CEO of National Heart Institute to conduct research study on

the post myocardial infarction patients of the hospital.

3. Myocardial Infarction patients were informed that participation in the study was voluntary and were guaranteed that data would be treated anonymously. The confidentiality of data was maintained.
4. Written informed consent was obtained from each patient for being part of the study.

### Data Collection Tool And Technique

The objective of the study was to assess the effect of cardiac rehabilitation program on health status and treatment compliance amongst post myocardial infarction patients in a cardiac centre, New Delhi for which researcher has developed a cardiac rehabilitation program booklet.

The tool consists of four sections described as follows:

#### Tool 1

**Section I:** This section consists of questionnaires to assess the demographic variable which includes age, gender, marital status, employment status, education level, bad habit & treatment advised and baseline data includes BMI and BP of post myocardial infarction patients during discharge period.

**Section II:** This section consists of the record maintained that includes number of missed doses of medication, follow up and number of hospitalization after discharge.

**Section III:** This section consists of questionnaires during first follow up which consists of assessment of baseline data which includes BMI and BP; level of treatment compliance to diet and exercises which includes deep breathing, chest expansion, neck, walking, both upper and lower limb exercises as per cardiac rehabilitation program in post myocardial infarction patients.

**Section IV:** This section consists of same questionnaires during second follow up.

#### Tool 2

A cardiac rehabilitation program booklet which includes health record of patient, the maintenance of medication chart for 4 weeks taught by the researcher, diet chart as advised and exercises as demonstrated by the researcher which includes deep breathing, neck exercises, shoulder exercises, walking, chest expansion exercises, leg exercises and upper limb exercises at the time of discharge.

#### Validity Of The Tools

The validity of the tool was obtained by submitting the tools to 6 experts and it was valid. All the rectification was as suggested by the experts.

#### Reliability of the Tools

The reliability of the structured tool to evaluate the effect of cardiac rehabilitation program on health status and treatment compliance amongst post myocardial infarction patients was determined using Guttman split half coefficient and the reliability coefficient was 0.9.

**Procedure for Final Data Collection**

Formal permission was obtained from the concerned authorities to conduct the final study by using purposive sampling technique according to research design.

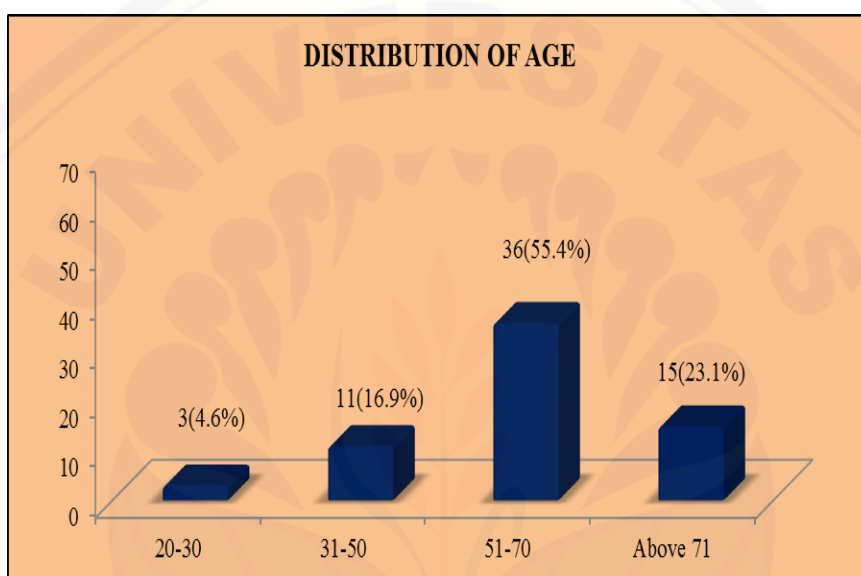
The finalized data from this study was collected between 20<sup>th</sup> December 2019 to 31<sup>st</sup> April 2020. During the discharge procedure the patients were handed over a self-assessment cardiac rehabilitation booklet along with usage guidelines by NHI. The first follow up of the patients was scheduled after 7 days as per the protocol. On the 1st follow up the patients were interviewed and evaluated with baseline data, treatment compliance, number of cardiac related hospitalization and self-assessment cardiac rehabilitation program booklet including medication assessment. Thereafter, patients

were informed regarding their second follow up due after 30 days. All the parameters mentioned in the first follow up assessment were re-evaluated in the second follow up. Adequate measures were taken to maintain uniformity for all the activities conducted with the selected samples.

**RESULTS AND DISCUSSIONS**

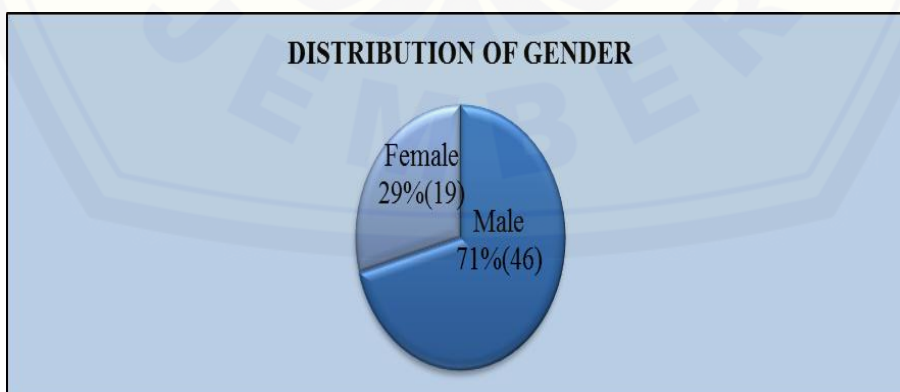
**Section I:- Distribution of demographic variables among post myocardial infarction patients**

A purposive sampling of 65 post myocardial infarction patients was drawn from the selected settings, based on the selection criteria. The data obtained are summarized in frequency and percentages in figure- 1 to 7 and table- 1 to 11.



**Figure 1: Bar diagram showing frequency and percentage distribution of post MI patients with regards to age (N=65).**

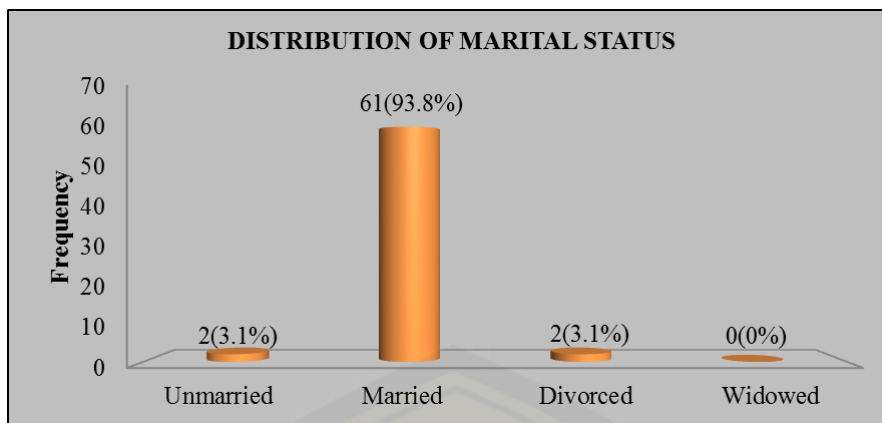
Figure 1: Indicates that out of the total samples, maximum are in the age group of 51-70 years (55.4%), above 71years (23.1%), 31-50 years (16.9%) and remaining in 20-30years (4.6%) of age.



**Figure 2: Pie chart showing frequency and percentage distribution of post MI patients with regards to gender (N=65).**

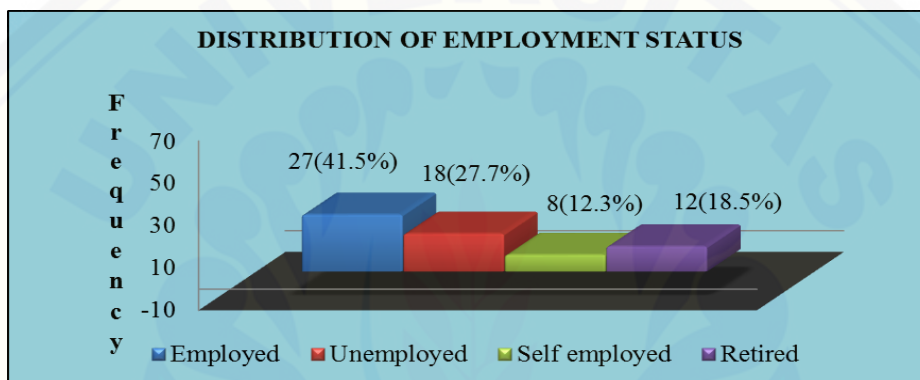
Figure 2: Indicates that out of the total sample taken majority of the patients were male (71%) and only a small fraction of it were female (29%).





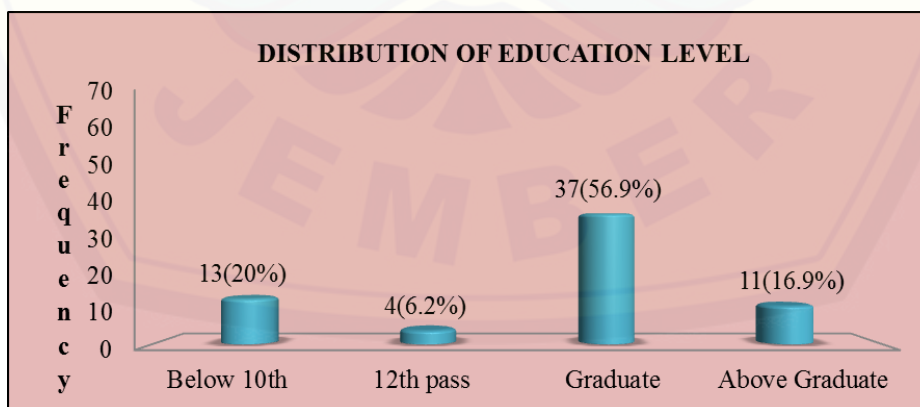
**Figure 3: Column graph showing frequency and percentage distribution of post MI patients with regards to marital status (N=65).**

Figure 3: Indicates that out of all total samples, majority (93.8%) of the samples were married, both unmarried (3.1%) and divorced (3.1%) samples were same and none of the sample was widowed (0%).



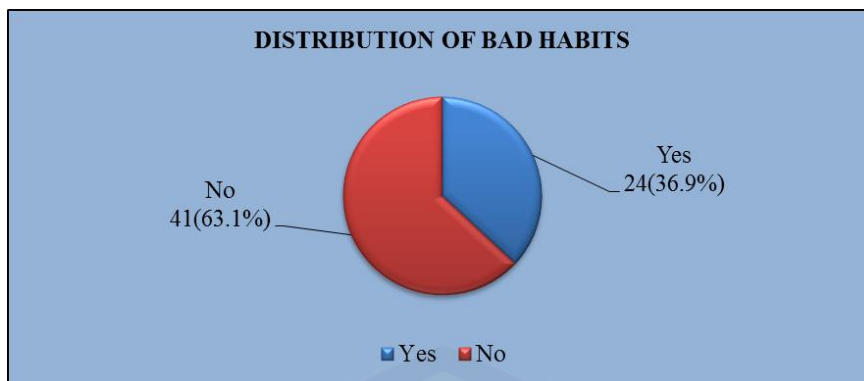
**Figure 4: Column graph showing frequency and percentage distribution of post MI patients with regards to employment status (N=65).**

Figure 4: Indicates that of the total samples, employed were 41.5%, unemployed were 27.7%, retired were 18.5% and remaining 12.3% were self employed.



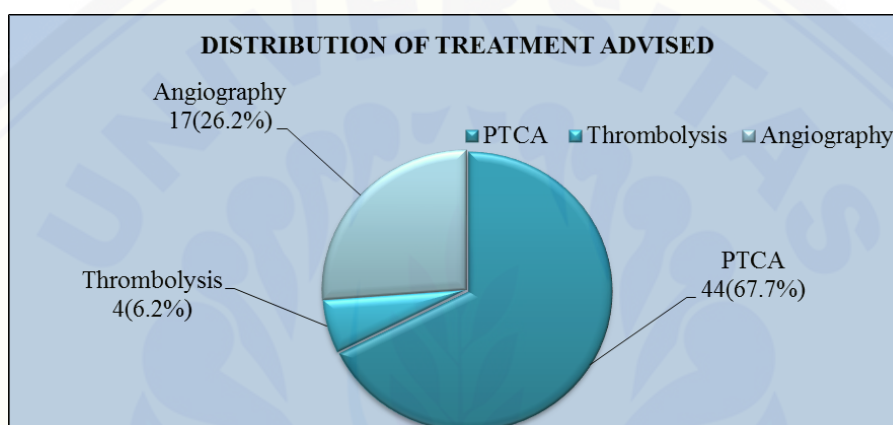
**Figure 5: Column graph showing frequency and percentage distribution of post MI patients with regards to education level (N=65).**

Figure 5: Indicates that among all samples, graduates were 56.9%, below 10<sup>th</sup> pass were 20%, above graduate were 16.9% and remaining 6.2% were 12<sup>th</sup> pass.



**Figure 6:** Pie chart showing frequency and percentage distribution of post MI patients with regards to bad habits (N=65).

Figure 6: Indicates majority of samples do not have bad habit (63.1%) and remaining 36.9% had bad habit.



**Figure 7:** Pie chart using frequency and percentage distribution of post MI patients with regards to treatment advised (N=65).

Figure 7: Indicates amongst all samples treatment advised for majority of them was PTCA (67.7%), angiography (26.2%) and minimal treatment advised was thrombolysis (6.2%).

**Section II:- Effectiveness of cardiac rehabilitation program on health status of post myocardial infarction patients**

This section deals with the analysis and interpretation of data related to effect of cardiac rehabilitation program on health status in terms of BMI and blood pressure in 1<sup>st</sup> and 2<sup>nd</sup> follow up of post myocardial infarction patients.

**Table 1:** Table showing the frequency and percentage distribution of health status among post myocardial infarction patients (N= 65).

S. No	Health Status	1 <sup>st</sup> follow up		2 <sup>nd</sup> follow up	
		f	%	f	%
1.	<b>Body mass index</b>				
	Under weight	4	6.15%	2	3.07%
	Normal weight	22	33.84%	28	43.07%
	Pre Obesity	21	32.30%	19	29.23%
	Obesity class 1	12	18.46%	12	18.46%
	Obesity class 2	5	7.69%	3	4.61%
	Obesity class 3	1	1.53%	1	1.53%
2.	<b>Blood pressure</b>				
	Normal	19	29.23%	20	30.76%
	Elevated	19	29.23%	22	33.84%
	Stage 1	19	29.23%	22	33.84%
	Stage 2	8	12.30%	1	1.53%
	Hypertensive crisis	0	0%	0	0%

Data presented in table 1 shows the frequency and percentage distribution of health status in terms of BMI and blood pressure in 1<sup>st</sup> and 2<sup>nd</sup> follow up of post myocardial infarction patients. In the subject to BMI of patients in 1<sup>st</sup> and 2<sup>nd</sup> follow up, underweight (6.15%, 3.07%), normal weight (33.84%, 43.07%), pre obesity (32.30%, 29.23%), obesity class 1 (18.46%, 18.46%),

obesity class 2 (7.69%, 4.61%) and obesity class 3 (1.53%, 1.53%). In the subject to blood pressure of patients in 1<sup>st</sup> and 2<sup>nd</sup> follow up shows, normal (29.23%, 30.76%), elevated (29.23%, 33.84%), stage 1 (29.23%, 33.84%), stage 2 (12.30%, 1.53%) and hypertensive crisis (0%, 0%).

**Table 2:** Table showing the comparison of health status between first and second follow-up among post myocardial infarction patients using paired ‘t’ test (N=65).

Comparison	Mean	SD	MD	Calculated ‘t’ value	Table ‘t’ value	p value
First follow-up	5.185	1.402	0.261	2.133	1.997	0.037*
Second follow-up	4.923	1.216				

Level of significance 0.05; df= 64 \*significant

Data presented in the table 2 shows;  $t_{\text{tabulated value}}$  is 1.997 at 0.05 level. Hence  $t_{\text{calculated value}}$  is more than  $t_{\text{tabulated value}}$ . Then calculated  $t$  is significant. Hence we fail to accept null hypothesis, eventually accepting the research hypothesis. Therefore, there is a significant difference in health status following the completion of cardiac rehabilitation program.

**Section III:- Effectiveness of cardiac rehabilitation program on treatment compliance**

This section deals with the analysis and interpretation of data related to effect of cardiac rehabilitation program on treatment compliance in terms of medication, diet, exercises and follow up in 1<sup>st</sup> and 2<sup>nd</sup> follow up among post myocardial infarction patients.

**Table 3:** Table showing the frequency and percentage distribution of treatment compliance in terms of medication, diet, exercises and follow up among post myocardial infarction patients. (N=65).

S. No.	Treatment Compliance	Compliance criteria	1 <sup>st</sup> follow up		2 <sup>nd</sup> follow up	
			f	%	f	%
1	Medication Compliance	Good Compliance	61	93.8%	34	52.30%
		Moderate Compliance	03	4.61%	31	47.69%
		Poor Compliance	01	1.53%	00	0%
2	Diet Compliance	Good Compliance	18	27.69%	03	4.61%
		Moderate Compliance	47	72.3%	62	95.38%
		Poor Compliance	00	0%	00	0%
3	Exercise Compliance	Good Compliance	32	49.23%	40	61.53%
		Moderate Compliance	32	49.23%	25	38.46%
		Poor Compliance	1	1.53%	0	0%
4	Follow up Compliance	Compliance	65	100%	52	80%
		Non Compliance	00	0%	13	20%

Data presented in table 3 shows the frequency and percentage distribution of treatment compliance in terms of medication, diet, exercise and follow up among post myocardial infarction patients. On the subject to medication compliance of patients in 1<sup>st</sup> and 2<sup>nd</sup> follow up, good compliance (93.8%, 52.3%), moderate compliance (4.61%, 47.67%) and poor compliance (1.53%, 0%). On the subject to diet compliance of patients in 1<sup>st</sup> and 2<sup>nd</sup> follow up, good compliance

(27.69%, 4.61%), moderate compliance (72.3%, 95.38%) and poor compliance (0%, 0%). On the subject to exercise compliance of patients in 1<sup>st</sup> and 2<sup>nd</sup> follow up, good compliance (49.23%, 61.53%), moderate compliance (49.23%, 38.46%) and poor compliance (1.53%, 0%). And on the subject to follow up compliance of patients in 1<sup>st</sup> and 2<sup>nd</sup> follow ups, compliance (100%, 80%) and non compliance (0%, 20%).

**Table 4:** Table showing the comparison of medication compliance between first and second follow-up among post myocardial infarction patients using paired ‘t’ test. (N=65).

Comparison	Mean	SD	MD	Calculated ‘t’ value	Table ‘t’ value	p value
First follow up	1.077	0.322	0.400	5.311	1.997	0.001*
Second follow up	1.477	0.503				

Level of significance 0.05; df= 64 \*significant

Data presented in the table 4 shows;  $t_{\text{tabulated value}}$  is 1.997 at 0.05 level. Hence  $t_{\text{calculated value}}$  is more than  $t_{\text{tabulated value}}$ . Then calculated  $t$  is significant. Hence we fail to accept null hypothesis, eventually accepting the research hypothesis. Therefore, there is a significant

difference in health status following the completion of cardiac rehabilitation program.



*difference in medication compliance following the completion of cardiac rehabilitation program.*

**Table 5:** Table showing the comparison of diet compliance between first and second follow-up among post myocardial infarction patients using paired ‘t’ test. (N=65).

Comparison	Mean	SD	MD	Calculated ‘t’ value	Table ‘t’ value	p value
First Follow up	14.185	0.827	0.738	5.592	1.997	0.001*
Second Follow up	3.446	0.884				

**Level of significance 0.05; df= 64 \*significant**

Data presented in the table 5 shows;  $t_{\text{tabulated value}}$  is 1.997 at 0.05 level. Hence  $t_{\text{calculated value}}$  is more than  $t_{\text{tabulated value}}$ . Then calculated  $t$  is significant. Hence we fail to accept null hypothesis, eventually accepting the

research hypothesis. Therefore, there is a significant difference in diet compliance following the completion of cardiac rehabilitation program.

**Table 6:** Table showing the comparison of exercise compliance between first and second follow-up among post myocardial infarction patients using paired ‘t’ test. (N=65).

Comparison	Mean	SD	MD	Calculated ‘t’ value	Table ‘t’ value	p value
First follow-up	6.431	1.984	0.585	2.781	1.997	0.007*
Second follow-up	5.846	1.427				

**Level of significance 0.05; df= 64 \*significant**

Data presented in the table 6 shows,  $t_{\text{tabulated value}}$  is 1.997 at 0.05 level. Hence  $t_{\text{calculated value}}$  is more than  $t_{\text{tabulated value}}$ . Then calculated  $t$  is significant. Hence we fail to

accept null hypothesis, eventually accepting the research hypothesis. Therefore, there is a significant difference in exercises compliance following the completion of cardiac rehabilitation program.

**Table 7:** Table showing the comparison of follow-up compliance between first and second follow-up among post myocardial infarction patients using paired ‘t’ test. (N=65).

Comparison	Mean	SD	MD	Calculated ‘t’ value	Table ‘t’ value	p value
First follow-up	1.000	0.000	0.200	4.001	1.997	0.001*
Second follow-up	1.200	0.403				

**Level of significance 0.05; df= 64 \*significant**

Data presented in the table 7 shows;  $t_{\text{tabulated value}}$  is 1.997 at 0.05 level. Hence  $t_{\text{calculated value}}$  is more than  $t_{\text{tabulated value}}$ . Then calculated  $t$  is significant. Hence we fail to accept null hypothesis, eventually accepting the

research hypothesis. Therefore, there is a significant difference in follow up compliance following the completion of cardiac rehabilitation program.

**Table 8:** Table showing the comparison of treatment compliance (in terms of medication, diet, exercises and follows up) between first and second follow-up among post myocardial infarction patients using paired ‘t’ test. (N=65).

Comparison	Mean	SD	MD	Calculated ‘t’ value	Table ‘t’ value	p value
First Follow up	22.631	2.491	0.615	2.207	1.997	0.031*
Second Follow up	22.015	1.883				

**Level of significance 0.05; df= 64 \*significant**

Data presented in the table 8 shows;  $t_{\text{tabulated value}}$  is 1.997 at 0.05 level. Hence  $t_{\text{calculated value}}$  is more than  $t_{\text{tabulated value}}$ . Then calculated  $t$  is significant. Hence we fail to accept null hypothesis, eventually accepting the research hypothesis. Therefore, there is a significant difference in treatment compliance (in terms of medication, diet, exercises and follows up) following the completion of cardiac rehabilitation program.

**Section IV:- Effectiveness of cardiac rehabilitation program on hospitalization**

This section deals with the analysis and interpretation of data related to effect of cardiac rehabilitation program on hospitalization in 1<sup>st</sup> and 2<sup>nd</sup> follow up among post myocardial infarction patients.

**Table 9: Showing the frequency and percentage distribution of hospitalization in 1<sup>st</sup> and 2<sup>nd</sup> follow up among post myocardial infarction patients. (N=65).**

S. No.	Hospitalization	1 <sup>st</sup> follow up		2 <sup>nd</sup> follow up	
		f	%	f	%
1	No hospitalization	63	96.9%	45	69.23%
2	1-2 times hospitalized	2	3.07%	20	30.76%
3	More than 3times hospitalized	0	0%	0	0%

Data presented in table 9 shows the frequency and percentage distribution of hospitalization in first and second follow up. In first follow up, majority of patients (96.9%) were not hospitalized, minimal (3.07%) had 1-2 times hospitalized. In second follow up, maximum

percentages (69.23%) of patients were not hospitalized and minimal patients (30.76%) were 1-2 times hospitalized. None of the patients were hospitalized more than 3 times in both the follow ups.

**Table 10: Table showing comparison of hospitalization between first and second follow-up among post myocardial infarction patients using paired ‘t’ test. (N=65).**

Comparison	Mean	SD	MD	Calculated ‘t’ value	Table ‘t’ value	p value
First follow-up	1.308	0.465	0.277	4.609	1.997	0.001*
Second follow-up	1.031	0.174				

Level of significance 0.05; df= 64 \*significant

Data presented in the table 10 shows,  $t_{\text{tabulated value}}$  is 1.997 at 0.05 level. Hence  $t_{\text{calculated value}}$  is more than  $t_{\text{tabulated value}}$ . Then calculated  $t$  is significant. Hence we fail to accept null hypothesis, eventually accepting the research hypothesis. Therefore, there is a significant reduction in hospitalization following the completion of cardiac rehabilitation program.

**Section V:- Correlation between health status and treatment compliance**

Pearson correlation coefficient was computed to find the correlation between health status and treatment compliance.

**Table 11: Table showing correlation coefficient of health status with treatment compliance (N=65).**

Parameters	First follow-up	Second follow- up
	Pearson correlation coefficient	Pearson correlation coefficient
Health status	$r=0.109^{**}$	$r=-0.081^{**}$
Treatment compliance	$p=0.386$	$p=0.519$

\*\*Non-significant

Data presented in table 11 shows at 5% level of probability the tabulated value is more than calculated value. Hence we fail to accept research hypothesis, eventually accepting the research hypothesis. Therefore there is no significant correlation among two dependent variables of health status in terms of blood pressure and BMI and treatment compliance in terms of medication, diet, exercises and follows up.

**DISCUSSION**

Compliance towards medical advises is a key factor to discover health status of the patient. Negligence towards compliance critically affects patient’s health and further substandard the disease. Cardiac rehabilitation is designed to help the patients to improve health status and recover from cardiovascular diseases. Patients who are compliant to cardiac rehabilitation program have good health status and do not get hospitalized easily. Hence, a cardiac rehabilitation program was carried out among post myocardial infarction patients in order to assess the effectiveness of cardiac rehabilitation program and reduction in the hospitalization rates.

This study evaluated the effectiveness of the cardiac rehabilitation program on health status and treatment compliance among post myocardial infarction patients. The result of the study indicates that there is a significant difference in health status and treatment compliance following the completion of cardiac rehabilitation program assessed through a structured questionnaire which further interviewed and evaluated with baseline data, treatment compliance, number of cardiac related hospitalization and self-assessment cardiac rehabilitation program booklet including medication assessment indicating effectiveness of cardiac rehabilitation program.

The findings of the study have been discussed in reference to the objectives and hypothesis which are as follows:

**Effect of cardiac rehabilitation program on health status**

In this study noteworthy difference was observed in the health status following the completion of cardiac

rehabilitation program. The findings of the study were supported by another study which indicates marked improvement in the functional capacity and health status in patients with continuous-flow LVADs who attended cardiac rehabilitation program.<sup>[42]</sup>

Findings of the similar study depicts that cardiac rehabilitation significantly improves the functional capacity and some hemodynamic responses, post coronary artery bypass grafting. Therefore, patients need to be referred to rehabilitation units.<sup>[43]</sup>

### **Effect of cardiac rehabilitation program on treatment compliance**

In this study significant difference was noticed in treatment compliance (in terms of medication, diet, exercises and follows up) following the completion of cardiac rehabilitation program. The findings were consistent with a previous study in which exercise based cardiac rehabilitation alone was accredited with reduction of almost half of the mortality rates and reduction in the major risk factors like smoking. An improvement in tolerated metabolic equivalents by 33% and maximal oxygen consumption by 16% are amongst a few other beneficial effects which are observed as an output of cardiac rehabilitation.<sup>[11]</sup>

Similar study supported the findings of this study which was resulted in 20% reduction in total mortality and 26% reduction in cardiac mortality rates, with exercise-based rehabilitation compared to usual medical aid.<sup>[34]</sup> Similar studies were carried out which further put light on the matter that CR program enhanced the physical function of elderly and ability to do work independently.<sup>[34]</sup>

### **Effect of cardiac rehabilitation program on hospitalization**

In the current study remarkable reduction in hospitalization was seen following the completion of cardiac rehabilitation program. The finding of the study was supported by another study which depicted promising results with patients complying with the CR process with reduction in readmission rates and mortality post MI. Thus efforts have to be made at improving awareness amongst MI patients which would eventually improve participation rates and result in positive healthcare outcomes.<sup>[19]</sup>

Another study was conducted among 100 patients with myocardial infarction pour light on the observable improvement within the cardiac status, functional status and quality of life of the patients and also reduced recurrent MI, repeated hospitalization and future mortality.<sup>[30]</sup>

### **CONCLUSIONS**

From the findings, it can be concluded that highest percentage (55.4%) of them were in the age group of 51-70 years, were male (71%), were married (93.8%), were

graduate (56.9%), do not have bad habits (63.1%) and were advised PTCA for treatment (67.7%).

After completion of cardiac rehabilitation program highly significant differences were observed related ( $P > 0.05$ ) to the health status in terms of BMI and blood pressure, treatment compliance in terms of medication, diet, exercise and follow up and a noteworthy individualized developments observed in medication, diet, exercises and follow up compliance.

Marked reduction in hospitalization was observed among the myocardial infarction patients following ( $P > 0.05$ ) the completion of cardiac rehabilitation program.

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## A STUDY TO ASSESS THE EFFECTIVENESS OF ICE PACK APPLICATION ON PAIN AND PHYSIOLOGICAL PARAMETERS DURING REMOVAL OF INVASIVE LINES IN A TERTIARY CARE CARDIAC CENTRE, NEW DELHI

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### ABSTRACT

Nowadays many efforts are being done to decreasing cardiovascular diseases which is expeditiously increasing owing to physiological constraints and unhealthy lifestyle. Many patients undergo cardiothoracic surgery, following a cardiothoracic surgery invasive lines are inserted which gives worst experience of pain during removal. The need for pain relief is an important concern today in the society. Hence it is better to add up a non-pharmacological therapy along with medical treatment to maximize the pain control. Ice pack application has a significant short term analgesic effect on pain and physiological parameters of reducing the painful nerve conductions by acting on the gate control system. The non-pharmacological therapies always have its own merits with less side effects which the nurses by their standing orders can implement to the post- surgical patients to lesion the severity of pain.

**KEYWORDS:** Ice pack application, pain, physiological parameters, invasive lines.

### INTRODUCTION

Our societies are confronting profound challenges globally due to the high rise of cardiovascular diseases (CVDs). Meeting these challenges require assessment of how overall worldwide health trends affect. According to a Global Burden of Disease (GBD) 2015, 422.7 million cases are estimated of CVDs. It remains a major cause of health loss for all regions of the world. CVDs directly demand attention and surgical intervention for improving the quality of life.<sup>[1]</sup>

In the last 50 years cardiac surgeries, globally whether through cardiovascular diseases, congenital defects, rheumatic heart disease or generalized degradation of craniological function. In India 50,000- 60,000 cardio thoracic operations are performed every year, from 2006 - 2016 isolated surgical AVR were performed 61.2%, AVR with coronary artery bypass grafting (CABG) in 23.9%, AVR with mitral valve replacement (MVR) in 7%, and transcatheter aortic valve implantation (TAVI) in 2.3% of patients.<sup>[2]</sup>

During surgical intervention invasive lines are placed for multiple reasons. For giving IV fluids, medication, haemodynamic monitoring and determine if a patient is

dehydrated or has received an adequate amount of fluid to support bodily functions. The presence of invasive lines is associated with considerable discomfort in the conscious mind.<sup>[3]</sup>

The placement of invasive lines is a common experience of pain in thousands of patients. It is unpleasant feeling for patient which increase anxiety and trigger an autonomic response. The long term presence of invasive lines causes pain, infection and infiltration which increased length of hospital stay, and economical liability. Although analgesics drugs are the most effective measures to nurses but it have some side effect. Side by side the non-pharmacological measures like ice pack, massage, relaxation technique are great source to relief from pain.<sup>[4]</sup>

Cold application is an effective technique for pain relief. This technique reduces the speed of nervous conductance and pain. Similarly, based on the gate control theory of pain, stimulation of thick fibres through methods such as cooling may close the gate and reduce pain. Cold application can be used to reduce or reverse pain impulses via activating descending inhibitory neurons,



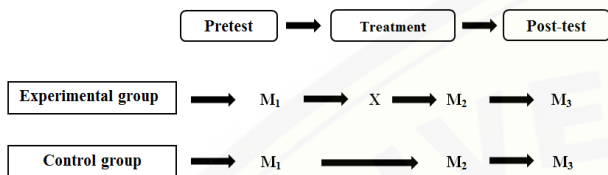
which block ascending nociceptive nerves originating from the substantial gelatinosa.<sup>[5]</sup>

## MATERIAL AND METHODS

### Research Design

The research design selected for the study was Quasi-experimental pre-test post-test control group research design which was considered appropriate for the present study to assess the effectiveness of ice pack application on pain and physiological parameters during removal of invasive lines.

The diagrammatic representation of research design is-



The diagrammatic representation of research design Where

**M**= Measurement

**X**= Treatment (Ice pack application 10 min. prior to invasive line removal.

**M<sub>1</sub>**= Measurement of pain, HR, RR, BP taken before the treatment.

**M<sub>2</sub>**= Measurement of pain, HR, RR, BP taken at zero minute after the treatment.

**M<sub>3</sub>**= Measurement of pain, HR, RR, BP taken at Fifteen minute after the treatment

**Experimental group:** - ice pack application given to the patient for 10 min.

**Control group:** -control group taking routine care

### Statement of problem

A study to assess the effectiveness of ice pack application on pain and physiological parameters during removal of invasive lines in a tertiary care cardiac centre, New Delhi.

### Aim of the Study

To assess the effectiveness of ice pack application on pain and physiological parameters during removal of invasive lines.

### Research Question

How much effective is ice pack application on pain and physiological parameters changes during removal of invasive lines?

### Objectives of study

1. To identify the effect of ice pack application on pain amongst post-surgical patients during invasive line removal.
2. To identify the effect of ice pack on physiological parameters (Blood pressure, respiration rate, and Heart rate).

3. To find out association between pain scores and selected demographic variables.

### Operational Definitions

- **ASSESS**-It is a statistical measurement of the effectiveness of ice pack application on pain by assessing visual analogue pain intensity scale in pre and post intervention.
- **EFFECTIVENESS**- In this study it refers to the degree to which objectives are achieved or the ability to produce intended result.
- **ICE PACK APPLICATION**-It refers to wrapping of ice pack in a clean towel and placing it around the invasive lines site for 10 minutes prior to removal of invasive line.
- **PAIN**- It refers to the intensity of pain experienced by the patient during invasive lines removal which was assessed subjectively and objectively using visual analogue pain intensity scale within 15 minutes of the invasive lines removal.
- **PHYSIOLOGICAL PARAMETERS**- Human health state is defined as variety of physiological parameters for understanding of normal body function. Heart rate, respiration rate and blood pressure are the main parameters which come under this study.
- **HEART RATE**- The number of heartbeats per unit of time, usually per minute. The heart rate is based on the number of contractions of the ventricles. It will be measured via the cardiac monitor.
- **RESPIRATION RATE**-The number of breaths per minute or, more formally, the number of movements indicative of inspiration and expiration per unit time. It is usually determined by counting the number of times the chest rises or falls per minute, it will be measured manually.
- **BLOOD PRESSURE**- Blood pressure is the force of the blood pushing against the artery walls during contraction and relaxation of the heart, measured using sphygmomanometer.
- **INVASIVE LINE**- Invasive line is the thin tube which is inserted in to the body for therapeutic or diagnostic purposes. In this study it includes chest tube, central line, pacing wire and arterial line.
- **CHEST TUBE**-A chest tube is a hollow, flexible tube placed into the chest. It drain blood, fluid, or air around lungs, heart, or oesophagus.
- **CENTRAL LINE**-An IV line that is inserted into a large vein (Internal jugular vein and subclavian vein) typically in the neck or near the heart for therapeutic or diagnostic purposes to administer medicines or fluids or withdraw blood.
- **PACING WIRE**- Pacing wire is an intervention that helps the heartbeat get back to a normal pace if it has been temporarily out of rhythm. Wires are inserted through the chest (during heart surgery) and are directly connected to the heart which delivers a current to the heart to make it beat normally.

- **ARTERIAL LINE**-An arterial line is a thin catheter inserted into an artery. It is most commonly used to monitor blood pressure directly and in real-time (rather than by intermittent and indirect measurement) and to obtain samples for arterial blood gas analysis.

#### Variable under study

**Independent Variable:** - Ice pack application

**Dependent Variable:** - pain, heart rate, respiration rate and blood pressure.

**Extraneous Variable:** -Demographical variables like age, gender, education, employment status, type of work, habits.

#### Assumption

**The Study is based on the assumption that**

1. Majority of the patient during invasive line removal experience pain.
2. Ice pack application is a method to close the gate hence helps alleviating pain as per gate control theory (GCT).
3. Physiological parameters fluctuation in post-surgical cardiac patients will cause complication and become lethal.

#### Conceptual framework

The conceptual framework for the study was based on Wiedenbachs Helping Art of Clinical Nursing Theory.

#### Setting

The study is conducted at National Heart Institute, East of Kailash, New Delhi. It is a 104 bedded super-specialty hospital having eight bedded post recovery unit and equipped with 2 cardiac operation theatre offering cardiac surgeries including CABG. In tertiary cardiac care hospital average 30 cardiac surgeries carried out per month.

#### Sample and Sampling Technique

##### Population

Population for the present study was post- surgical cardiac patients who were admitted in National Heart Institute, New Delhi.

##### Sample

The sample of the study was post- surgical cardiac patients who were having four invasive lines (Chest tube, Arterial line, Pacing wire and central line) admitted in National Heart Institute, New Delhi.

##### Sampling technique

The purposive sampling technique was used for the present study.

##### Inclusion criteria

**Sample were collected from patient who were**

1. Patients above 20-yearsto be part of study.
2. Fully conscious, ability to understand numerical pain intensity scale.

3. Body mass index of < 30 kg/m<sup>2</sup>.
4. Hemodynamically stable

##### Exclusion criteria

**The patient who were**

1. Oversensitivity to cold.
2. Visual or auditory defects.
3. Inability to verbally report pain.
4. Received analgesic less than 4 hours before intervention and drug dependency

##### Sampling size

Sampling size for the present study was 60 (30 experimental group), (30 control group) post- surgical cardiac patient who were admitted in post- surgical cardiac unit of National Heart Institute, New Delhi.

##### Ethical consideration

1. Formal scientific advisory, research and ethical committee clearance certificate was Ethics Committee of All India Heart Foundation (AIHF) of East of Kailash, New Delhi.
2. Formal permission was obtained from CEO of National Heart Institute to conduct research study on the post- surgical cardiac patients of the hospital.
3. Post- surgical cardiac patients were informed that participation in the study was voluntary and were guaranteed that data would be treated anonymously. The confidentiality of data was maintained.
4. Written informed consent was obtained from each patient for being part of the study.

##### Data collection tools and technique

In the present study, based on the objectives the tools were divided into 2 sections:-

**Section I-** A Semi structured interview schedule was prepared to collect the sample characteristic. The characteristics include patient's age, gender, educational status, occupation, type of work, personal habits, any previous surgery, number of invasive lines, and duration of removal of invasive lines.

**Section II –** It includes pain medications received within past four hours, and assessment of physiological parameters involving pain, respiration rate, heart rate and blood pressure assessed in three intervals, before removal of invasive line as well as at zero minute of removal of invasive line and after 15 minutes of removal of invasive lines by visual analogue pain intensity scale.

##### Validity of the tools

The validity of the tool was obtained by submitting the tools to 6 experts and it was valid. All the rectification was as suggested by the experts.

##### Reliability of the tools

The Test–retest reliability method was used to test the reliability of tool and reliability was found 0.828 of pain, 0.771 of respiratory rate, 0.988 of heart rate, 0.887 of systolic blood pressure, and 0.828 of diastolic blood pressure.

**Procedure for final data collection**

Formal permission was obtained from the concerned authorities to conduct the final study by using purposive sampling technique according to research design.

The data was collected between the periods of three months. The demographic Performa was given to the patient who undergone cardiac surgery and having four invasive lines. Pain medications which was received within past four hours was checked. Then baseline data of respiration rate is checked manually, heart rate was checked through a cardiac monitor and blood pressure was checked using a sphygmomanometer before removal of invasive lines. Then intervention of ice pack application was given to experimental group for 10 minutes, as well as the control group taking routine care. Then again physiological parameters (HR, BP, R. R) was assessed at zero minutes of removal of invasive lines and after 15 minutes of removal of invasive lines. Pain was assessed using visual analogue pain intensity scale. On

an average it took 45 minutes to collect data from each patients.

**RESULT AND DISCUSSION****Section 1: - Description of demographic variables in post-surgical cardiac patient.**

This section described demographic variables of post-surgical cardiac patients. A total of 60 subjects were selected for the study. There were total two groups and each group contained 30 subjects. This section contain demographic characteristics of the sample such as age, gender, education, occupation, type of work, personal habits, operative procedure number of invasive lines, previous surgeries, time of removal of all invasive lines. The data was gathered from post -operative cardiac patients and the data collected was tabulated and analysed to obtain frequency and percentage distribution of patients.

**Table 1: Frequency and percentage distribution of post-surgical patients according to demographic data (N=60).**

Demographic variables	Experimental group		Control group		Total	
	f	%	f	%	f	%
<b>Age(in years)</b>						
20-35	03	10	02	6.7	05	8.3
36-50	02	6.7	20	66.7	22	36.7
51-65	08	26.7	07	23.3	15	25.0
65 and above	17	56.7	01	3.3	18	30.0
<b>Gender</b>						
Male	19	63.3	19	63.3	38	63.3
Female	11	36.7	11	36.7	22	36.7
<b>Education</b>						
Primary	07	23.3	03	10.0	10	16.7
High school	13	43.3	09	30.0	22	36.7
Higher secondary	07	23.3	10	33.3	17	28.3
Graduate & above	03	10.0	08	26.7	11	18.3
<b>Occupation</b>						
Unemployed	08	26.7	07	23.3	15	25.0
Skilled	10	33.3	19	63.3	29	48.3
Unskilled	05	16.7	00	00	05	8.3
Retired	07	23.3	04	13.3	11	18.3
<b>Type of work</b>						
Sedentary work	13	43.3	15	50.0	28	46.7
Moderate work	16	53.3	11	36.7	27	45.0
Heavy work	01	3.3	04	13.3	05	8.3
<b>Personal habits</b>						
Smoking	03	10	04	13.3	07	11.7
Alcoholic	05	16.7	11	36.7	16	26.7
Chewing tobacco	06	20.0	04	13.3	10	16.7
None	16	53.3	11	36.7	27	45.0
<b>Operative procedure</b>						
Coronary Artery Bypass Graft.	22	73.3	20	66.7	42	70.0
Valve replacement surgeries	03	10.0	07	23.3	10	16.7
Device closure	04	13.3	01	3.3	05	8.3
Any other	01	3.3	02	6.7	03	5.0
<b>Any previous surgeries</b>						
Minor	01	3.3	01	3.3	02	3.3



Major	00	00	01	3.3	01	1.7
Nil	29	96.7	28	93.4	57	95.0

In table 1 data reveals that in relation to the age wise distribution of patients, the highest percentage (36.7%) were in the age group of 36-50 years and the lowest percentage (8.3%) were in the age group of 20-35 years.

The gender wise distribution of patients depicts that the highest percentage (63.3%) were of male and (36.7 %) were of female.

The highest percentage (36.7%) of the total sample were educated till high school, (28.3%) completed their higher secondary education, (18.3%) of them were graduate and above and only (16.7%) were educated till primary.

With regards to occupation, out of the total sample (48.3%) were skilled, (25 %) were unemployed, (18.3%) of them were retired and only (8.3%) were unskilled.

Almost (46.7%) were doing sedentary work and (45%) of the sample were doing moderate work and only (8.3%) were doing heavy work.

More than (45%) does not have personal habits and (26.7%) were having habits of alcohol consumption. However (16.7 %) were having habits of chewing tobacco only (11.7%) were having smoking habits.

Majority of the patients (70%) had undergone coronary artery bypass Graft and (16.7%) had undergone valve replacement surgeries. However only (5%) of the sample had undergone any other surgeries.

Majority (95%) of the patient have not undergone any previous surgeries. Out of all the total sample only (3.3%) and (1.7%) had previously undergone minor and major surgeries respectively.

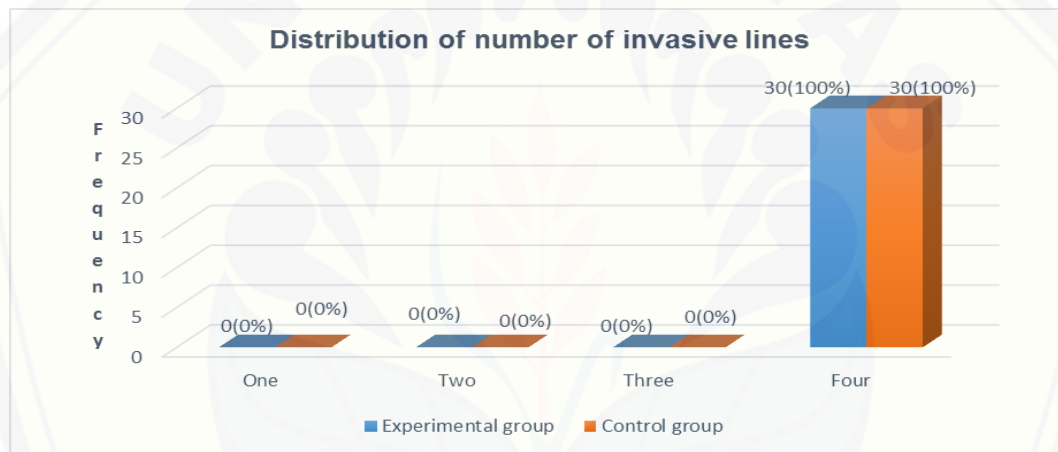


Figure 1: A bar diagram shows the Frequency distribution of post-surgical patients with regards to number of invasive lines (n=30).

In figure 1 data reveals that 100% of the sample have all the four invasive lines.

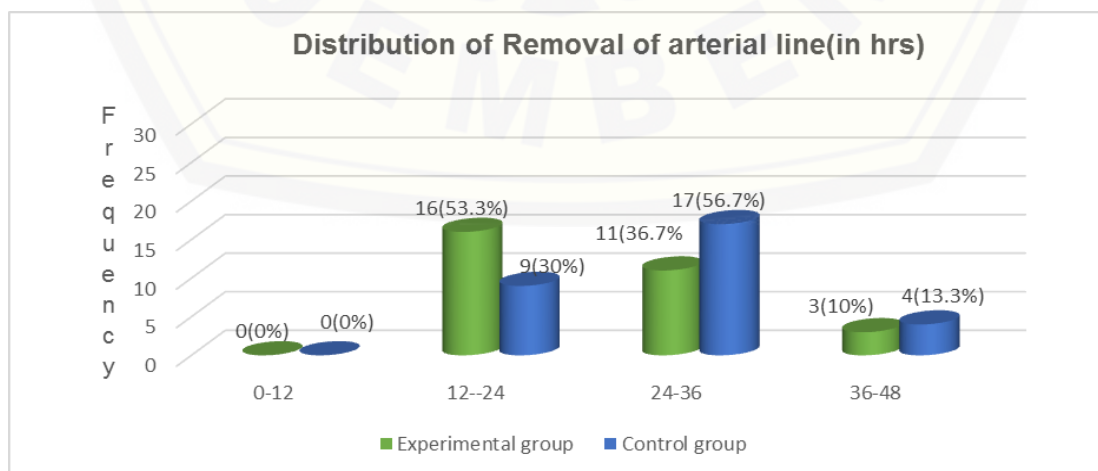


Figure 2: A bar diagram shows the Frequency distribution of post-surgical patients with regards to removal of arterial line (n=30).

Above figure shows that (46.7 %) (41.7%) (11.7%) had their arterial line removal after cardiac surgery within in

24-36 hours, 12- 24 hours and in 36-48 hours respectively.

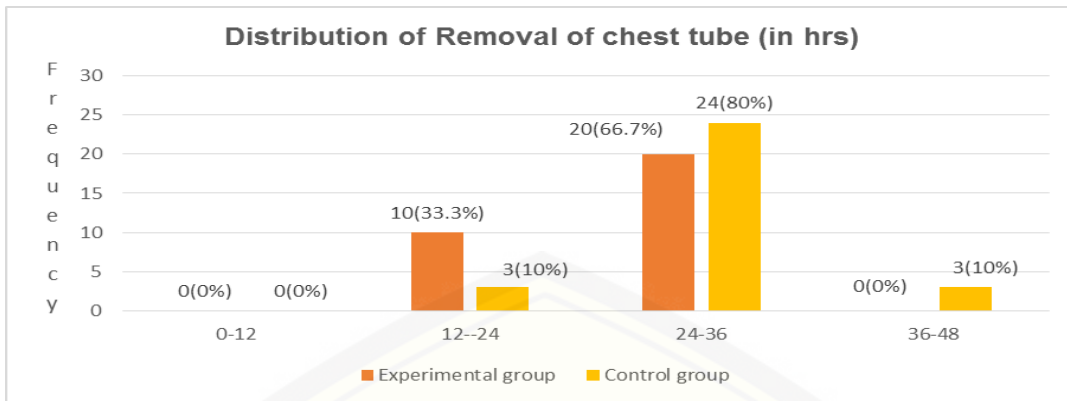


Figure 3: Frequency distribution of post-surgical patients with regards to removal of chest tube (n=30).

Above figure shows that (68.3%) (21.7 %) (5.8%) had their chest tube removal after cardiac surgery within 24-

36 hours, 12- 24 hours and in 36-48 hours respectively.

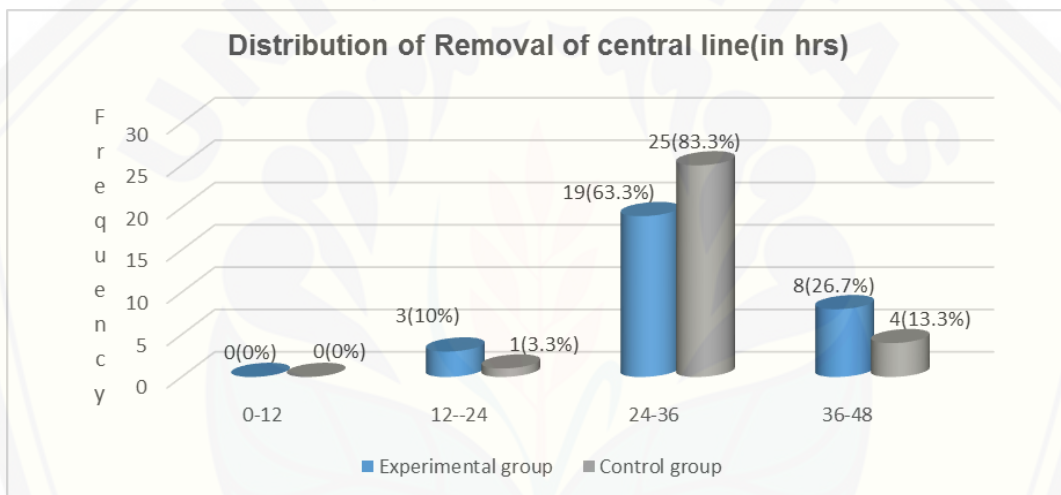


Figure 4: A bar diagram shows the Frequency distribution of post-surgical patients with regards to removal of central line (n=30).

Above figure depict that (73.3%), (20%), (6.7%) had their chest tube removal after cardiac surgery within 24-

36 hours, 36- 48 hours and in 12-24 hours respectively.

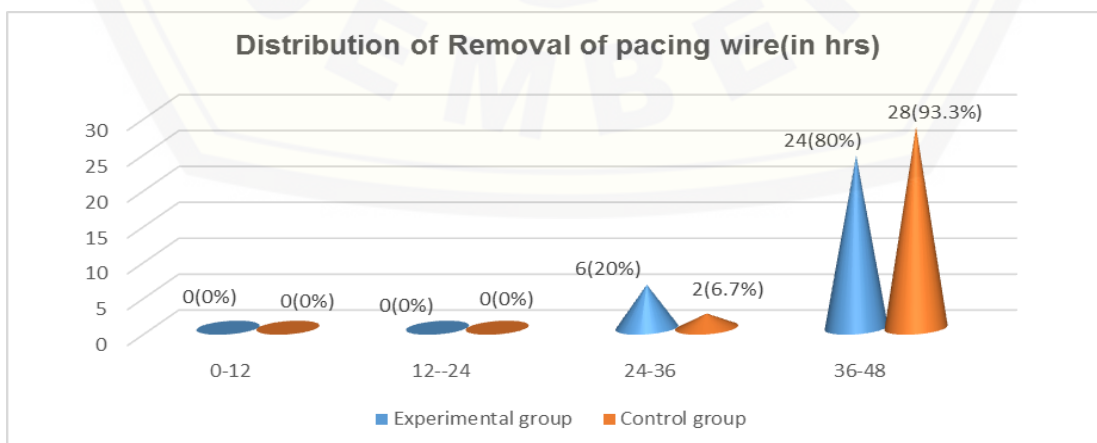


Figure 5: A bar diagram shows the Frequency distribution of post-surgical patients with regards to removal of pacing wire (n=30).

Above figure shows that (86.7%), (13.3%), had their chest tube removal after cardiac surgery within 36-48hours, and in 24-36 hours respectively.

pain medication within past four hours. The data was analysed to obtain frequency and percentage distribution of patient who received pain medication within past four hours.

**SECTION 2:- Pain medication received by patient within past four hours**

This section described the patient who were received

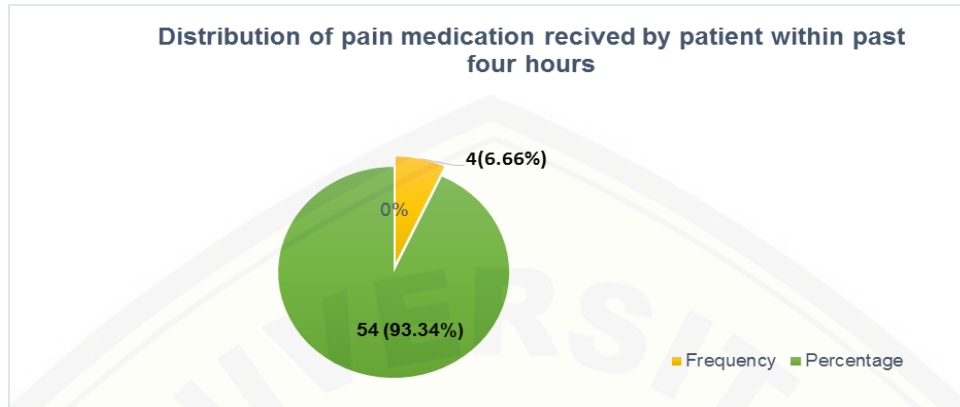


Figure 6: Shows the percentage wise distribution of pain medication received within past four hours (N=60).

The data presented in figure 6 indicated that, Pain medication received within past four hours by patient shows 6.66% before removal of invasive lines. Hence it can be interpreted that 93.34% of the patients have not taken any pain medication within past four hours of removal of invasive line.

surgical cardiac patients. The data was analysed by using mean, standard deviation, unpaired 't' & 'p' test and repeated measure ANOVA test comparing all together within the groups.

**SECTION 3:-Effectiveness of ice pack application on pain among post- surgical cardiac patient during invasive line removal.**

This section described the effectiveness of ice pack application on pain during invasive line removal in experimental group and control group among post-

**Objective-1** To identify the effect of ice pack application on pain among post-surgical patients during invasive line removal.

**H<sub>1</sub>**. There will be significant difference in the mean pre-test and post- test pain scores on ice pack application during removal of invasive lines.

Table 2: Comparison of pre-test and post-test of pain among post- surgical cardiac patients (N=60).

Invasive lines	Group	Comparison	Mean	SD	Unpaired 't' & p value		Repeated measures ANOVA
					Post-test1 EXP-CON	Post-test2 EXP-CON	EXP
Chest tube removal	Exp.	Pre-test	0.133	0.507	9.834 p=0.001*	1.115 p=0.270**	40.067 df=(2,58) p=0.001*
		Post-test 1	1.733	0.981			
		Post-test 2	0.401	0.814			
	Con	Pre-test	0.000	0.000			
		Post-test 1	4.267	1.015			
		Post-test 2	0.2	0.551			
Arterial line removal	Exp.	Pre-test	0.101	0.403	10.999 p=0.001*	0.336 p=0.738**	2.760 df=(2,58) p=0.072**
		Post-test 1	0.367	0.765			
		Post-test 2	0.067	0.365			
	Con	Pre-test	0.2	0.610			
		Post-test 1	3.4	1.302			
		Post-test 2	0.1	0.402			
Pacing wire removal	Exp.	Pre-test	0.000	0.000	11.062 p=0.001*	1,795 p=0.78**	11.528 df=(2,58)
		Post-test 1	0.533	0.861			
		Post-test 2	0.000	0.000			
	Con	Pre-test	0.000	0.000			
		Post-test 1	3.033	0.889			



		Post-test 2	0.2	0.610			p=0.002*
Central line removal	Exp.	Pre-test	0.2	0.610	10.5665	1.828	6.067 df=(2,58)
		Post-test 1	0.767	1.006			
		Post-test 2	0.133	0.507			
	Con	Pre-test	0.2	0.610			
		Post-test 1	3.6	1.069			
		Post-test 2	0.467	0.860			
					p=0.001*	p=0.073**	p=0.04*

Level of significance 0.05; df =58\*significant \*\*non-significant

Data in table 2 depict that ice pack application on pain score among post-surgical cardiac patients by using repeated measure ANOVA was found to have significant effects during chest tube removal (p=0.001), pacing wire removal (p=0.002) and central line removal (P=0.04). However ice pack application has no significant effect during arterial line removal (p=0.072) with respect to pain score.

**SECTION 4:- Effectiveness of ice pack application on physiological parameters during invasive line removal**

This section describes the effectiveness of ice pack application on physiological parameters during invasive

line removal between control group and experimental group. The data was analysed to obtain mean, standard deviation unpaired 't' & p by comparing post-land post-test-2 between experimental and control group. Repeated measures of ANOVA test was compared within the experimental group.

**Objective 2:** To identify the effect of ice pack on physiological parameters (respiration rate, heart rate and blood pressure) during invasive lines removal.

**H<sub>2</sub>-** There will be significant difference in the mean pre-test and post- test of respiratory rate on ice pack application during removal of invasive lines.

**Table 3: Comparison of pre-test and post-test of respiratory rate score among post- surgical cardiac patients (N=60).**

Invasive lines	Group	Comparison	Mean	SD	Unpaired 't' & p value		Repeated measures ANOVA
					Post-test1 EXP-CON	Post-test2 EXP-CON	EXP
Chest tube removal	Exp.	Pre-test	19.5	2.129	0.513	0.000	11.677 df=2,58
		Post-test 1	21.2	2.001			
		Post-test 2	20.667	1.647			
	Con.	Pre-test	19.667	1.295			
		Post-test 1	20.967	1.473			
		Post-test 2	20.667	1.348			
Arterial line removal	Exp.	Pre-test	19.467	1.358	2.114	1.095	4.863 df=2,58
		Post-test 1	20.433	1.654			
		Post-test 2	20.301	1.664			
	Con.	Pre-test	19.833	1.858			
		Post-test 1	21.433	1.994			
		Post-test 2	20.833	2.085			
Pacing wire removal	Exp.	Pre-test	19.667	1.647	1.283	3.285	3.227 df=2,58
		Post-test 1	20.433	1.736			
		Post-test 2	19.467	1.383			
	Con.	Pre-test	19.867	1.852			
		Post-test 1	21.033	1.884			
		Post-test 2	20.733	1.596			
Central line removal	Exp.	Pre-test	19.633	1.586	0.693	0.419	1.698 df=2,58
		Post-test 1	22.267	9.577			
		Post-test 2	20.05	1.978			
	Con.	Pre-test	19.6	1.613			
		Post-test 1	21.033	1.829			
		Post-test 2	20.7	1.704			
					p=0.610*	p=1.000**	p=0.001*
					p=0.039*	p=0.278**	p=0.011*
					p=0.205**	p=0.002*	p=0.047*
					p=0.491**	p=0.676**	p=0.676**

Level of significance 0.05; df= 58 \*significant \*\*non-significant

Data in table 3 shows that ice pack application on respiratory rate among post-surgical cardiac patient have significant effects during chest tube removal (p=0.001),

arterial line removal (p=0.011), and pacing wire removal (p=0.047). Whereas it was found to be insignificant during central line removal (p=0.676).

**Table 4: Comparison of pre-test and post-test of heart rate score among post-surgical cardiac patients (N=60).**

Invasive lines	Group	Comparison	Mean	SD	Unpaired 't' & p value		Repeated measures ANOVA
					Post-test1 EXP-CON	Post-test2 EXP-CON	EXP
Chest tube removal	Exp.	Pre-test	89.333	13.649	0.635  p=0.528**	0.476  p=0.636**	4.120  df=2,58  p=0.021*
		Post-test 1	91.4	13.52			
		Post-test 2	90.267	13.245			
	Con.	Pre-test	91.367	14.089			
		Post-test 1	93.567	12.894			
		Post-test 2	91.9	13.309			
Arterial line removal	Exp.	Pre-test	87.033	10.159	1.909  p=0.045*	1.165  p=0.249**	1.655  df=2,58  p=0.201**
		Post-test 1	88.433	10.602			
		Post-test 2	88.967	11.242			
	Con.	Pre-test	91.567	12.048			
		Post-test 1	94.0	11.942			
		Post-test 2	92.533	12.442			
Pacing wire removal	Exp.	Pre-test	86.333	10.812	2.054  p=0.045*	2.231  p=0.030*	1.145  df=2,58  p=0.325**
		Post-test 1	88.367	10.313			
		Post-test 2	87.333	10.895			
	Con.	Pre-test	90.4	9.298			
		Post-test 1	93.633	9.536			
		Post-test 2	93.067	8.913			
Central line removal	Exp.	Pre-test	84.867	9.511	3.078  p=0.003*	2.919  p=0.05*	7.437  df=2,58  p=0.001*
		Post-test 1	87.000	9.906			
		Post-test 2	86.6	9.765			
	Con.	Pre-test	92.633	9.182			
		Post-test 1	94.533	9.031			
		Post-test 2	94.067	10.048			

Level of significance 0.05; df= 58 \*significant \*\*non-significant

The data presented in table 4 shows that ice pack application on heart rate among post-surgical cardiac patient have significant effects during chest tube removal

(p=0.001) and arterial line removal (p=0.011). Whereas it was found to be insignificant during arterial line removal (p=0.201) and pacing wire removal (p=0.325).

**Table 5: Comparison of post-test 1 and post-test 2 of systolic blood pressure score among post-surgical cardiac patients (N=60).**

Invasive Lines	Group	Comparison	Mean	SD	Unpaired 't' & p value		Repeated measures ANOVA
					Post-test1 EXP-CON	Post-test2 EXP-CON	EXP
Chest tube removal	Exp.	Pre-test	111.211	14.079	1.572  p=0.121**	0.962  p=0.340**	0.646  df=2,58  p=0.528**
		Post-test 1	111.231	14.014			
		Post-test 2	112.323	15.16			
	Con.	Pre-test	114.831	14.156			
		Post-test 1	116.623	13.751			
		Post-test 2	115.971	13.773			
Arterial line removal	Exp.	Pre-test	111.772	11.318	1.455  p=0.151**	1.846  p=0.070**	0.434  df=2,58  p=0.650**
		Post-test 1	112.934	12.224			
		Post-test 2	112.672	10.026			
	Con.	Pre-test	116.501	11.688			
		Post-test 1	117.632	12.791			
		Post-test 2	117.772	11.331			

Pacing wire removal	Exp.	Pre-test	109.213	9.402	1.717	3.053	6.214
		Post-test 1	112.302	7.865			
		Post-test 2	110.435	8.904			
	Con.	Pre-test	114.701	10.554			
		Post-test 1	116.732	11.75			
		Post-test 2	117.802	9.845			
				p=0.091**	p=0.003*	p=0.04*	
Central line removal	Exp.	Pre-test	112.638	8.799	1.765	1.461	0.325
		Post-test 1	113.421	9.538			
		Post-test 2	13.821	9.026			
	Con.	Pre-test	117.421	10.407			
		Post-test 1	117.834	11.573			
		Post-test 2	117.401	10.036			
				p=0.083**	p=0.150**	p=0.724**	

Level of significance 0.05; df= 58 \*significant \*\*non-significant

In table 5 the above data depict that ice pack application on systolic blood pressure among post –surgical cardiac patient have significant effects during pacing wire removal (p=0.04).Whereas it was found to be

insignificant effects during chest tube removal, arterial line removal, and central line removal (p=0.528), (p=0.650), (p=0.724) respectively.

**Table 6: Comparison of post-test 1 and post-test 2 of diastolic blood pressure score among post- surgical cardiac patients (N=60).**

Invasive lines	Group	Comparison	Mean	SD	Unpaired 't' & p value		Repeated measures ANOVA
					Post-test1 EXP-CON	Post-test2 EXP-CON	EXP
Chest tube removal	Exp.	Pre-test	64.267	8.959	0.778	1.179	2.663
		Post-test 1	66.23	7.916			
		Post-test 2	66.66	7.985			
	Con.	Pre-test	65.267	7.899			
		Post-test 1	67.967	9.290			
		Post-test 2	68.900	7.097			
				p=0.440**	p=0.243**	p=0.078**	
Arterial line removal	Exp.	Pre-test	66.767	7.118	0.808	2.165	2.344
		Post-test 1	66.267	8.855			
		Post-test 2	66.301	7.773			
	Con.	Pre-test	68.167	7.096			
		Post-test 1	68.133	9.031			
		Post-test 2	70.533	7.366			
				p=0.422**	p=0.034*	p=0.912**	
Pacing wire removal	Exp.	Pre-test	67.179	6.561	2.203	3.040	0.0228
		Post-test 1	66.201	8.619			
		Post-test 2	66.067	6.158			
	Con.	Pre-test	69.6	7.6			
		Post-test 1	70.8	7.513			
		Post-test 2	71.133	7.741			
				p=0.032*	p=0.004*	p=0.797**	
Central line removal	Exp.	Pre-test	66.3	5.44	2.093	1.263	2.402
		Post-test 1	65.9	5.695			
		Post-test 2	68.167	6.497			
	Con.	Pre-test	70.0	6.868			
		Post-test 1	69.6	7.833			
		Post-test 2	70.267	6.384			
				p=0.041*	p=0.212**	p=0.099**	

Level of significance 0.05; df =58 \*significant \*\*non-significant

In table 6 the data represent that ice pack application on diastolic blood pressure among post –surgical cardiac patient have insignificant effects during chest tube removal (p=0.078), arterial line removal(p=0.912), pacing wire removal(p=0.797) and central line removal (p=0.099). Hence it is interpreted that the patient have

slight changes on diastolic blood pressure after ice pack application.

**SECTION 5:- Association between pain scores and selected demographic variables**

This section describes the association between post- test pain score during chest tube removal with selected



demographic variables of post- surgical cardiac patients of experimental group and control group. The data was analysed to obtain chi square and p value.

**H<sub>5</sub>**- There will be significant association between post-test pain scores and selected demographic variables.

**Objective:** To find out association between pain scores and selected demographic variables.

**Table 7: Association between post-test pain scores during chest tube removal with selected demographic variables of post- surgical cardiac patients in experimental group (n=30).**

Sl. No	Demographic variables	f	Level of pain		Chi square	df	Table value	P value
			No pain	Mild pain				
1	<b>Age(in years)</b>				2.472	3	7.815	0.480**
	20-35	03	03	00				
	36-50	02	02	00				
	51-65	08	07	01				
	65 and above	17	12	05				
2	<b>Gender</b>				2.907	1	3.841	0.088**
	Male	19	17	02				
	Female	11	07	04				
3	<b>Education</b>				1.291	3	7.815	0.731**
	Primary	07	05	02				
	High school	13	10	03				
	Higher secondary	07	06	01				
	Graduate & above	03	03	00				
4	<b>Occupation</b>				1.696	3	7.815	0.638**
	Unemployed	08	06	02				
	Skilled	10	08	02				
	Unskilled	05	05	00				
	Retired	07	05	02				
5	<b>Type of work</b>				0.343	2	5.991	0.843**
	Secondary work	13	10	03				
	Moderate work	16	13	03				
	Heavy work	01	01	00				
6	<b>Personal habits</b>				6.562	3	7.815	0.087**
	Smoking	03	03	00				
	Alcoholic	05	05	00				
	Chewing tobacco	06	06	00				
	None	16	10	06				
7	<b>Operative procedure</b>				2.727	3	7.815	0.436**
	Coronary Artery Bypass Graft.	22	16	06				
	Valve replacement surgeries	03	03	00				
	Device closure	04	04	00				
	Any other	01	01	00				
8	<b>Any previous surgeries</b>				0.259	1	3.841	0.611**
	Minor	01	01	00				
	Nil	29	23	06				
9	<b>Number of Invasive lines</b>				No cross table			
	Four	30	24	06				
10	<b>Removal of Arterial line (in hrs.)</b>				1.129	2	5.991	0.569**
	12- 24	16	13	03				
	24-36	11	08	03				
	36-48	03	03	00				
11	<b>Removal of chest tube (in hrs.)</b>				0.000	1	3.841	1.000**
	12- 24	10	08	02				
	24-36	20	16	04				

12	<b>Removal of central line (in hrs.)</b>				1.505	2	5.991	0.471**
	12- 24	03	03	00				
	24-36	19	14	05				
	36-48	08	07	01				
13	<b>Removal of pacing wire (in hrs.)</b>				0.052	1	3.841	0.819**
	24-36	06	05	01				
	36-48	24	19	05				

Level of significance 0.05 \*\* non significant

In table 8 Chi-square values was calculated to find out the association between the post-test pain score during chest tube removal in experimental group with their selected demographic variables which reveals that there is no significant association between post-test pain score during chest tube removal with age, gender, educational

status, occupation, type of work, personal habits, operative procedure, previous surgery, number of invasive line and removal of all invasive lines. Hence, it can be interpreted that there is no association of post- test pain score of chest tube removal with demographic variables in the experimental group.

**Table 9: Association between post-test pain scores of chest tube removal and selected demographic variables of post- surgical cardiac patients in control group (n=30).**

Sl. No	Demographic variables	f	Level of pain		Chi square	df	Table value	P value
			No pain	Mild pain				
1	<b>Age(in years)</b>				1.104	3	7.815	0.776**
	20-35	02	02	00				
	36-50	20	16	04				
	51-65	07	7	00				
65 and above	01	1	00					
2	<b>Gender</b>				3.997	1	3.841	0.136**
	Male	19	18	01				
	Female	11	08	03				
3	<b>Education</b>				10.333	3	7.815	0.111**
	Primary	03	01	02				
	High school	09	08	01				
	Higher secondary	10	09	01				
Graduate & above	08	08	00					
4	<b>Occupation</b>				2.152	2	5.991	0.708**
	Unemployed	07	05	02				
	Skilled	19	17	02				
	Retired	04	04	00				
5	<b>Type of work</b>				0.839	2	5.991	0.933**
	Secondary work	15	13	02				
	Moderate work	11	09	02				
	Heavy work	04	04	00				
6	<b>Personal habits</b>				6.989	3	7.815	0.072**
	Smoking	04	02	02				
	Alcoholic	11	11	00				
	Chewing tobacco	04	03	01				
	None	11	10	01				
7	<b>Operative procedure</b>				2.679	3	7.815	0.443**
	Coronary Artery Bypass Graft.	20	18	02				
	Valve replacement surgeries	07	06	01				
	Device closure	01	01	00				
	Any other	02	01	01				
8	<b>Any previous surgeries</b>				0.33	2	5.991	0.847**
	Minor	01	01	00				
	Major	01	01	00				
	Nil	28	24	04				

9	<b>Number of Invasive lines</b> Four	30	26	04	No cross tabulation			
10	<b>Removal of Arterial line (in hrs.)</b>				0.928	2	5.991	0.628**
	12- 24	09	08	01				
	24-36	17	14	03				
	36-48	04	04	00				
11	<b>Removal of chest tube (in hrs.)</b>				1.514	2	5.991	0.469**
	12- 24	03	02	01				
	24-36	24	21	03				
	36-48	03	03	00				
12	<b>Removal of central line (in hrs.)</b>				1.175	2	5.991	0.555**
	12- 24	01	01	00				
	24-36	25	21	04				
	36-48	04	04	00				
13	<b>Removal of pacing wire (in hrs.)</b>				0.252	1	3.841	0.615**
	24-36	02	02	00				
	36-48	28	24	04				

Level of significance 0.05,\*\* non- significant

In table 9 Chi-square values was calculated to find out the association between the post- test pain score of chest tube in control group with their selected demographic variables which reveals that there is no significant association between pain scores during chest tube removal with age, gender, educational status, occupation, type of work, personal habits, operative procedure, previous surgery, number of invasive line and removal of all invasive lines. Hence, it can be interpreted that there is no association of pain score during chest tube removal with demographic variables.

## DISCUSSION

Cold application is an effective technique for pain relief. This technique reduces the speed of nervous conductance and pain. Similarly, based on the gate control theory of pain, stimulation of thick fibres through methods such as cooling may close the gate and reduce pain.<sup>[5]</sup> Ever since pain is the most common complication in post-cardiac surgery patient that cause discomfort. So proper intervention in preventing and reducing the occurrence has become the essential nursing intervention for nurses who are taking care of post-surgical patient.

This study assess the effectiveness of ice pack application on pain and physiological parameters during removal of invasive lines. Total 60 post- surgical cardiac patient were selected and divided in to two equal groups. Experimental group taken ice pack application where the control group taken routine care. The result indicate that there is a significant improvement on pain by ice pack application and this low cost measure are free from any side effect.

### Effectiveness of ice pack application on pain

In the present study the effectiveness of ice pack application on pain during chest tube showed significant difference ( $p=0.001$ ) at zero minute and after fifteen minutes ( $p=0.270$ ) among post- surgical cardiac patient.

Hence the study showed that ice pack application was effective method ( $p=0.01$ ) during chest tube removal.

A similar study conducted by Nurcan Ertug, to assess the effectiveness of cold application on pain during chest tube removal showed significant difference ( $1.13\pm 1.31$ ;  $0.27\pm 0.44$ ;  $0.27\pm 0.44$ ) in pre- test and post- test ( $8.57\pm 0.49$ ;  $8.73\pm 0.57$ ;  $8.63\pm 0.48$ ) at zero minute and 15 minute. Which is statistically significant at ( $p < 0.05$ ) level. Hence the study resulted that ice pack application found to be effective on pain during chest tube removal.<sup>[25]</sup>

### Effect of ice pack application on physiological parameters during invasive line removal

The present study assessed the effect of ice pack application on heart rate during invasive line removal among post- surgical cardiac patient. Which showed that there is significant difference in post- test-1&2 ( $p=0.045$ ), ( $p=0.249$ ). Which revealed that HR shows significant changes ( $p=0.201$ ) during invasive line removal, which was statistically proved ( $p < 0.05$ ) Hence the study interpreted the effect of ice pack application showed significant changes on heart rate.

A similar study conducted by Erdogan A to assess the pain intensity after ice pack application on heart rate among cardiac surgery patents. The findings of the study shows that the pain occurred at different levels cause change in heart rate during ice application. The pain score after ice pack was ( $7.36 \pm 1.34$  and  $7.88 \pm 0.79$ ) of the study. Thus the study concluded that there was a significant changes in heart rate after ice pack application.<sup>[32]</sup>

### Association between post- test pain score with selected demographical variable

In the present study the association between post-test and selected demographical variable were checked and found that there was no association between age ( $p=0.776$ ),



gender ( $p=0.136$ ), educational status( $p=0.111$ ), occupation, type of work, personal habits, operative procedure, any previous surgery, no of invasive lines and removal of all invasive lines. The result is consistent with the study conducted by Irene Lie published that there was no association between the level of pain with selected demographic variables such as age,(80%) of elderly,(60%) of older adults gender( $F = 40\%$ ), ( $M = 35\%$ ). Which is statistically significant at ( $p < 0.05$ ) level.<sup>[46]</sup>

## CONCLUSION

The present study assessed the effectiveness of ice pack application on pain and physiological parameters during removal of invasive lines among post- surgical cardiac patients. The major findings of the study revealed that there is significant difference in pre- test and post- test pain score. Which depict that ice pack application is effective on pain and physiological parameters during invasive line removal. This intervention can be added as an adjunct treatment for patients. This nursing intervention is simple and free from side effect so patient can use at home also to reduce pain.

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## EFFECTIVENESS OF VIDEO ASSISTED TEACHING PROGRAMME ON KNOWLEDGE REGARDING CARE OF CHILDREN ON MECHANICAL VENTILATOR AMONG STAFF NURSES WORKING IN PEDIATRIC INTENSIVE CARE UNITS OF SELECTED HOSPITALS AT BELGAUM

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### ABSTRACT

**Background:** Mechanical ventilation is a method to mechanically assist or replace spontaneous breathing. This may involve a machine called a ventilator or the breathing may be assisted by a physician or other suitable person compressing a bag or a set of bellows. Traditionally divided into negative-pressure ventilation, where air is essentially sucked into the lungs, or positive pressure ventilation, where air (or another gas mix) is pushed into the trachea. Owing to the anatomy of the human pharynx, larynx, and esophagus and the circumstances in which ventilation is required then additional measures are often required to "secure" the airway during positive pressure ventilation to allow proper passage of air into the trachea and avoid air enters into the esophagus and stomach. **Method:** This was pre-experimental study a total of 500 subjects was selected through non-probability convenient sampling technique. Pre-experimental one group pre-test, post-test design was used. Data was collected by structured knowledge questionnaire. Data collected under the 2 sections (socio-demographic data, knowledge questionnaires). The reliability of the tool was established by spilt half method formula. The reliability result of knowledge was  $r = 0.902829$ . Video assisted teaching programme was developed effective for staff nurses regarding the care of children on ventilators, Content validity of the tool was established by six experts. Data was analyzed by using descriptive statistics and inferential statistically in terms of frequency, percentage, mean, standard deviation, Chi-square values. **Results:** With regard to the pre-test knowledge assessment, the mean percentage of response was 66.97 %, with mean and SD of  $17.62 \pm 2.43$ , which increased to 91.67% with mean and SD of  $29.43 \pm 1.82$  in the post-test. Further effectiveness of planned video assisted teaching programme was tested by inferential statistics using paired 't' test [ $t = 90.4970, P < 0.05$ ]. On the whole, the analysis revealed that the video assisted teaching programme was very effective in increasing the knowledge of staff nurses on care of children on ventilator. **Conclusion:** Video assisted teaching programme was effective in increasing the knowledge of staff nurses regarding care of children on ventilator

**KEYWORDS:** Effectiveness; video assisted teaching; ventilator; pediatric intensive care unit.

### 1. BACKGROUND

Mechanical ventilation is often a life-saving intervention, but carries many potential complications, including pneumothorax, airway injury, alveolar damage, and ventilator-associated pneumonia. Healthy and active children are beautiful gift to the world. Unfortunately, children get disease, some from the environment and some from heredity. Nurses should be very skillful in care of children, especially in Pediatric Intensive Care

Units (PICU).<sup>[1]</sup> Increasing complexity of pediatric critical care has required corresponding evolution in the sophistication of Pediatric Critical Care Nursing. The role of nursing in this setting is multifaceted. The nurse serves as a form of local system monitor, continually monitoring all physiological parameters and treatment devices as well as the child's body. The nurse should be very skillful in handling devices like mechanical ventilators, infusion pumps, bedside multi parameter



monitors and other ancillary equipment in Pediatric ICU.<sup>[2]</sup>

The incidence of ventilator associated pneumothorax in pediatric ICUs has been reported to be between 4.5%-8%, ventilator associated pneumonia 20-25 % and accidental extubation around 4.1 %, according to the research studies from different parts of the world.<sup>[3]</sup> In United States 12.8%/ 100000 population suffer ventilator associated lung injury..and.among. These Patients, 9% Died.due.to.this.lung.injury.every.year.<sup>[4]</sup>

Many deaths occur in Pediatric ICU's due to ventilator associated complications. The common complications are ventilator associated pneumonia, accidental extubation, septicemia etc. The incidence of mortality rate in pediatric ICU's is around 14%. The Pediatric ICU Nurse should have adequate knowledge and aptitude in ventilator care.<sup>[5]</sup> The mortality in Pediatric ICU can be reduced by standardizing the protocols of care of children on ventilators. Assessing the knowledge level of the individual staff in the PICU will help in identifying the lacunae in their skill, knowledge and evolve strategies to improve the training of critical care nurses.<sup>[6]</sup> 'Each child is a precious gift of lord', so no complication occurs in the PICU's due to lack of knowledge and skill in nurses.<sup>[7]</sup>

## 2. Methods

**2.1 Study Area:** The study was conducted from July 1 2019 to August 1 2019 in the selected Pediatric intensive care unit hospitals at Belagavi.

### 2.2 Study design

One-group pre-test post-test design judges the effect of the treatment by the difference between the pre-test and post-test scores without comparing the control group.

### 2.3 Sample size determination

Convenient sampling techniques were used to select staff nurses.

### 2.4 Data collection procedures

Data was collected in selected pediatric intensive care unit hospitals from 1-10-2019 to 1-11-2019 after obtaining the permission from concerned authorities. The pre test was conducted using structured knowledge questionnaire and video assisted teaching program was administered. A post test was conducted on same subjects seven days after the administration of video assisted teaching programe using the same structured questionnaire as used for the pre-test.

### 2.5 Data processing and analysis

Data was analyzed using both descriptive and inferential statistics. Distribution of subjects with respect to demographic variables was represented using frequency and percentage. Mean, standard deviation, and mean percentage were used to describe the knowledge of Staff nurses regarding the care of children on mechanical

ventilation. The Statistical significance of the effectiveness of the video assisted teaching programme will be analyzed by paired't' test. Data will be presented in tables, graphs and diagrams. Chi-square test will be used to find out the association between knowledge of staff nurses and selected socio-demographic variables.

## 2.6 Ethical Consideration

An Ethical clearance was obtained before conducting this research from the Himalayan University College of health and medical sciences. All study participants were informed about the purpose of the study, their right to deny participation, anonymity and confidentiality of the information.

## 3. RESULT

### 3.1. Description of socio-demographic characteristics of sample.

Table 1: 341 respondents age group between 31 to 40 years are 68.20 percent 110 respondents age group between 41 years are 22.0 percent and 49 respondents are age group between 21-30 years are 9.80 percent.339 respondents are male staffs 67.80 percent and 161 respondents are female staffs 32.20 percent.223 respondents are Muslim religion, 44.60 percent, 188 respondents are Christian religion 37.60 and 89 respondents are Hindu religion 17.80percent. Most (66.20%) of staff nurses had General Nursing Midwifery education. 17.80 percent of them completed Basic B.Sc Nursing education and16.00 Percentage PB B.Sc. Nursing education. 49.80 percent of staff nurses were married and 30.40 percent of unmarried remaining 19.80 were widowed. 41.20 percent of staff nurses attended the training program on care of children on ventilator and 58.80 percent of them did not attend the training program. Most 39.80 percent of staff nurses had 7 years of experience, 35.80 percent of them had 1-3 years and 24.40 percent of them had an experience of 4 to 6 years.

### 3.2: Comparison of pretest and posttest levels of knowledge of respondents

Table; 2: Categorization of the staff nurses on the basis of their level of knowledge was done as follows: pretest 18.60 percent low knowledge scores 65.80 percentage average knowledge levels and 15.60 percentage high level knowledge. Posttest knowledge score of staff nurses having high score.

### 3.3: Association between pretest knowledge levels with demographic characteristics

Table;3: Assessment of the level of pretest knowledge of staff nurses with demographic characteristics. Age group between 21-30 years of age group had low knowledge 4.8 percent knowledge and 31-40 age group staff nurses had high knowledge 68.2 percent knowledge regarding care of children on ventilator. Gender pretest knowledge of staff nurses male had high knowledge 67.8 percent and female staff nurse had low knowledge 32.2 percent knowledge regarding care of children on ventilator. Religion pretest knowledge of staff nurse's Muslim

religion had high knowledge 44.6 percent. Hindu religion had low knowledge 17.8 percent regarding care of children on ventilator educational status. Diploma nursing had high knowledge 66.2 percentage Bsc nursing 17.8 percentages and 16.00 percentage PB Bsc nursing had low knowledge regarding care of children on ventilator. Marital status married had high knowledge 49.8 percentage single had knowledge 30.4 percentage and widow had 19.8 percentage low knowledge regarding care of children on ventilator. 58.8 percent of staff nurses not attended any educational programme and 41.2 percent of staff nurses attended educational programme on care of children on ventilator. 39.8 percent of staff nurses had 7 years of experiences 35.8 percent of 1-3 year of experiences and 24.4 percent of 4-6 years of work experiences.

### 3.4 Association between posttest knowledge levels with demographic characteristics

Table; 4: Assessment of the level of posttest knowledge of staff nurses with demographic characteristics. Age group between 21-30 years of age group had low knowledge 4.8 percent knowledge and 31-40 age group staff nurses had high knowledge 68.2 percent knowledge regarding care of children on ventilator. Gender pretest knowledge of staff nurses male had high knowledge 67.8 percent and female staff nurse had low knowledge 32.2 percent knowledge regarding care of children on ventilator. Religion pretest knowledge of staff nurse's Muslim religion had high knowledge 44.6 percent. Hindu religion had low knowledge 17.8 percent regarding care of children on ventilator educational status. Diploma nursing had high knowledge 66.2 percentage Bsc nursing 17.8 percentages and 16.00 percentage PB Bsc nursing had low knowledge regarding care of children on ventilator. Marital status married had high knowledge 49.8 percentage single had knowledge 30.4 percentage and widow had 19.8 percentage low knowledge regarding care of children on ventilator. 58.8 percent of staff nurses not attended any educational programme and 41.2 percent of staff nurses attended educational programme on care of children on ventilator. 39.8 percent of staff nurses had 7 years of experiences 35.8 percent of 1-3 year of experiences and 24.4 percent of 4-6 years of work experiences.

**Table 1: Association between pre-test knowledge scores of staff nurses regarding care of children on ventilator and selected socio-demographic variables.**

Demographic Profile	No of Respondents	% of Respondents
<b>Age groups- 21-30 years</b>	49	9.80
31-40 yrs	341	68.20
41+ yrs	110	22.00
<b>Gender- Male</b>	339	67.80
Female	161	32.20
<b>Religion -Hindu</b>	89	17.80
Christian	188	37.60
Muslim	223	44.60
<b>Educational status-GNM</b>	331	66.20
Basic Bsc/P.B. BSc Nursing	89	17.80

### 3.5 Comparison of pretest and posttest total knowledge and its component scores by dependent t test

Table;5: Comparison of mean percentage of the knowledge scores of the pretest and posttest and its component scores by dependent t test, total knowledge pretest mean 17.62 and SD 2.43 and post test reveals an increase of mean 29.43 SD 1.82 and mean percentage effect of 66.97. Comparison of area wise mean and SD of the knowledge score in the area of general information on "care of children on ventilator" shows that the pre-test mean percentage of knowledge score was 7.0 and 1.73. whereas post test mean percentage of knowledge score was 80.33 percent with mean and SD 12.63±0.96. mechanical ventilator shows that pre-test mean percentage of knowledge score was 53.73 percent with mean and SD 3.56±0.90. Whereas post test mean percentage of knowledge score was shows mean and SD 5.48±0.64. Prevention of ventilator associated complications shows that percentage score was 36.66 percent with pretest mean and SD 2.55±0.79. Whereas post test mean percentage of knowledge score was shows mean and SD 3.48±0.54. Care of child shows that mean percentage score was 111.63 percent with pretest mean and SD 1.11±0.62. Whereas post test mean percentage of knowledge score was shows mean and SD 2.33±0.59. Care of ventilator mean percentage score was 61.67 percent with pretest mean and SD 3.40±0.80. Whereas post test mean percentage of knowledge score was shows mean and SD 5.50±0.83.

**Section D: Testing of Hypothesis:** To evaluate the effectiveness of video assisted teaching a research hypothesis was formulated.

### H<sub>1</sub> - A Significant Difference will be found between post-test and pre-test knowledge scores with 0.05 level of significance

Paired 't' test was used to find out the significant difference between the pre-test and post-test knowledge scores of staff nurses regarding care of children on ventilator.

Post graduate nursing	80	16.00
<b>Marital status -Single</b>	152	30.40
Married	249	49.80
Widowed/Divorced	99	19.80
<b>Educational programme- Yes</b>	206	41.20
No	294	58.80
<b>Work experience as staff nurse</b>		
-1-3 years	179	35.80
4-6 years	122	24.40
7+ years	199	39.80
<b>Total</b>	<b>500</b>	<b>100.0</b>

Table II: Comparison of pretest and posttest levels of knowledge of respondents.

Levels of knowledge	Pretest	%	Posttest	%
Low level	93	18.60	0	0.00
Average	329	65.80	0	0.00
High level	78	15.60	100	100.00
Total	500	100.00	100	100.00

Table III: Association between pretest knowledge levels with demographic characteristics.

Characteristics	Pretest levels of knowledge								Chi-square	df	p-value
	Low level	%	Average	%	High level	%	Total	%			
<b>Age groups -21-30yrs</b>	14	28.57	33	67.35	2	4.08	49	9.80	11.2066	4	0.0244*
31-40 yrs	56	16.42	232	68.04	53	15.54	341	68.20			
41+ yrs	23	20.91	64	58.18	23	20.91	110	22.00			
<b>Gender -Male</b>	61	17.99	224	66.08	54	15.93	339	67.80	0.2932	2	0.8637
Female	32	19.88	105	65.22	24	14.91	161	32.20			
<b>Religion -Hindu</b>	15	16.85	58	65.17	16	17.98	89	17.80	7.1148	4	0.1300
Christian	45	23.94	113	60.11	30	15.96	188	37.60			
Muslim	33	14.80	158	70.85	32	14.35	223	44.60			
<b>Education -G.N.M</b>	79	23.87	220	66.47	32	9.67	331	66.20	37.4899	4	0.0001*
Basic Bsc/P.B. BSc Nursing	6	6.74	57	64.04	26	29.21	89	17.80			
Post graduate nursing	8	10.00	52	65.00	20	25.00	80	16.00			
<b>Marital status -Single</b>	26	17.11	101	66.45	25	16.45	152	30.40	3.3379	4	0.5030
Married	44	17.67	170	68.27	35	14.06	249	49.80			
Widowed/Divorced	23	23.23	58	58.59	18	18.18	99	19.80			
<b>educational programme -Yes</b>	21	10.19	143	69.42	42	20.39	206	41.20	19.1547	2	0.0001*
No	72	24.49	186	63.27	36	12.24	294	58.80			
<b>Work experience 1-3 years</b>	41	22.91	114	63.69	24	13.41	179	35.80	7.8377	4	0.0977
4-6 years	14	11.48	89	72.95	19	15.57	122	24.40			
7+ years	38	19.10	126	63.32	35	17.59	199	39.80			
Total	93	18.60	329	65.80	78	15.60	500	100.0			

Table IV: Association between posttest knowledge levels with demographic characteristics.

Characteristics	Posttest levels of knowledge							
	Low level	%	Average	%	High level	%	Total	%
<b>Age groups -21-30yrs</b>	0	0.00	0	0.00	49	100.0	49	9.80
31-40 yrs	0	0.00	0	0.00	341	100.0	341	68.20
41+ yrs	0	0.00	0	0.00	110	100.0	110	22.00
<b>Gender -Male</b>	0	0.00	0	0.00	339	100.0	339	67.80
Female	0	0.00	0	0.00	161	100.0	161	32.20
<b>Religion -Hindu</b>	0	0.00	0	0.00	89	100.0	89	17.80
Christian	0	0.00	0	0.00	188	100.0	188	37.60
Muslim	0	0.00	0	0.00	223	100.0	223	44.60
<b>Education -G.N.M</b>	0	0.00	0	0.00	331	100.0	331	66.20
Basic Bsc/P.B. BSc Nursing	0	0.00	0	0.00	89	100.0	89	17.80
Post graduate nursing	0	0.00	0	0.00	80	100.0	80	16.00
<b>Marital status -Single</b>	0	0.00	0	0.00	152	100.0	152	30.40



Married	0	0.00	0	0.00	249	100.0	249	49.80
Widowed/Divorced	0	0.00	0	0.00	99	100.0	99	19.80
<b>Educational programme -Yes</b>	0	0.00	0	0.00	206	100.0	206	41.20
No	0	0.00	0	0.00	294	100.0	294	58.80
<b>Work experience -1-3 years</b>	0	0.00	0	0.00	179	100.0	179	35.80
4-6 years	0	0.00	0	0.00	122	100.0	122	24.40
7+ years	0	0.00	0	0.00	199	100.0	199	39.80
<b>Total</b>	<b>0</b>	<b>0.00</b>	<b>0</b>	<b>0.00</b>	<b>500</b>	<b>100.0</b>	<b>500</b>	<b>100.0</b>

**Table V: Comparison of pretest and posttest total knowledge and its component scores by dependent t test.**

Variables	Time	Mean	SD	Mean Diff.	SD Diff.	%of effect	Paired t	P-value
Total knowledge	Pretest	17.62	2.43					
	Posttest	29.43	1.82	-11.80	2.92	-66.97	-90.4970	0.0001*
General information on care of children	Pretest	7.01	1.73					
	Posttest	12.63	0.96	-5.63	1.89	-80.33	-66.7289	0.0001*
Mechanical ventilator	Pretest	3.56	0.90					
	Posttest	5.48	0.64	-1.91	1.04	-53.73	-41.0163	0.0001*
Prevention of ventilator associated complications	Pretest	2.55	0.79					
	Posttest	3.48	0.54	-0.93	0.90	-36.66	-23.1873	0.0001*
Care of children	Pretest	1.11	0.62					
	Posttest	2.33	0.59	-1.23	0.78	-111.03	-35.2959	0.0001*
Care of ventilator	Pretest	3.40	0.80					
	Posttest	5.50	0.83	-2.10	1.14	-61.67	-41.1611	0.0001*

#### 4. DISCUSSION

The present study was conducted to evaluate the effectiveness of video assisted teaching programme on care of children on mechanical ventilator. In order to achieve the objectives of the study, pre-experimental one group pre-test post-test design with an evaluative approach was adopted. The sample was selected by convenient sampling technique. The sample comprised of 500 staff nurses and the data was collected using a structured questionnaire from them before and after the administration of video assisted teaching programme.

**4.1 Description of the socio-demographic variables of the staff nurses:** Findings revealed that the most (68.20%) of staff nurses were in the age of 31-40 years and 29.80% of staff nurses were in the age of 21-30 years and 22 % of staff nurses 41 years and above each. 67.80 percent of them were males and 32.20 percent of them were females. Majority of staff nurses 44.60 percent were belonging to Muslim religion and 37.60 percent of them were Christian. And 17.80 percent of them were Hindu religion.

Distribution of staff nurses according to their educational status shows that 66.20 percent of staff nurses had general nursing midwifery, 17.80 percent of them completed Basic B.Sc and 16.00 percent PB BSc. Nursing and no staff nurses with post graduation in nursing. 49.80 percent of staff nurses were married, 30.40 percent of them were unmarried and 19.80 percent were widow.

41.20 percent of staff nurses attended the training program on care of children on mechanical

ventilator. 58.80 Percent of staff nurses not attended any educational programme. Most 39.80 percent of staff nurses had 7 years of experience, 24.40 percent of them had 4-6 years, and 35.80 percent of them had an experience of 1-3 years.

#### 4.2 Assessment of the pre-test knowledge of staff nurses on care of children on mechanical ventilator

Findings of the present study showed that majority (65.80%) of the staff nurses had only average knowledge and 18.60 percent of the sample had Low knowledge and there were only 15.60 percent of staff nurses had high knowledge.

A experimental study was designed to assess the knowledge of staff nurses regarding care of children on mechanical ventilator. Results showed that the majority of staff nurses had moderately adequate knowledge regarding care of children on mechanical ventilator. The staff nurses' level of education had a significant association with their practice.<sup>[8]</sup>

#### 4.3: Area-wise assessment of knowledge scores of staff nurses on care of children on mechanical ventilator

Comparison of mean percentage of the knowledge scores of the pretest and posttest and its component scores by dependent t test, total knowledge pretest mean 17.62 and SD 2.43 and post test reveals an increase of mean 29.43 SD 1.82 and mean percentage effect of 66.97. Comparison of area wise mean and SD of the knowledge score in the area of general information on "care of children on ventilator" shows that the pre-test mean percentage of knowledge score was 7.0 and 1.73. whereas post test mean percentage of knowledge score was 80.33 percent with mean and SD 12.63±

0.96. mechanical ventilator shows that pre-test mean percentage of knowledge score was 53.73 percent with mean and SD  $3.56 \pm 0.90$ . Whereas post test mean percentage of knowledge score was shows mean and SD  $5.48 \pm 0.64$ . Prevention of ventilator associated complications shows that percentage score was 36.66 percent with pretest mean and SD  $2.55 \pm 0.79$ . Whereas post test mean percentage of knowledge score was shows mean and SD  $3.48 \pm 0.54$ . Care of child shows that mean percentage score was 111.63 percent with pretest mean and SD  $1.11 \pm 0.62$ . Whereas post test mean percentage of knowledge score was shows mean and SD  $2.33 \pm 0.59$ . Care of ventilator mean percentage score was 61.67 percent with pretest mean and SD  $3.40 \pm 0.80$ . Whereas post test mean percentage of knowledge score was shows mean and SD  $5.50 \pm 0.83$ . 4.4 Shortage of Trained Health Workers

#### 4.4: Evaluation of the effectiveness of video assisted teaching programme on care of children on mechanical ventilator

##### 4.4.1: Comparison of level of knowledge of staff nurses in pre-test and post-test

In pretest knowledge score majority 65.80 percent of staff nurses had average knowledge, 18.60 percent of staff nurses had low knowledge and only 15.60 percent of the staff nurses had High knowledge regarding care of children on ventilator. Whereas in post test knowledge scores all the staff nurses had High knowledge.

##### 4.4.2: Area-wise effectiveness of video assisted teaching programme on care of children on mechanical ventilator

Comparison of mean percentage of the knowledge scores of the pretest and posttest and its component scores by dependent t test, total knowledge pretest mean 17.62 and SD 2.43 and post test reveals an increase of mean 29.43 SD 1.82 and mean percentage effect of 66.97. Comparison of area wise mean and SD of the knowledge score in the area of general information on "care of children on ventilator" shows that the pre-test mean percentage of knowledge score was 7.0 and 1.73. whereas post test mean percentage of knowledge score was 80.33 percent with mean and SD  $12.63 \pm 0.96$ . mechanical ventilator shows that pre-test mean percentage of knowledge score was 53.73 percent with mean and SD  $3.56 \pm 0.90$ . Whereas post test mean percentage of knowledge score was shows mean and SD  $5.48 \pm 0.64$ . Prevention of ventilator associated complications shows that percentage score was 36.66 percent with pretest mean and SD  $2.55 \pm 0.79$ . Whereas post test mean percentage of knowledge score was shows mean and SD  $3.48 \pm 0.54$ . Care of child shows that mean percentage score was 111.63 percent with pretest mean and SD  $1.11 \pm 0.62$ . Whereas post test mean percentage of knowledge score was shows mean and SD  $2.33 \pm 0.59$ . Care of ventilator mean percentage score was 61.67 percent with pretest mean and SD  $3.40 \pm 0.80$ . Whereas post test mean percentage of knowledge score was shows mean and SD  $5.50 \pm 0.83$ .

#### 4.5: Testing of Hypothesis

##### 4.5.1: Significance of difference between pre-test and post-test knowledge scores of staff nurses

Paired 't' test was used to find out the significance of difference between pre-test and post-test knowledge scores of staff nurses on care of children on mechanical ventilator. Findings revealed that the difference between mean pre-test ( $17.62 \pm 2.43$ ) and post-test ( $29.43 \pm 1.82$ ) knowledge scores of staff nurses found to be statistically significant at 0.05 level of significance [ $t = 90.4970$ ,  $p < 0.05$ ]. It indicated that video assisted teaching programme was very effective in improving the knowledge of staff nurses on care of children on mechanical ventilator.

A study was carried out aiming at assessing the effects of a training program on the knowledge, attitude and practices (KAP) of health care workers (HCWs) in pediatric intensive care unit regarding care of children on ventilator. Results showed significant improvements in the knowledge of the trained staff nurses after training, the 500 staff nurses obtained higher mean comprehension score ( $17.62 \pm 2.43$ ), higher mean practice score ( $29.43 \pm 1.82$ ), and higher mean general scores ( $32.3 \pm 4.6$ ) compared to the mean scores they obtained in the pre-test ( $5.7 \pm 1.5$ ;  $7.4 \pm 2.2$  and  $25.7 \pm 4.4$ , respectively). These differences were statistically significant ( $P < 0.001$ ).<sup>[45]</sup>

##### 4.6: Association between Pre-test knowledge scores of staff nurses and selected socio-demographic variables

Findings revealed that no significant association was found between pre-test knowledge scores of the staff nurses and socio demographic variables such as Age, Gender, Religion, Educational status, Marital status, Training attended on care of children on mechanical ventilator, Work experience as staff nurse.

#### 5. CONCLUSION

Most of the staff nurses (68.20%) were of 31-40 years of age. Majority (67.80%) of the staff nurse were Males. Most of the staff nurses (44.60%) were belonging to Muslim religion. Majority (66.20%) of staff nurse had General nursing midwifery training. Most of the staff nurses (49.80%) were married. Majority (58%) of the staff nurses were attended the training programme on care of children on mechanical ventilator. Most of the staff nurses (39%) had an experience of 7 years.

Majority (65.80%) of staff nurses had average level of knowledge regarding care of children on ventilator and 18.60 percent of them had Average level of knowledge and only 15.60 percent staff nurse had high level of knowledge.

A significant difference was found between the pre-test and post-test knowledge scores of staff nurse. The study showed that the video assisted teaching programme was highly effective in improving the knowledge of staff nurse on care of children on ventilator. There was no

significant association found between pre-test knowledge scores of the staff nurse and socio demographic variables such as Age , Gender, Religion, Educational status, Marital status, Training attended in care of children on ventilator, Work experience as staff nurse, Experience in pediatric intensive care unit, Present working area.

#### What is known about this topic

- Staff nurses having lack of knowledge regarding care of children on ventilator by this study.
- Why ventilator children's are suffering with ventilator associated complications.

#### What this study adds

- This study helps to identify staff nurses knowledge regarding care of children on ventilator
- After assessing knowledge about staff nurses regarding ventilator care, provided video assisted teaching programme
- Staff nurses gain knowledge regarding care of children on ventilator
- It helps to reduce mortality and morbidity rate of children

#### Competing interests

- The authors declare no competing interest.

#### Authors' contributions

Sanjay shinde wrote the proposal, involved in the data collection, analysis and interpretation. Nagarajappa. D was involved in data collection, analysis and interpretation of statistical outputs and drafted the manuscript. Pritam kabade was involved in data collection, analysis and interpretation of statistical outputs. All authors read and approved the final manuscript.

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## EFFECT OF EMPAGLIFLOZIN ON HR VARIABILITY AND QT DISPERSION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS T2DM

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### ABSTRACT

**Background:** Individuals with type 2 Diabetes Mellitus(T2DM) are at high risk for development of cardiovascular complications. Treatment with empagliflozin may affect on impaired heart rate variability and impaired ventricular repolarization heterogeneity which associated with the risk of sudden cardiac death(SCD). **Objective:** the present study aims to assess the effects of empagliflozin on QT dispersion(QTd) and HR variability (HRV) in patients with T2DM. **Materials and Methods** This is prospective study conducted in the department of cardiology in Tishreen University Hospital-Lattakia - Syria from September 2019 to September 2020. Patients with T2DM who aged 42 to 80 with indication for treatment with empagliflozin were enrolled in the study. QT dispersion, HR variability were recorded before starting empagliflozin and at the end of follow up. **Results:** A total of 40 patients were included, Median age was 52.5 years, 22 (55%) were male, hypertension was detected in 28(70%) of the patients. Empagliflozin reduced glycemia ( $186.10 \pm 54.9$  vs  $125.72 \pm 33.3$ ,  $p:0.0001$ ), systolic blood pressure SBP( $132.3 \pm 12.7$  vs  $124.9 \pm 9.8$ ,  $p:0.001$ ), QTd ( $62.22 \pm 21.4$  vs  $52.15 \pm 22.6$ ,  $p:0.003$ ), and increased SDNN( $89.15 \pm 22.2$  vs  $96.40 \pm 21.2$ ,  $p:0.03$ ) in the study participants. Spearman's correlation analysis revealed positive correlation between changes in SBP and QTd(Spearman's  $=0.6$ ,  $P=0.0001$ ) and negative correlation with SDNN(Spearman's  $=-0.3$ ,  $P=0.02$ ). Reduction in glycemia was correlated with increased in QTd(Spearman's  $=-0.2$ ,  $P=0.07$ ) and decreased in SDNN(Spearman's  $=0.1$ ,  $P=0.3$ ). **Conclusion:** Empagliflozin alters ventricular repolarization indices and impaired HRV, and this could be the mechanism by which empagliflozin reduced cardiovascular events.

**KEYWORDS:** Type 2 Diabetes Mellitus, empagliflozin, HR variability, QT dispersion.

### INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder in which prevalence has been increasing steadily all over the world, and these patients are predisposed to serious cardiovascular complications.<sup>[1]</sup> Intensive glycemic control reduced incidence of microvascular disease but had limited effects on cardiovascular events including SCD.<sup>[2]</sup>

Empagliflozin, a Sodium-glucose co -transporter 2(SGLT2)inhibitor represents a new milestone in treatment of T2DM.It has pleiotropic effects beyond its glucose control effect through different mechanisms.<sup>[3]</sup> EMPA-REG OUTCOME trial is the first of the positive cardiovascular outcome trials of empagliflozin in patients with T2DM.<sup>[4]</sup>

Among the suggested mechanisms mediating the beneficial effects of empagliflozin on cardiovascular mortality is reversing ventricular repolarization heterogeneity,<sup>[5]</sup> and also through the effects on cardiac sympathetic and parasympathetic activity.<sup>[6]</sup> The current study was designed to investigate effects of empagliflozin on ventricular repolarization indices and heart rate variability HRV.

### Study design and data collection

We prospectively studied patients with T2DM aged 42 to 80 years who presented to the department of endocrinology in Tishreen University Hospital -Lattakia-Syria from September 2019 to September 2020. Patients with one of the following: evidence of presence atrial fibrillation, chronic renal failure stage IV and V, treatment with antiarrhythmic drugs except of beta blockers, and patients with disorders in serum

electrolytes (potassium K ,sodium Na, magnesium Mg, calcium Ca) were excluded. Demographic data including age, sex and related to co-morbidities were recorded. All the following measurements were recorded before the treatment with empagliflozin and at the end of follow up: SBP, fasting blood glucose, QT dispersion, QTC, SDNN.

**Heart rate variability (HRV):** is the physiological phenomenon of the variation in the time interval between consecutive heart beats in milliseconds, and it may provide a non-invasive tool for the early diagnosis of cardiac autonomic neuropathy(CAN) in patients with DM.<sup>[7,8]</sup>

**SDNN(ms):** The Standard deviation of all normal RR intervals in the entire 24 –hour ECG record, and represents one of HRV indices measured by Time-domain method. It reflects the parasympathetic component of autonomic function, and classified into normal SDNN: above 100 ms, and abnormal SDNN below 100ms.<sup>[8]</sup>

**QT dispersion:** is defined as the difference between the longest and shortest QT intervals on a standard 12-lead ECG, and this may provide an indirect measure of underlying inhomogeneity of myocardial repolarization. It classified into three subgroups: normal <40

ms,prolonged:40-80 ms, very prolonged ≥80 ms.<sup>[9]</sup>

**Statistical Analysis**

Statistical analysis was performed by using IBM SPSS version 20. Basic Descriptive statistics included means, standard deviations (SD) Frequency and percentages.

Differences of distribution examined by using chi-square test or Fisher exact test if it need. Paired sample t-test was performed to compare indices before and after treatment. Correlations were analysed using Spearman's rank correlation coefficient. Variables with p less than 0.05 were included in the model.

**RESULTS**

A total of 40 patients with T2DM (median age: 52.5 year; 22 males, hypertension in 70%) who presented to the department of endocrinology from September 2019 to September 2020 were included in the study. The baseline characteristics of patients are as given in table(1).

As shown below, 57.5% of the patients had prolonged QTd,25% had very prolonged QTd, and 70% had abnormal SDNN.

**Table 1: Demographic characteristics and electrocardiographic parameters of the study population.**

<b>Variable</b>	
Age(years)	52.5(42-80)
<u>Sex-n(%)</u>	
Male	22(55%)
female	18(45%)
<u>Co=morbidities:</u>	
HTN	28(70%)
T2DM (duration >10 years)	23(57.5%)
CAD	15(37.5%)
HFrEF	8(20%)
Follow up duration(day)	56.5
<u>QTd(ms):</u>	
Normal	7(17.5%)
Prolonged	23(57.5%)
Very prolonged	10(25%)
<u>SDNN(ms)</u>	
Normal	12(30%)
Abnormal	28(70%)

There was a significant relationship between QTd subgroups and presence hypertension (p=0.03) before treatment Table 2.

**Table 2: Comparison between QTd subgroups and Co=morbidities.**

	<b>QTd</b>		
	<b>Normal</b>	<b>Prolonged</b>	<b>Very prolonged</b>
Hypertension	3(10.7%)	15(53.6%)	10(35.7%)
HFrEF	0	6(75%)	2(25%)

The relationship between SDNN subgroups and presence of hypertension (p=0.04), T2DM with duration longer

than 10 years(p=0.001), HFrEF(p=0.03) was significant, Table 3.

**Table 3: Comparison between SDNN subgroups and Co=morbidities.**

	SDNN	
	Normal	Abnormal
Hypertension	6(21.4%)	22(78.6%)
T2DM (duration>10 years)	2(8.7%)	21(91.3%)
HFrEF	0	8(100%)

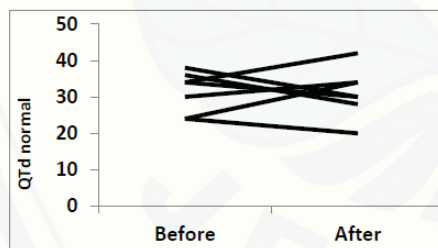
SBP reduced significantly after the treatment (p<0.05). There wasn't any significant difference in serum electrolyte, mean HR after treatment(p>0.05).

significant reduction in QTd(62.22±21.4 vs 52.15±22.6 ,p0.003) in particular in very prolonged QTd subgroup, Fig1 and significant increased in SDNN, table(4).

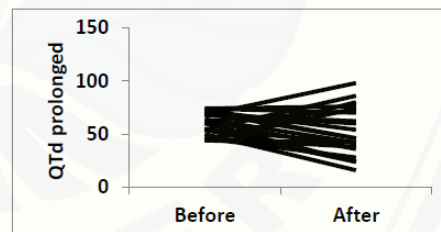
Among ventricular repolarization indices, there is a

**Table (4): Changes in parameters in T2DM patients after treatment with empagliflozin(n=40).**

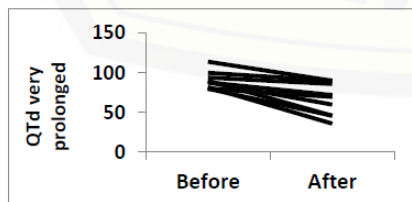
	Before	After	P-value
Blood glucose	186.10±54.9	125.72±33.3	0.0001
<u>Serum electrolyte</u>			
Na	138.32±3.09	138±2.7	0.6
K	4.17±0.43	4.16±0.4	0.4
Ca	8.9±0.38	8.9±0.4	0.4
Mg	1.9±0.29	1.9±0.33	0.8
SBP	132.3±12.7	124.9±9.8	0.001
Mean HR	77.3±9.5	78.6±11.7	0.2
<u>QTd</u>	62.22±21.4	52.15±22.6	0.003
Normal	31.4±5.6	31.1±6.7	0.9
Prolonged	59.6±10.5	52.2±22.5	0.1
Very prolonged	89.6±10.8	66.6±19.2	0.001
<u>QTc</u>	429.8±23.5	431.9±27.4	0.5
SDNN	89.15±22.2	96.40±21.2	0.03



a-Normal QTd subgroup



b- prolonged QTd subgroup



c-very prolonged subgroup

**Figure 1: Changes in QTd after administration empagliflozin in the three subgroups of QTd, with decreasing rate by 100% in very prolonged subgroup.**

There was a positive correlation between changes in SBP and changes in QTd (Spearman's =0.6, P=0.0001) and a

negative correlation with changes in SDNN Figure 2.



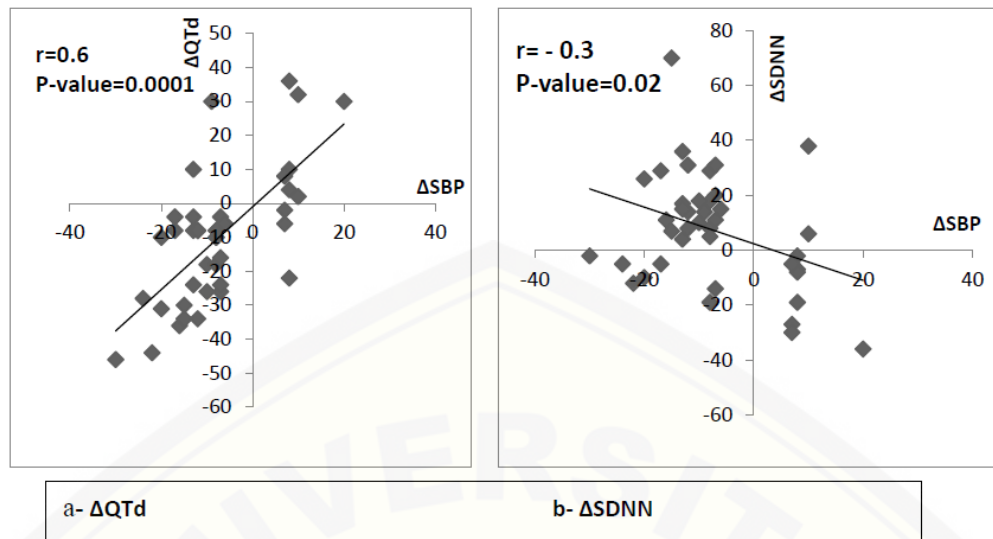


Figure 2: Correlation of changes in SBP with changes in QTd(a) and changes in SDNN(b).

There was a negative correlation between changes in glycemia and changes in QTd (Spearman's  $r = -0.2$ ,

$P=0.07$ ) and a positive correlation with changes in SDNN (Spearman's  $r = 0.1$ ,  $P=0.3$ ), Figure 3.

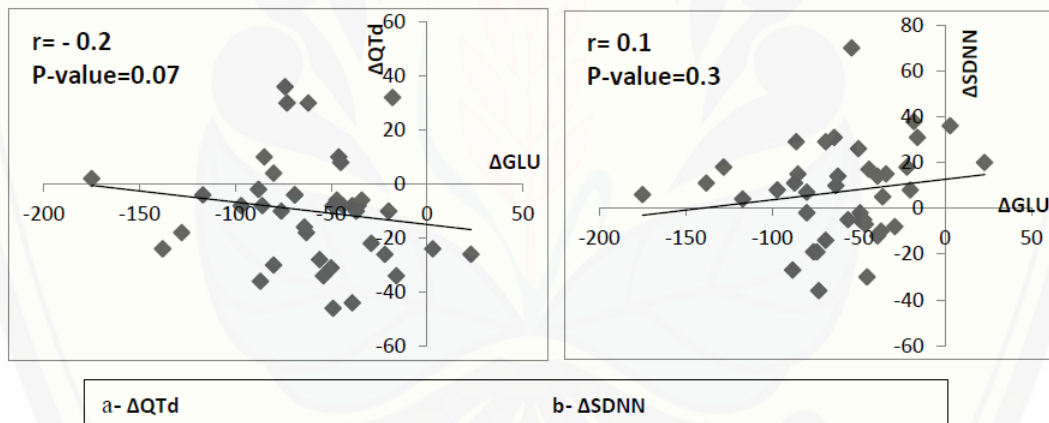


Figure 3: Correlation of changes in glycemia with changes in QTd(a) and changes in SDNN(b).

**DISCUSSION**

This prospective study demonstrated changes in heart rate variability and QT dispersion in patients with T2DM aged 42 to 80 years after treatment with empagliflozin. This changes include reduction in SBP and QTd (more significantly in the very prolonged QTd subgroup), increasing in SDNN. Reduction in SBP was correlated with decreased QTd and increased in SDNN. Reduction in glycemia was correlated with increased in QTd and decreased in SDNN without any statistical significance.

The exact mechanism responsible for cardio protective effects of empagliflozin in patients with T2DM is not fully understood, and there are many supposed mechanisms.

Systemic effects of empagliflozin are modulated by hemodynamic actions via natriuresis (sustained reduction in intravascular volume and BP lead to reduction in cardiac preload and afterload),<sup>[10,11]</sup> and metabolic actions via glycosuria and increasing circulating levels of ketones which are taken up by myocardial cells leading to decreased of myocardial oxygen consumption and cardiac sympathetic nerve activity.<sup>[12,13]</sup>

Direct effects could potentially mediate through their abilities to attenuate cardiac inflammation, oxidative stress, mitochondrial dysfunction and ionic dyshomeostasis. As result of the previous mechanisms improving both systolic and diastolic LV function, prevent cardiac arrhythmia in cardiac ischemic/reperfusion, and improving cardiac morphologic changes.<sup>[14,15]</sup>

The results of our study are consistent with the results of a previous studies.

Sato et al 2017 in Japan showed that treatment with empagliflozin reduced SBP(133±18 vs 126±12 mmHg) without changes in heart rate, QTd(48.8 vs 44.2 ,p 0.006), more significantly in the very prolonged QTd subgroup, and positive correlation of changes in SBP with changes in QTd (Spearman's = 0.32, P=0.03).<sup>[16]</sup> Shimizu et al,2020 found similar results in multicenter randomized trial included patients with acute myocardial infarction with T2DM which revealed improvement in SDNN after treatment with empagliflozin without significant difference in comparison with placebo.<sup>[6]</sup>

In contrast to that, Vinay et al ,2020 showed that treatment with empagliflozin reduced SBP(may explain reduced left ventricular mass index observed by MRI),but without significant changes in SDNN(100.2±45.8 vs 108.3±29.9,p:0.4) and this difference with our study might be explained by the low number of patients with HF<sub>r</sub>EF in Canadian study(3% vs 20%) and normal SDNN in most patients.<sup>[17]</sup>

## CONCLUSION

Empagliflozin appears to be a promising option in reducing lethal cardiovascular complications in patients with T2DM by its effects on impaired ventricular repolarization heterogeneity and impaired HRV.

## List of abbreviations

T2DM: Type 2 Diabetes Mellitus

HF<sub>r</sub>EF: Heart failure with reduced ejection fraction.

SDNN: standard deviation of NN.

HTN: hypertension

CAD: Coronary artery disease

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## EFFECT OF SACUBITRIL/VALSARTAN ON HEART RATE VARIABILITY HRV AND QT DISPERSION IN HEART FAILURE WITH REDUCED EJECTION FRACTION

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### ABSTRACT

**Background:** Treatment of heart failure with reduced ejection fraction(HFrEF) by using Sacubitril/Valsartan reduces sudden cardiac death, but the precise mechanism underlying the beneficial effect on reducing cardiovascular mortality is still not clear. **Objective:** the present study aims to assess effects of Sacubitril/Valsartan on QT dispersion and HR variability in symptomatic patients with HFrEF.

**Materials and Methods:** This is prospective study conducted in the department of Cardiology in Tishreen University Hospital-Lattakia -Syria from September 2019 to September 2020. Patients with HFrEF classified according to the NYHA in II-IV who aged 39 to 82 years were enrolled in the study. QT dispersion, SDNN were reordered before starting Sacubitril/Valsartan and after one month of the therapy.

**Results:** A total of 22 patients were included, Median age was 50 years, 13 (59.10%) were female, hypertension was present in 15(68.2%) of the patients. Sacubitril/Valsartan reduced QTd (65.09±25.3 vs 51.72±21.7, p:0.004), OTc(435.04±27.6 vs 425.40±27.1.p:0.1), QRS(94.54±19.22 vs 93.40±16.39,p:0.6), and increased SDNN(93.22±24.7 vs 111.81±37.2,p:0.01) in the study participants. Spearman's correlation analysis revealed negative correlation between changes in SDNN and dyspnea degree (Spearman's = -0.2, P:0.04) and a positive correlation between changes in QTD and dyspnea degree (Spearman's = 0.3, P:0.01). Increased dose of drug was correlated with decreased QTd(Spearman's = - 0.1, P:0.5) and increased SDNN(Spearman's = 0.1, P:0.4). **Conclusion:** Based on our results, Sacubitril/Valsartan alters ventricular repolarization indices which associated with clinical improvement, so it could be an effective approach in treating patients with HFrEF.

**KEYWORDS:** Sacubitril/Valsartan, QT dispersion, HR variability, HFrEF.

### INTRODUCTION

Heart failure (HF) is a clinical syndrome in which symptoms result from impairment of ventricle filling or ejection of blood or both. HFrEF occurs when the left ventricular ejection fraction (LVEF) is 40% or less and is accompanied by progressive left ventricular dilatation and adverse cardiac remodeling.<sup>[1,2]</sup>

Worldwide, the burden of heart failure has increased and approximately 50% of cases are HFrEF which represents a major public health concern with substantial morbidity and mortality.<sup>[3]</sup>

Sacubitril/Valsartan is known as an angiotensin receptor neprilysin inhibitor(ARNI). It blocks harmful effects of renin-angiotensin-aldosterone system(RAAS) activation, and also raising levels of natriuretic peptides that are

degraded by neprilysin. Therapy with Sacubitril/Valsartan successfully improved outcomes in patients with HFrEF.<sup>[4,5]</sup> The absence of local studies prompted us to carry out this research to assess the effects of Sacubitril/Valsartan on ventricular repolarization parameters in HFrEF patients.

### MATERIALS AND METHODS

#### Study design and data collection

We prospectively studied patients with HFrEF aged 39 to 82 years who presented to the department of Cardiology in Tishreen University Hospital –Lattakia-Syria from September 2019 to September 2020. Patients with one of the following: evidence of presence atrial fibrillation, renal failure stage IV and V, treatment with antiarrhythmic drugs except of beta blockers, and patients with disorders in serum electrolytes (potassium

K, sodium Na, magnesium Mg, calcium Ca) were excluded. Demographic data including age, sex and related to co-morbidities were recorded. All the following measurements were recorded before starting treatment with Sacubitril/Valsartan and after one month: blood glucose, serum electrolytes, QT dispersion, QRS, QTC, SDNN.

### Definitions

**Heart rate variability (HRV):** fluctuations in the RR intervals, can be measured by three methods: time domain measures, frequency domain measures, nonlinear/complexity based measures.<sup>[6]</sup>

**SDNN(ms):** The Standard deviation of all normal RR intervals in the entire 24-hour ECG record, and represents one of HRV indices measured by Time-domain method. It reflects the parasympathetic component of autonomic function, and classified into normal SDNN: above 100 ms, and abnormal SDNN below 100ms.<sup>[7]</sup>

**QT dispersion:** defined as the difference between the longest (QT max) and the shorter (QT min) QT intervals within a 12 lead ECG. Patients are classified into three

subgroups: normal <40 ms, prolonged:40-80 ms, Very prolonged  $\geq 80$ ms.<sup>[8]</sup>

### Statistical Analysis

Statistical analysis was performed by using IBM SPSS version 20. Basic Descriptive statistics included means, standard deviations (SD), Frequency and percentages.

Differences of distribution examined by using chi-square test or Fisher exact test as needed. Paired sample t-test was performed to compare indices before and after treatment. Correlations were analysed using Spearman's rank correlation coefficient. Variables with p less than 0.05 were included in the model.

### RESULTS

A total of 22 patients with HFrEF (median age: 50 year; 13 females, hypertension in 68.2%) who presented to the department of Cardiology from September 2019 to September 2020 were included in the study. The baseline characteristics of patients are as given in table(1).

As shown below, 40.9% of the patients had prolonged QTd, and 50% had abnormal SDNN.

**Table 1: Demographic characteristics and electrocardiographic, echocardiographic parameters of the study population.**

Variable	
Age (years)	50(39-82)
Sex-n(%)	
Male	9(40.90%)
female	13(59.10%)
Smoking	12(54.5%)
Co=morbidities	
HTN	15(68.2%)
CAD	14(63.6%)
Diabetes mellitus	11(50%)
Dyslipidemia	10(45.5%)
Renal diseases	6(27.3%)
EF	32.7 $\pm$ 4.9(20-40%)
QTd(ms)	
Normal	5(22.7%)
Prolonged	9(40.9%)
Very prolonged	8(36.4%)
SDNN(ms)	
Normal	11(50%)
Abnormal	11(50%)

There was a significance decrease in SPB after treatment with Sacubitril/Valsartan (p 0.0001) Fig 1, without any significant difference in laboratory parameters (p>0.05).

Among ventricular repolarization indices, there is a significant reduced in QTd (65.09 $\pm$ 25.3 vs 51.72 $\pm$ 21.7, p=0.004) in particular in Very prolonged QTd subgroup (Fig 2), and significant increased in SDNN without any difference between SDNN subgroups, table(2).

Table 2: Laboratory and electrocardiographic data before and after one month of therapy with Sacubitril/Valsartan.

	Before	After	P-value
SBP	133.2±18.9	122.7±15.2	0.0001
Blood glucose	127.68±47.5	133.59±58.2	0.2
Hemoglobin (Hb)	10.68±1.2	10.49±0.9	0.06
Creatinine (Cr)	1.34±1.06	1.36±0.9	0.6
Serum electrolyte			
Na	134.09±5.2	133.5±3.5	0.3
K	4.27±0.6	4.21±0.1	0.6
Ca	8.9±0.5	9.03±0.5	0.2
Mg	2.09±0.3	2.05±0.2	0.4
QTd	65.09±25.3	51.72±21.7	0.004
Normal	30±7.07	28±14.3	0.7
Prolonged	62±14.1	52.9±17.3	0.09
Very prolonged	90±8.4	65.2±18.6	0.01
QTc	435.04±27.6	425.40±27.1	0.1
QRS(ms)	94.54±19.22	93.40±16.39	0.6
SDNN	93.22±24.7	111.81±37.2	0.01

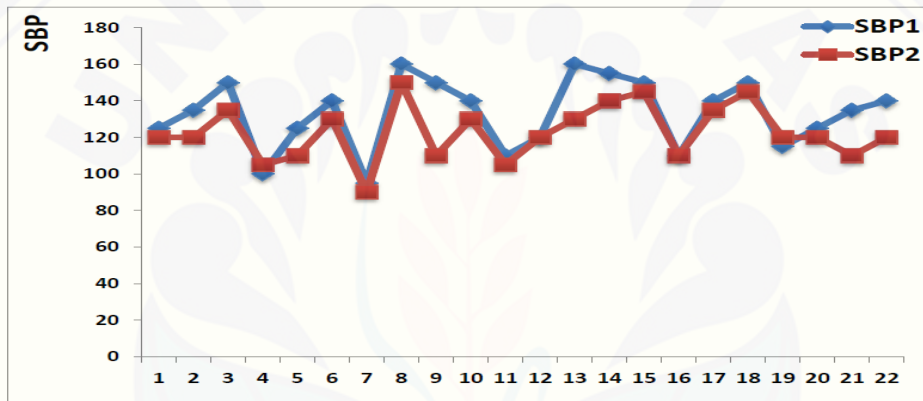
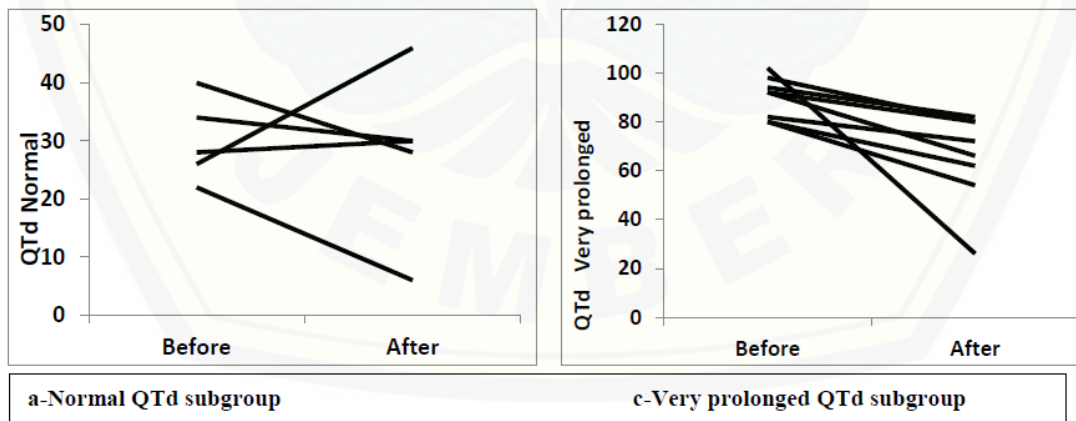
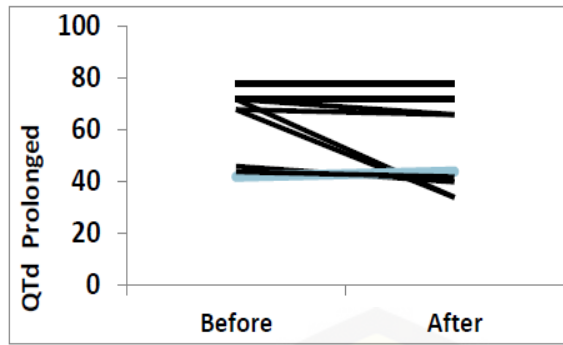


Figure 1: Changes in systolic blood pressure SBP after treatment with Sacubitril/Valsartan,(p 0.0001).







b-prolonged QTd subgroup

Figure 2: Changes in QTd after administration Sacubitril/Valsartan in the three subgroups of QTd, decreasing average is by 100% in Very prolonged QTd subgroup.

There wasn't relationship between presence of diabetes mellitus DM and changes in QTd, SDNN, table 3.

There wasn't relationship between previous use of Valsartan and changes in QTd, SDNN, table4.

Table 3: Comparison SDNN, QTd according to presence DM.

	Before	After	p-value
<b>Present</b>			
SDNN	89.1±24.4	109±44.2	0.05
QTd	51.6±25.8	44.1±20.9	0.1
<b>Absent</b>			
SDNN	97.2±25.6	114.2±30.8	0.1
QTd	78.5±16.7	59.2±20.8	0.01

Table 4: Comparison SDNN, QTd according to presence of previous use of Valsartan.

	Before	After	p-value
<b>Present</b>			
SDNN	88±30.3	96.5±23.6	0.3
QTd	68±18.4	53±17.2	0.1
<b>Absent</b>			
SDNN	94.4±24.2	115.2±39.3	0.02
QTd	64.4±27.03	51.4±23.09	0.01

There was a negative correlation between changes in SDNN and dyspnea degree (Spearman's  $r = -0.2$ ,  $P=0.04$ ),

and a positive correlation between changes in QTd and dyspnea degree (Spearman's  $r = 0.3$ ,  $P=0.01$ ), Fig3.

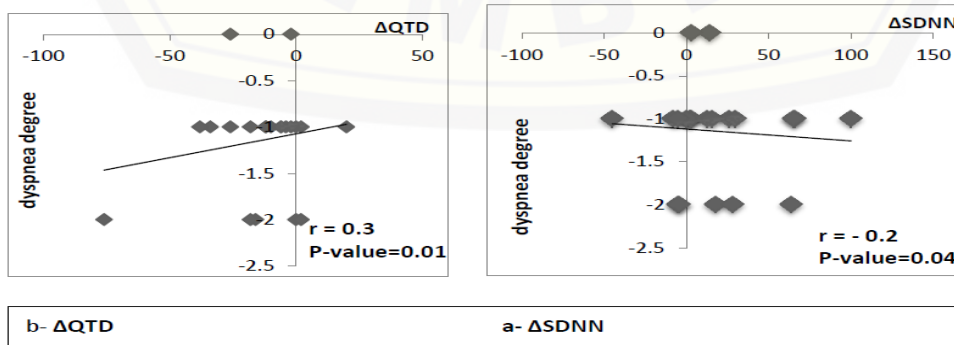


Figure 3: Correlation of dyspnea degree with changes in SDNN (a) and changes in QTd(b).

There was a positive correlation between sacubitril/valsartan dose and changes in SDNN

(Spearman's  $r = 0.1$ ,  $P = 0.4$ ), and negative correlation with changes in QTd (Spearman's  $r = -0.1$ ,  $P = 0.5$ ), Fig4.

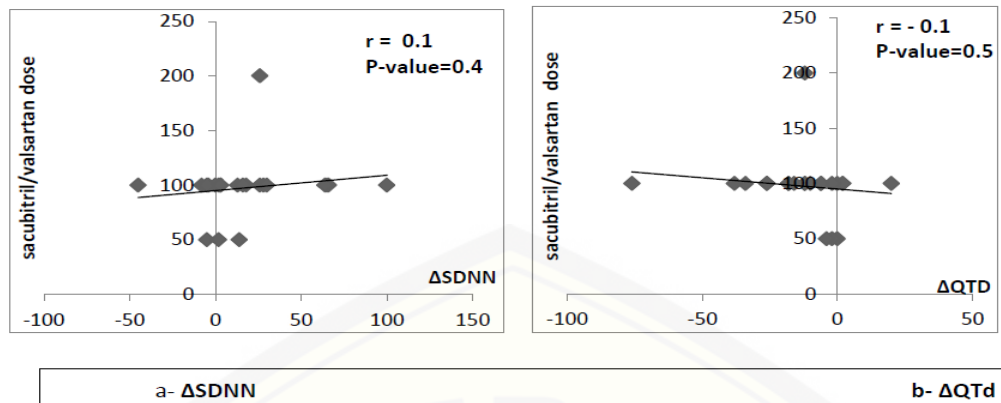


Figure 4: Correlation of sacubitril/valsartan dose with changes in QTd (a) and SDNN(b).

## DISCUSSION

This prospective study demonstrated changes in heart rate variability and QT dispersion in patients with HFrEF aged 39 to 82 years after treatment with Sacubitril/Valsartan. These changes include reduction in QTd (more significantly in the very prolonged QTd subgroup) and QTc, increasing in SDNN without significant changes in QRS. Reduction in QTd and increasing in SDNN were correlated with clinical improvement in dyspnea, without any effect of previous use of Valsartan on changes in QTd, SDNN. Increased dose of drug was correlated with decreased QTd and increased SDNN.

Sacubitril/Valsartan drug acts on two pathways activated in HF: it inhibits neprilysin and blocks angiotensin II receptor.<sup>[9]</sup> Inhibition of neprilysin has a positive impact on heart by a vasodilating action and improvement in the availability of natriuretic peptides which leads to an increase in natriuresis and diuresis, as a result reduction in intravascular volume and BP, in addition to that reduction in left ventricular and vascular remodeling.<sup>[10]</sup> Blocking angiotensin II receptor reverses unfavorable effects such as: cardiac hypertrophy, fibrosis, cardiomyocyte dysfunction which contributes to proarrhythmic effect. This reduces ventricular premature beats and tachyarrhythmias, consequently reducing sudden cardiac death.<sup>[11,12]</sup>

The trial that led to approve Sacubitril/Valsartan in patients with HFrEF is PARADIGM-HF which showed reduction in mortality in patients treated with this drug.<sup>[13]</sup>

A trial by de Diego et al found that adding Sacubitril/Valsartan to the medical therapy for heart failure reduce ventricular tachycardia, increase in biventricular pacing by reduction in premature ventricular contraction.<sup>[14]</sup>

Sercan et al 2018 showed significant decreasing in QTc after treatment with Sacubitril/Valsartan ( $415.2 \pm 19.7$  vs  $408.5 \pm 20.8$ ,  $p = 0.022$ ) and this consisted with the result of our study.<sup>[15]</sup>

António et al also found that treatment with Sacubitril/Valsartan reduced QTc interval ( $451.9$  vs.  $426.0$  ms,  $p < 0.001$ ), QRS duration ( $125.1$  vs.  $120.8$  ms,  $p = 0.033$ ), but decreasing QRS in our study wasn't significant.<sup>[16]</sup>

Simon et al, 2019 reported a case of 44 old woman with HFrEF showed improvement in SDNN after switching from candesartan to Sacubitril/Valsartan ( $82$  ms to  $162$  ms).<sup>[17]</sup> On the contrary, Francisco et al 2018 showed that treatment with Sacubitril/Valsartan was not associated with any improvement in SDNN ( $42.1 \pm 11.5$  vs  $38.2 \pm 12.3$ ,  $p = 0.1$ ), and this may be explained by insufficient drug dose that used or period of the therapy is short.<sup>[18]</sup>

## CONCLUSION

The analysis of ECG changes can be used as useful predictor for monitoring effects of the treatment with Sacubitril/Valsartan and its correlation with clinical improvement.

## List of abbreviations

HFrEF heart failure with reduced ejection fraction HR: heart rate

NYHA: New York Heart Association SDNN: standard deviation of NN. HTN: hypertension

CAD: Coronary artery disease

## ACKNOWLEDGEMENTS

We would like to thank all doctors in department of Cardiology for assistance.

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## OUTCOME OF IMMUNE THROMBOCYTOPENIC PURPURA (ITP). EXPERIENCE IN A TERTIARY CARE CHILDREN HOSPITAL OF BANGLADESH

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### ABSTRACT

**Background:** The pathogenesis of Childhood Idiopathic Thrombocytopenic Purpura(ITP), a common hematological disease involves antibody-mediated platelet destruction and reduced platelet production. Though in large number of cases it resolve spontaneously but we the pediatricians very frequently use steroid or IV Immunoglobulin due to lack of experience. **Object:** The objective of this study was to review the presenting features, natural history and remission rate of ITP cases spontaneously or to therapy. **Method:** This is a retrospective study conducted in the Department of Pediatric Haematology & Oncology of Dhaka Shishu (Children) Hospital during the period January 2018 to December 2019 and there was review and analysis of natural history and treatment response in children diagnosed with ITP age ranged of 9 months to 14 years. **Results:** Of 64 patient with ITP with a age range of 9 months to 14 years (mean age  $6.1 \pm 1.6$  yrs) and female predominance 36 (56 %) female and 28 (44 %) male. Male female ratio was 1: 1.3. Ten (15.6%) children had major hemorrhage. The platelet counts were 6,000/cmm to 1.25,000/cmm (mean 19,000/cmm). Bone marrow study was done in 14 (22%) cases with no alteration in diagnosis. Regarding outcome, 25 (39%) patients had been achieved spontaneous remission and 39 (61%) needed intervention with corticosteroid. Among the patients treated with corticosteroid 26 (67%) patients responded to corticosteroid and 13 (33%) had gone to chronic stage. Out of 13 chronic ITP patients 6 had received Anti D Ig: of these 6 patients 100% patients maintained platelet count  $>30,000$ /cmm for variable periods, and 7 patients received oral Eltrombopag-a newer drug of ITP treatment: of these 7 patients 5(71%) had responded and maintaining platelet count  $>50,000$ /cmm for longer duration than Anti D and 2(29%) did not respond. These 13 of 64 (20%) patient remained as chronic ITP. Chronic ITP developed in older children. **Conclusion:** The overall prognosis in childhood ITP is excellent. Spontaneous remission occurred in good number of cases (39 %) and overall about 90% cases resolved with therapy or observation. Anti-D Immunoglobulin and Eltrombopag are promising in chronic ITP though further larger study is needed.

**KEYWORDS:** ITP, Outcome.

### INTRODUCTION

Pediatric immune thrombocytopenia (ITP) is an acquired immune-mediated disorder characterized by isolated thrombocytopenia.<sup>[1,2]</sup> ITP is characterized by autoreactive antibodies that bind to platelets targeting them for phagocytosis by macrophages in spleen and liver.<sup>[3,4]</sup> Other mechanisms, including B-cell hyperactivity, T-cell mediated cytotoxicity and impaired platelet production, have also been demonstrated to cause ITP.<sup>[5-7]</sup>

ITP can be classified based on patients age (childhood versus adult), duration of illness (acute versus chronic)

and presence of an underlying disorder (primary versus secondary). Persistence of thrombocytopenia ( $<1,50,000$  /cmm) for longer than 12 months are defined as chronic ITP.<sup>[8]</sup>

Although ITP is often self-limiting, about 20-30% of children develop chronic ITP, defined as persistence of thrombocytopenia ( $<150 \times 10^9/L$ ) for longer than 12 months.<sup>[9]</sup> In the chronic form, therapeutic choices are complex and focused on improving health-related quality of life<sup>[10]</sup> and controlling bleeding symptoms.<sup>[11,12]</sup>

Corticosteroids and IVIG are recommended as first-line treatments. If first-line therapy fails, therapeutic options

for managing chronic ITP include immunosuppressive drugs (such as rituximab, mycophenolate mofetil, and sirolimus).<sup>[2,13]</sup> splenectomy or, more recently, thrombopoietin receptor agonists (TPO –RAs).<sup>[14,15]</sup>

Clarification of the major pathways that lead to childhood ITP have influenced our approach to therapy and may ultimately aid in the early identification of individuals who may need more aggressive intervention versus no treatment at all. By decreasing the risk of hemorrhage and minimizing the long-term side effects of treatment, these insights have greatly improve the care of patients with ITP.<sup>[16-18]</sup> With this view this study was done to see the percentage of spontaneous recovery and to disseminate it for general pediatricians.

**METHODS AND MATERIALS**

This retrospective study was performed by reviewing the patient’s files / records and statistical analysis on all ITP patients admitted in the Paediatric Haematology & Oncology Department of Dhaka Shishu (Children) Hospital from January 2018 to December 2019. Diagnosis was done from clinical findings, peripheral blood count. Initially patients were kept in observation for spontaneous remission when initial platelet count was >10000/cmm and there was no massive haemorrhage. Platelet count was followed every day. When platelet count was <10,000/cmm or there was massive haemorrhage or suspicion of ICH, intervention was done

with oral corticosteroid (3-4 mg/kg/day for 7 -10 days and then tapered). Anti D Ig was given at the dose of 50 - 75 µg / kg and Eltrombopag at the dose of 25-50 mg /day. A complete response (CR) to treatment was defined as achieving a platelet count>150x10<sup>9</sup>/L and resolution of bleeding symptoms, a partial response (PR), achieving a platelet increment of >20x10<sup>7</sup>L. and improvement in bleeding symptom

**RESULT**

Total number of patients were 64. Their age range from 9 months to 14 years (mean age 6.1±1.5 years). Their age is given in Table-1. There was female predominance, 36 (56%) female and 28 (44%) male. Male female ratio was 1: 1.3.

**Table-1: Age distribution of Patients (n=64).**

Age of patients	Number of Patients	Percentage
<1 Year	04	6%
1-10 Years	47	74%
<10 Years	13	20%

Bone marrow study was done in 14 (22%) patients with no alteration in diagnosis.

The platelet counts ranged from 6,000/cm to 1, 25,000/cmm (mean 19,000/cmm) (Table-2).

**Table-2: Distribution of Platelet count (n=64).**

Platelets Count	No of Patients	Percentage of Patients
Less than 20,000/cmm	42	64%
20,000 – 30,000/cmm	16	28%
More than 30,000/cmm	06	8%

Regarding outcome- 25 (39%) out of 64 patients went into spontaneous remission and 39(61%) needed

intervention with corticosteroid (Table-3). 39(61%) needed intervention with corticosteroid (Table-3).

**Table-3: Distribution of Remission Pattern (n=64).**

Total Patients	Spontaneous Remission	Need Intervention
64 (100%)	25 (39%)	39 (61%)

After intervention with corticosteroid- 26 (67%) out of 39 patients responded to corticosteroid and 13 (33%) had gone into chronic stage. Out of 13 chronic ITP patients Anti-D Ig was given in 6 patients with 100% response to maintaining platelet count> 30,000/cm for variable period and 7 received oral Eltrombopag- a newer drug of

ITP (Table-4). Among these 7 patients of Eltrombopag 5(71%) responded and maintaining platelet count more than 50,000/ for longer duration than Anti D group and 2(29%) did not respond.These 13 patients remained as chronic cases till now.

**Table 4: Distribution of different treatment regimen & their response.**

Treatment Regimen	Remission	Not in Remissionmq
Corticosteroid (39)	26 (67%)	13 (33%)
Anti D Immunoglobulin (6)	06 (100%)	Nil
Eltrombopag (7)	05 (71%)	02 (29%)

In all the responded (spontaneous & intervention) patients, platelet count began to rise at 3<sup>rd</sup> day and

continue to rise up to 7<sup>th</sup> day except in Eltrombopag group where count began to rise at 7<sup>th</sup> day & continue to rise at 25<sup>th</sup> day (Table-5).

We found that 3 (50%) patients maintaining platelet count >50,000/cmm for at least 15 weeks.

**Table 5: Mean Platelet count (Thousand/ Cmm.) at treatment.**

Treatment	Day 0	Day 3	Day 7	Day 15	Day 25
No treatment	17	28	85	173	230
Corticosteroid	08	35	95	165	250
Anti D Ig	10	30	145	170	185
Eltrombopag	12	12	>25	>100	160

The incidence of chronic ITP is more in older children (>10 years of old).

## DISCUSSION

The age of the study population ranged from 9 months to 14 years (mean age 6.1± 1.5 yrs) which correlates with the studies of the International Childhood ITP Study Group and others.<sup>[19,20]</sup>

In our study there was slight female predominance, 36 (56%) female, 28 (44%) female, Male Female ratio was 1 : 1.3. This was similar to the studies done by Victor Blanchette et al.<sup>[19,21]</sup> in Hospital for the Sick Children, Toronto and others.

The platelet counts in our study subjects were 6000/cm to 1,25,000/cmm (mean 19000/cmm) which correlates with the study done by Watts RG in Children Hospital of Alabama, Bermingham.<sup>[19]</sup>

In our study the spontaneous remission rate was 25 (39%) out of 64 patients which correlates with the study of Desiree Medeiros MD et al<sup>[22]</sup> but lower than the other studies.<sup>[19,23-25]</sup> The lower spontaneous remission rate in our patients might be due to starting of early corticosteroid by receiving junior doctors on admission of the patients in the Hospital. The spontaneous remission might be due to cessation of production as well as disappearance of responsible antibodies from circulation.

The response rate to corticosteroid was 26 (67%) out of 39 patient which correlates with studies of guideline for the American Society of Haematology and others (24,26) but lower than the study performed by Watts RG in Children Hospital of Alabama, Bermingham.<sup>[19]</sup> The mechanism of action of corticosteroid in ITP remains uncertain. Corticosteroid may inhibit the phagocytosis of antibody-coated platelets, may suppress antibody production in lymphocytes and may maintain capillary integrity.

The incidence of chronic ITP was 13 of 64 (20%) which is also close to the studies abroad.<sup>[19,25,29]</sup>

The response rate to Anti-D Ig was 100% maintaining platelet count >30,000/cm which is higher than the study by Watts RG.<sup>[19]</sup> and here IV Ig acts by competitive inhibition of monocyte/phagocyte systems affected by the preferential sequestration of autologous erythrocytes

sensitized by alloantibody present in the Ig G preparations.<sup>[30]</sup>

The response rate to Eltrombopag was 5(71%) in 7 patient and maintaining platelet count >50,000/cmm which correlates with the studies done abroad.<sup>[31,32,33]</sup>

Chronic ITP developed in older children in our study which had been shown in the studies performed by Watts RG.<sup>[19]</sup>

## CONCLUSION

The overall prognosis in childhood ITP is excellent. Spontaneous response occurred in good number of cases (39%) and overall about 90% cases resolved with therapy or observation. Ant-Immunoglobulin and Eltrombopag are promising in chronic ITP though further larger study is needed.

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## EFFECTIVENESS OF STRUCTURED TEACHING PROGRAMME ON KNOWLEDGE OF WOMEN REGARDING MENOPAUSAL CHANGES IN SELECTED RURAL AREAS OF MYSURU, KARNATAKA

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### ABSTRACT

**Background:** Menopause is a unique stage of female reproductive life cycle, a transition from reproductive to non-reproductive stage. It is characterized by cessation of menstruation and women may view menopause as a transition from middle age to old age. Various problems which women experience are depression, anxiety, irritability, low self-esteem, lack of confidence, memory changes, and difficulty in concentration, fatigue and inferiority feelings, vasomotor, instability, hot flashes, headaches, dizziness, diaphoresis, sleeplessness, wrinkling and dying of the skin and loss of hair. Thus women may be hesitant and ignore the unusual and hormonal related symptoms may go undetected resulting in a delay in diagnosis and treatment. Awareness about menopausal symptoms is necessary for women as she is vulnerable to physical and psychological stress and ability to manage and cope up with those symptoms effectively. **Methods:** The main objective of the study was to determine the effectiveness of structured teaching program on knowledge of women regarding menopausal changes. The research design selected for this study was Pre-experimental - One group pre test post-test design. 30 women were selected from rural areas of Mysuru through convenience sampling technique. Personal proforma was used to assess the selected personal variables of rural women and structured knowledge questionnaire to assess the knowledge of women regarding menopausal changes. **Results:** The structured teaching programme was effective in increasing the knowledge of rural women regarding menopausal changes as the computed paired 't' = 19.2 p < 2.045) is found to be significant at 0.05 level of significance. **Conclusion:** The study reinforces the need to organize teaching programs which sensitize the rural women to enhance the knowledge regarding menopausal changes.

**KEYWORDS:** Structured teaching programme, knowledge, women, menopausal changes.

### INTRODUCTION

Menopause means permanent cessation of menstruation at three end of the reproductive life due to loss of ovarian follicular activity. It is the point of time when last and final menstruation occurs.

The average women are postmenopausal for one third her life, the incidence of certain conditions (e.g. coronary artery diseases, diabetes, breast cancer, cervical cancer, and osteoporosis) increase after menopause. Menopause is an unavoidable changes that every women will experience, assuming she reaches middle age and beyond. Menopause is important phase in a women's life which produces physical, physiological as well as social changes. This will help in early reorganization of symptoms, reduction of discomfort and fear and enable to seek appropriate medical care if necessary.

Menopause is the most misunderstood biological and physiological changes that happen to women. Most of the women are not aware about the menopausal problems and it needs intervention. So, it is important to bring awareness about menopausal symptoms and its management among menopausal women and get appropriate treatment which should be used by everyone in all level of economical background.

Menarche and menopause are the turning point in the life of a woman. "Menopause is a stage of life not a disease" - such as diet and physical activity climate and women's roles- as factors in women's experiences with menopause. Post menopausal women have to face a lot of problems, both physically and psychologically. They have to cope with these changes and accept their new role in the society and family.



Menopause is a unique stage of female reproductive life cycle, a transition from reproductive to non-reproductive stage. It is characterized by cessation of menstruation and women may view menopause as a transition from middle age to old age. Some women may look upon this with pleasant anticipation as time of relative freedom from such worries as undesired pregnancies and the stress of child bearing. Many women may have fear during this period because of the anticipated losses. Thus women may be hesitant and ignore the unusual and hormonally related symptoms may go undetected resulting in a delay in diagnosis and treatment.

A descriptive study was conducted to assess relationship between knowledge, attitude and health behaviour among menopausal women. A random sample of 250 menopausal women was studied. The data was collected by using a questionnaire and study showed that 7(28%) women had good knowledge only 27(11%) women had a positive attitude and 40(16%) women had healthy behaviour regarding menopausal duration. The result of this study revealed that there is a positive correlation between knowledge, attitude and healthy behaviour.

Awareness about her physiological changes is necessary for women as she is vulnerable to physical and psychological stress. The individual age, physical emotional status and environment influences the regulatory of her periods. Women's health care is generally focused on the pregnant adult women however childhood, menarche, pregnancy, menopause and the menopausal years are defined by anatomic and physiologic parameters<sup>16</sup>.

The above facts made the investigation to realize the importance of problem in current situation and created an intention to administer a structured teaching program to assess the knowledge of the women in menopausal stage regarding the menopausal symptoms. Thereby enhancing their awareness on menopausal symptoms and ability to manage and cope up with those symptoms effectively.

## OBJECTIVES

1. To assess the knowledge of women regarding menopausal changes before and after administration of structured teaching program on menopausal changes.
2. To determine the effectiveness of structured teaching program on knowledge of women regarding menopausal changes.
3. To find the association between knowledge of women regarding menopausal changes and their selected personal variables.

## Hypotheses

H<sub>1</sub>:-The post-test knowledge scores of women regarding menopausal changes will be significantly higher than their pre test knowledge score.

H<sub>2</sub>:- There will be significant association between level of knowledge of women regarding menopausal changes and their selected personal variables.

## METHODOLOGY

**Research Approach/Design-** The research design selected for this study was Pre-experimental - One group pre test post-test design.

### Variables Under Study

**Independent variable:** Structured teaching programme regarding menopausal changes. **Dependent variable:** Knowledge of women regarding menopausal changes.

**Selected personal variables:** Age, marital status, religion, monthly family income, education.

**Setting -** The setting for the present study is selected rural areas of Mysuru.

### Sample and Sampling Criteria

#### Inclusion criteria for sampling

1. Residing in selected rural areas of Mysuru
2. Aged between 45-50 years

#### Exclusion criteria

Women who are not willing to participate in the study.

#### Sampling Technique

In this study, convenience sampling will be used to select the samples from the selected rural areas in Mysuru.

#### Sampling Size

In this study, sample size will be 30 women from selected rural areas of Mysuru.

#### Data Collection Instrument

1. Personal proforma was used to assess the selected personal variables of rural women and
2. Structured knowledge questionnaire to assess the knowledge of women regarding menopausal changes.

RESULTS

Table 1: Frequency and percentage distribution of women according to their selected personal variables n=30.

Sl.no	Sample characteristics	Frequency(f)	Percentage (%)
1	Age(in years)		
	1.1 40-45	8	27%
	1.2 46-50	22	73%
2	Marital status		
	2.1 Married	26	87%
	2.2 Unmarried	4	13%
3	Religion		
	3.1 Hindu	24	80%
	3.2 Muslim	5	17%
	3.3 Christian	1	3%
4	Family income		
	4.1 Below 5000	2	7%
	4.2 5000-10000	8	27%
	4.3 10000-15000	16	53%
	4.4 Above 15000	4	13%
5	Educational status		
	5.1 primary school	16	53%
	5.2 high school	6	20%
	5.3 no formal education	8	27%

Table 2: Frequency and percentage distribution of level of knowledge of women in selected rural areas according to their pre test and post test scores n = 30.

Knowledge level	Pre test f (%)	Post test f(%)
Poor knowledge(0-11)	29(96%)	--
Average knowledge(12-17)	1 (4%)	12(40%)
Good knowledge(>18)	--	18(60%)

Table 3: Mean, Median, Standard deviation and Range of pre-test and post-test knowledge score of rural women n=30.

Test	Mean	Median	Range	SD
Pre test	7.36	7	2-12	±2.9
Post test	17.9	18	15-20	±1.5

Table 4: Mean, mean difference, standard deviation difference, standard error and paired 't' value of pre-test and post-test knowledge scores of rural women n=30.

Knowledge scores	Mean	Mean Difference	S.D. Difference	Standard Error	Paired 't' test value
Pre-test	7.36	10.54	±1.4	0.2	19.2*
Post-test	17.9				

T<sub>(29)</sub>=2.045; p<0.05\* significant.

To find the significant difference in mean knowledge scores, paired 't' test was computed and obtained value of paired 't'= 19.2, p<2.045 is found to be significant. It is inferred that there is significant improvement of knowledge of rural women regarding menopausal changes after structured teaching programme.

**Section 3: Association between level of knowledge and their selected personal variables among rural women.**

There was no statistically significant association between the level of knowledge of the rural women and their selected personal variables except for educational status. Hence, the null hypothesis is partially supported and it is inferred that level of knowledge of rural women regarding menopausal changes is influenced by their educational status.

## CONCLUSION

The structured teaching programme was effective in increasing the knowledge regarding menopausal changes as the computed paired  $t = 19.2$  ( $p < 2.045$ ) is found to be significant at 0.05 level of significance. Therefore, the study reinforces the need to organize teaching programs which sensitize the rural women to enhance the knowledge regarding menopausal changes.

## ACKNOWLEDGEMENT

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## **Acceptance Letter**

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**TITLE: INFLUENCE OF SYSTEM QUALITY, INFORMATION QUALITY, AND SERVICE QUALITY ON ORGANIZATION AT PUBLIC HEALTH CENTER PASURUAN CITY**

**Dear Nita Dwi Nur Aini, Farida Wahyu Ningtyias, Dewi Rokhmah**

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