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CONTENTS

Clinical Research

Microbiological profile of pre-debridement, post-debridement, and surgical wound infection on open fracture in orthopedic patients at soebandi general hospital

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ABSTRACT

Introduction: Open fractures are fairly common in developing countries. Infection is a common complication of open fractures. Pre-debridement, post-debridement, and surgical site infection (SSI) cultures are important to identify microbiological profiles to prevent infection.

Methods: We report microbiological profile of pre-debridement, post-debridement, and surgical site infection on open fracture in orthopedic patients at Soebandi General Hospital.
. 30 patients were taken into the study of all ages. Primarily, wound was examined and a description of the wound was recorded at 1st culture swab taken at the time of examination before debriment, followed by 2nd culture swab on 1st dressing after debridement, and 3rd culture swab if an infection continued further. Culture reports were collected for studying the pattern of bacterial isolate.

Results: In this study, 30 patients became the study samples. The results of pre-debridement from 15 patients who had positive culture, 9 patients (56.25%) showed growth of Klebsiella sp., 3 patients (18.75%) showed growth of Proteus sp., 2 patients (12.50%) showed growth of *Salmonella thypi*, 1 patient (6.25%) showed growth of *Shigella sonnei*, and 1 patient (6.25%) showed growth of *Staphylococcus aureus*, and one patient culture grew several organisms. In post-debridement culture in the operating room, the results of culture identification from 12 patients showed that 5 patients (41.67%) had Klebsiella sp., 3 patients (25.00%) had *Shigella sonnei*, 2 patients (16.67) had *Pseudomonas aeruginosa*, 1 patient (8.33%) had *Salmonella thypi*, 1 patient (8.33%) had Proteus sp. Nine patients (30%) developed surgical wound infection with 6 patients (85.71%) showed growth of *Staphylococcus aureus*, 1 patient (14.29%) showed growth of *Salmonella thypi*, and 2 others did not show any growth of microorganism.

Conclusion: Microbiological profile of pre-debridement, post-debridement, and surgical wound infection cultures of open fracture were different.

ABSTRAK

Pendahuluan: *Fraktur terbuka cukup banyak di negara-negara berkembang. Infeksi adalah komplikasi umum dari fraktur terbuka. Kultur pra-debridemen, pasca-debridemen, dan infeksi luka operasi penting untuk mengidentifikasi profil mikrobiologis untuk mencegah infeksi.*

Metode: *Kami melaporkan profil mikrobiologis pra-debridemen, pasca-debridemen, dan infeksi luka operasi pada fraktur terbuka pasien ortopedi di RSD dr. Soebandi. Tiga puluh pasien dengan patah tulang terbuka dimasukkan ke dalam studi ini, yang melibatkan semua umur, jenis kelamin, dan derajat patah tulang terbuka. Mula-mula luka diperiksa dan deskripsi luka dicatat, kemudian dilakukan swab kultur pertama yang diambil sebelum tindakan debridemen, diikuti oleh swab kultur kedua setelah tindakan debridemen, dan swab kultur ketiga jika masih ditemukan adanya infeksi pada luka. Laporan kultur dikumpulkan untuk mempelajari pola isolat bakteri.*

Hasil: *Dalam penelitian ini ada 30 pasien yang menjadi sampel penelitian. Hasil kultur dan identifikasi bakteri pra-debridemen pada 15 pasien, ditemukan 1 pasien memiliki pertumbuhan* multiple *organisme*, pertumbuhan Klebsiella sp ditemukan pada 9 pasien (56,25%), *Proteus sp. pada 3 pasien (18,75%),* Salmonella thypi *pada 2 pasien (12,50%),* Shigella sonnei *pada 1 pasien (6,25%), dan* Staphylococcus aureus *pada 1 pasien (6,25%). Pasca-debridemen di ruang operasi, hasil kultur dan identifikasi bakteri pada 12 pasien didapatkan Klebsiella sp. pada 5 pasien (41,67%),* Shigella sonnei *pada 3 pasien (25,00%),* Pseudomonas aeruginosa *pada 2 pasien (16,67),* Salmonella thypi *pada 1 pasien (8,33%), dan Proteus sp. pada 1 pasien(8,33%). Sembilan pasien (30%) menunjukkan infeksi luka operasi dengan hasil kultur dan identifikasi ditemukan bakteri* Staphylococcus aureus *pada 6 pasien (85,71%),* Salmonella thypi *pada 1 pasien (14,29%), dan 2 lainnya tidak ditemukan pertumbuhan bakteri.*

Kesimpulan: *Profil mikrobiologi pada kultur pra-debridemen, pasca-debridemen, dan infeksi luka operasi menunjukkan hasil yang berbeda.*

Keywords: Open fractures, Pre-debridement, Post-debridement, Surgical site infection.

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INTRODUCTION

The prevalence of open fracture in the world is quite high. The World Health Organization (WHO) noted that in 2011 there were more than 5.6 million people died due to accident and around 1.3 million people experienced physical disabilities. The incidence of fractures in the lower limbs has a high prevalence at around 40% of all accidents. Based on the data obtained from Soebandi General Hospital for 1 year, from July 2017 to June 2018, the number of patients with skeletal trauma was 1,008 patients. Open fractures have the highest percentage among the other types of trauma, which is found in 516 cases or 51%.[1,2]

Open fracture is one of the emergencies in orthopedics that requires quick and precise treatment for the success of saving lives and preventing life threats.[3] Open fractures require immediate surgery to clean the area of injury. Because of discontinuity in the skin, debris and bacteria can enter the fracture site and cause infection in the bone so that it becomes a problem that is difficult to treat.[4]

The incidence rate of surgical site infections (SSI) appears to be higher after emergency surgery due to several factors such as severity of the patient's trauma, surgical techniques, and lack preparation for preoperative patients. The incidence of SSI in emergency surgery cases were higher than elective surgery cases, which were 8.4% emergency cases compared to 2.5% elective cases.[5] Prevention of wound sepsis, healing of the fracture and return to optimum function are challenging goals for the treating surgeon. In addition, as surgeons, they need to give a definitive antibiotic as prophylactic treatment to prevent those risks. Due to lack of research about bacterial profile on open fractures at the Soebandi General Hospital, Jember, this research is very important. Pre-debridement, post-debridement, and SSI cultures are important to identify microbiological profiles in order to provide antibiotic therapy that can definitely prevent infection. The results of those cultures are expected to be a reference and evaluation for future management of open fractures. Furthermore, the results of this study can be a general picture related to the prognosis of open fracture with certain bacterial cultures.

METHODS

Study Design

This study used a descriptive method with a cross-sectional approach, where the identification of the type of bacteria was from the swab sample of the wound area in patients with open fracture. The operative procedure was carried out by orthopaedic surgeon. The first swab was the pre-debridement in Emergency Room, the post-debridement was collected in the Operating Room, and the third swab if SSI occured. The SSI was diagnosed based on the CDC criteria.[6] The sampling technique in this study was accidental sampling.

Inclusion and Exclusion Criteria

The Inclusion criteria of this research was all patients diagnosed with open fractures of the extremities in the emergency room starting from March 2019. All patients agreed to become the subject of this research and underwent medical procedures to post-operative care while in hospital. Also, all patients could communicate well. The exclusion criteria was patients with neglected fracture and open fracture in the calvaria, maxillofacial, vertebrae, or costae regions.

Sampling Procedure

Right after the patients delivered to the hospital, the first swab was taken as the pre-debridement sample. The post-debridement sample, or the second swab, was taken after the patient underwent the surgical debridement procedure. The third swab was taken if the patient develop further infection on their surgical site. All specimens were collected and cultured right after the swabs were taken. The specimens were cultured on Blood Agar Plate (BAP) and Mac-Conkey Agar Media.

Data Analysis

All data collected consisted of bacterial cultures from the pre-debridement, post-debridement, and SSI samples. All positive bacterial cultures were identified and described further in this research in observational descriptive way. The data obtained consisted of culture outcome variables and the incidence of SSI in open fracture of patients underwent operative therapy and the data was tabulated in the types of microorganism among the pre-debridement, post-debridement, and SSI.

RESULTS

Table 1. Gender and Age*

Characteristic	Category	Number	Percentage
Sex	Men	25	83.33%
	Women	5	16.67%
Age (Year)	Early teens (12-16)	0	0%
	Adolescent (17-25)	7	23.33%
	Early adulthood (26-35)	7	23.33%
	Adulthood (36-45)	2	6.67%
	Early eldery (46-55)	5	16.67%
	Eldery (56-65)	6	20%
	Old (66)	3	10%

**Age classification by Depkes RI*

Table 2. Open Fracture Causes

Causes	Number	Percentage
Traffic accident	23	76.67%
Work accident	6	20.00%
Fall from height	1	3.33%

Table 3. Open Fracture Region

Region	Number	Percentage
Upper extremity		
Humerus	1	2.70%
Antebrachii	2	5.40%
Manus	6	16.22%
Lower extremity		
Femur	2	5.40%
Cruris	12	32.43%
Pedis	12	32.43%
Pelvic	2	5.40%
Total	37*	100%

*Note : *7 out of 30 patients had multiple traumas, including head injury or maxillofacial*

Table 4. Open Fracture Classification by Gustillo

Classification	Number	Percentage
I	2	6.67%
II	14	46.67%
III	-	-
III A	7	2.33%
III B	5	16.67%
III C	2	6.67%

Table 5. Open Frcature Infection by Gustillo

Classifica-tion	Number	Infection	Percentage
I	2	-	0%
II	14	3	21.43 %
III	14	6	42.86 %
IIIA	7	4	57.14 %
IIIB	5	1	20 %
IIIC	2	1	50 %

Table 6. Time Interval Between Trauma and Surgery

Interval trauma-surgery	Number	Infection
<6 hours	1	0
>6 hours	29	9

average time for patients to come to the emergency department since the accident was about 321 minutes (5 hours and 21 minutes)

Table 7. Nutritional Status

Nutritional Status	BMI (Asian Criteria)	Number	Infection	Percentage
Underweight	<18.4	1	0	0%
Normal	18.5-22.9	17	9	52.94%
Overweight	23.0-24.9	8	0	0%
Pre-Obese	25.0-29.9	3	0	0%
Obese	≥30.0	1	0	0%
Obese Type 1 (Obese)	30.0-40.0	0	0	0%
Obese Type 2 (Morbid Obese)	40.1-50	0	0	
Obese Type 3 (Super Obese)	>50.0	0	0	

Table 8. Pre-debridement Microbiological Profile

Bacteria	Percentage (n=16)*
Klebsiella sp	9 (56.25%)
Proteus sp	3 (18.75%)
Salmonella thypi	2 (12.50%)
Shigella sonnei	1 (6.25%)
Staphylococcus aureus	1 (6.25%)

**from 15 patients with positive culture, it was found 1 patient growing multiple organisms*

Table 9. Post-debridement Microbiological Profile

Bacteria	Percentage (n=12)*
Klebsiella sp	5 (41.67%)
Shigella sonnei	3 (25.00%)
Pseudomonas aeruginosa	2 (16.67)
Salmonella thypi	1 (8.33%)
Proteus sp	1 (8.33%)

** 12 patients were found with positive culture*

Table 10. Microbiological Profile of SSI

Bacteria	Percentage (n=7)*
Staphylococcus aureus	6 (85.71%)
Salmonella thypi	1 (14.29%)

** from 9 patients with surgical site infections, 7 were found to have microorganisms growth on the culture*

DISCUSSIONS

The study was conducted at the RSD dr. Soebandi, Jember. From 30 patients who met the inclusion criteria, open fractures were mostly diagnosed in men compared to women in the range of late adolescent (17-25 years) and early adulthood (26-35 years). In an Indian study, 63 patients (90%) of 70 open fracture patients were male and 7 female (10%) with age mostly ranging between 21-40 years, i.e. 34 patients (48.57%).[7] This is supported by a research conducted in Africa with 98 patients with open fractures, 80 patients (83.6%) were male.[8] The incidence of fractures is more commonly experienced by men because men are more involved in outdoor work or activities.[9] The incidence of open fractures in male were mostly found to be between the age of 15 and 19 years at 54.5 per 100,000 people per year.[10]

The most common cause of open fractures is traffic accident. A research in India stated that the most common cause was due to traffic accident, i.e. 50 cases (71.42%)[7], among which 31.6% were motor vehicle accidents as the most common cause and 20.4% were pedestrian as the second largest cause.[8] This is supported by the study of Kale *et al*., in 2017[11], where 48 patients (75%) of open fractures were due to traffic accidents, other causes were crush injuries (10.93%), fell from height (6.25%), physical attack (6.25%) and sports injuries (1.56%).

In this study, the location of most open fractures occurred in the lower extremities, especially in the cruris (32.43%) and pedis (32.43%). In a study in India, it was found as many as 51 cases (72%) of open fractures occurred in the lower extremities, tibia bone was the most common.[7] Other study conducted in India supported this previous study, the location of the most fractures were in the tibia (40.62%), femur (21.87%), radius/ulna (15.62%), ankle (12.5%), hands (4.68%), and pedis (4.68%).[11] Cruris is part of a long bone consisting of tibia and fibula that often experiences open fractures with a percentage of 11.2%.[10]

Infection remains one of the most common challenges in the treatment of open fractures. Damage to the tissue barrier between the fracture and the environment creates a portal for contaminating agents. The culture result of the open fracture wounds found that most presence of germ colonies, based on the grade of open fractures according to Gustillo classification, were classified as grade IIIA. There were 7 patients in the grade IIIA, of which 4 patients (7.14%) had infections. This result is supported by a research conducted by Kale et al., in 2017[11], where the highest incidence of open fractures was grade III (80%) with the most dominant was the grade IIIB (46.66%). In a study conducted in Brazil, it was found a high infection rate in grade III open fractures of 72%, grade II of 24%, and grade I of 4%. The estimated rate of infection in grade I open fractures was 0-2%, grade II was 2-7%, and grade III was 10-25%.[12] These results indicated that the incidence of infection in open fractures increases following the grade of severity.[11]

The results of pre-debridement bacterial culture from 30 patients showed positive in 15 patients (50%) and there was 1 patient with multiple organism growth. The most bacteria that grew were from the gram-negative group consisting of 4 types of organisms. The most growing organism was Klebsiella sp. found in 9 patients. These results are different from the previous study which showed that the pre-debridement culture from 70 patients, 36 patients (51.42%) developed bacterial colonies, of which 24 patients (66.66%) had Gram (+) bacteria, Coagulase-negative *Staphylococcus aureus*, while gram (-) were found in 12 other patients (33.33%).[7] However, in another study conducted in Brazil in 2014, from 11 patients with open fractures with infection, it was found 11 organisms, mostly were gram-negative (66.70%), and the rest were gram-positive (33.30%).[12] Another study in Kenya in 2015-2016, it was found that 55.8% were gram-negative bacteria while the gram-positive were 44.15%.[8] In this study, gram-negative bacteria found in the pre-debridement consisted of 4 species of microorganisms with Klebsiella as the most common, which was found in 9 patients. Previous study reported that the most gram-negative microorganisms were Pseudomonas (11.7%) and Klebsiella sp. (10.4%).[8]

The results of post-debridement bacterial culture showed positive for 12 patients. All cultures contained gram-negative bacteria consisting of 5 types of organisms. Most organisms was Klebsiella sp. found in 5 patients. Post-debridement culture in this study showed an increase in the growth of gram-negative bacteria. This is supported by a research by Agarwal *et al*., in 2017[7], which showed reduced growth of gram-positive bacteria compared to the pre-debridement cultures, while the gram-negative bacteria in the post-debridement cultures showed the same amount as the pre-debridement cultures.[7] A research conducted by Sitati *et al*., in 2017[8], showed that the main gram-negative isolates found were Pseudomonas spp. (20.8%) and Klebsiella sp. (10.4%).[8]

Several studies from some developing countries reported a fairly high prevalence of Bacillus gram-negative species, Klebsiella, *E. Coli*, and *Pseudomonas aeruginosa* as significant pathogens for the incidence of SSI.[13] A research conducted by Gupta *et al*., in 2012[9], found that all organisms in the pre-debridement cultures were gram-negative. The results of this study indicated that there was a tren of change in the pathogenic bacteria that infected patients with open fractures from gram-positive to gram-negative. Also, the evolution of hospital-acquired pathogens which are mostly gram-negative were the main cause of infection.[9]

In this study, bacterial cultures analysis showed differences in the number of positive cultures between the pre-debridement and the post-debridement. Post-debridement cultures were found to be positive bacterial growth for 12 patients (73.33%) while pre-debridement cultures were positive in 15 patients. There was 1 patient with negative culture in the pre-debridement but showed positive culture in the post-debridement. This result is the same with the research conducted by Gupta *et al*., in

2012[9], in which from 25 patients with positive culture in the pre-debridement, 16 patients (64%) also showed culture that remained positive in the post-debridement.

Open fractures require immediate surgery to clean the injured area. Because of discontinuity in the skin, debris and bacteria can enter the fracture site and cause infection in the bone, making it a problem that is difficult to treat. Gustilo and Anderson reported that 50.7% of patients had positive wound culture at the initial evaluation. While 31% of patients who previously had negative culture, became positive at definitive closure. Therefore, it is necessary to prevent infection as early as possible.[4]

Irrigation and debridement are very important in the treatment of open fractures. Removing contaminated debris and reducing the content of bacteria that have the potential to cause infection can reduce the possibility of acute or chronic infection.[14] The purpose of irrigation of the wound by using normal saline in a large number in open fractures also aims to dissolve bacteria and eliminate foreign matter so that when debridement is carried out, the number of bacterial colonies and germs has decreased.[15,16]

The single most important factor in reducing the infection rate was the early administration of antibiotics that provide antibacterial activity against both gram-positive and gram-negative microorganisms.[17] Patzakis *et al*., in 1989 reported a reduction in open fracture wound infections from 13.9% in patients without antibiotic treatment to 2.3% in patients treated with antibiotics.[17] Antibiotics effectively prevented infections in open fractures. According to the recommendation from The EAST Practice Management Guideline, prophylactic antibiotics are given in large doses and should be started as soon as possible.[18]

The condition of the patient's nutritional adequacy is also one of the determining factors in the incidence of SSIs. Preoperative malnutrition has been identified in a number of studies as a risk factor for SSI.[19] Nutritional condition can actually be considered also as one of the postoperative infection-predicting factor since it should be admitted that wound healing also depends on this nutritional status. Malnutrition may predispose patients to SSI through several mechanisms. The first mechanism involves impairment in wound healing via diminished fibroblast proliferation and collagen synthesis. The second mechanism involves impairment in the ability of the immune system to fight infection, at least partially, through lymphocytopenia.[20] Nutritional status of the patients can be described based on their body mass index (BMI). But, unexpectedly, from all, 9 out of 9 patients that develop SSI came from the normal range BMI group.

Although there is a consensus that the initial treatment of these open fractures should ideally be handled in less than 6 hours, some studies evidently suggested that there is no association between time to debridement and infection rate. It may be prudent to delay definitive debridement so that better treatment by experienced surgeons and staff familiar with the equipment can be provided.[21] This also related to wide practical experience confirms that a senior surgeon operating in daytime with an experienced consistent team is better than urgent care out of hours with a less experienced team.[22] In a General or Peripheral hospital, where immediate access is not easily obtained, this delayed factor can be considered. Based on the data of this research, in average, patients come to the emergency department 5 hours after the accident because transportation and distance problems. Therefore, it is quite hard to maintain the 6 hours rules in most of our cases.

Analysis of the types of organisms found that there were differences of bacterial growth type in pre-debridement and post-debridement in 5 (33.33%) of 15 patients. A research in India in 2017 showed different patterns of organism growth in the first culture with subsequent cultures. Since there was microflora changes phenomenon in SSI patients during inpatient care, nosocomial infections can become the evidence enough as the cause of SSI in open fracture cases.[11]

The results of the third bacterial culture at the time of follow-up found 9 patients had SSI. One of the post-operative risk factors for SSI incidence is postoperative wound care. Postoperative wound care is determined by the technique of closure of the surgical wound area. The primary wound that has been closed must be kept clean with a sterile dressing for 1 to 2 days after surgery.[13] Risk factors for SSIs are also caused by poor sterilization and the length of time lag between fracture onset and surgery.[23]

Seven (7) out of the 9 patients showed positive culture. The SSI culture found gram-positive bacteria, *Staphylococcus aureus*, in 6 patients and gram-negative bacteria, *Salmonella*, in 1 patient. The result of the third culture of the open fracture wounds or when the SSI occur was different among the pre-debridement and the post-debridement.. A metanalysis research comparing prophylactic antibiotic vs placebo in open fractures showed a reduction in infection rate from 13.4% to 5.5% with the addition of intravenous antibiotics.[24] Giving antibiotics, especially in the first two hours can reduce bacterial infections in bones. The use of antibiotics, regardless of the type, is effective in reducing infections in bone and soft tissue.[25]

In a study conducted at the Bilaspur tertiary hospital in India, there were 37 cases of orthopedic surgery wound infections where the most common cause was *Staphylococcus aureus* found in 9 cases (24.3%).[26] Based on the research conducted by Oliveira in 2016,[27] the main causative agents in SSI are *Staphylococcus aureus* and Coagulase-negative Staphylococcus (CoNS). According to Oliveira, the highest incidence of SSI was in cases of open fractures.[25] Recent studies support the findings of previous studies of orthopedic implant surgery that underwent SSI, where it was found that the most causative organism was *Staphylococcus aureus* (54.54%).[28]

Staphylococcus aureus is a positive coagulase bacterium that most often causes infection, especially when the host immunity decreases. Other bacteria found in SSI isolates are normal human flora.[29] About 10-30% of healthy people carry *Staphylococcus aureus* in their nares. Infection by this organism can be caused by the patient himself, bedsheets, instruments, and surgical wound dressing, which can also become a reservoir for *Staphylococcus aureus*.[30] The microorganisms that cause SSI vary from different regions throughout the world but some are caused by *Staphylococcus aureus* and *Staphylococcus epidermidis*.[13]

The small number of cases in this series becomes a limitation for this study and larger studies are required before resolute recommendations can be made in terms of generic antibiotic selection. This research is better used as an analytical study. Further research needs to complete our limitations on antibiotic sensitivity.

CONCLUSION

Microbiological profile in the pre-debridement, post-debridement, and SSI on open fracture in orthopedic patients were found different.

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REFERENCES

1. World Health Organization [Internet]. Global Health Observatory Data Repository. c2011[cited 2019 month date]. Available from: http://apps.who.int/gho/data/?theme=main
2. Emergency Department dr. Soebandi General Hospital. Data Open Fracture 2017-2018. dr. Soebandi General Hospital 2018
3. Koval K.J. and Zuckerman J.D. *Handbook of Fractures*, 3rd Ed. Lippincott: Williams & Wilkins, 2006. pp: 20-9.
4. Gustilo R. B, Anderson J. T. Prevention of Infection in The Treatment of One Thousand Twenty Five Open Fractures of Long Bones: Retrospective and Prospective Analyses. The Journal of Bone & Joint Surgery—American. 1976; 58(4), 453-8.
5. Ercole FF, Chianca TC, Duarte D, Starling CE, Carneiro M. Surgical site infection in patients submitted to orthopedic surgery: the NNIS risk index and risk prediction. Rev Lat Am Enfermagem. 2011;19:269–76.
6. Center for Disease Control and Prevention (CDC). 2018. *Procedure-associated Module. Surgical Site Infection (SSI)* Overview.
7. Agarwal D, Maheshwari R, Agrawal A, Chauhan VD, Juyal A. To study the pattern of bacterial siolates in open fractures. J Orthop Traumatol Rehabil. 2015;8:1-5.
8. Sitati FC, Mosi PO, Mwangi JC. Early Bacterial Cultures from Open Fractures – Differences Before and After Debridement. The Annals of African Surgery. 2017;14(2).
9. Gupta S. et al. A Comparative Study of Efficacy of Pre and Post Debridement Culture in Open Fracture. The Internet Journal of Orthopedic Surgery. 2018; 19(3).
10. Sop JL, Sop A. Open Fracture Management [Updated 2019 Jan 20]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. 2019 Jan-.
11. Kale AR, Sonawane CS, Waghmare VU, Kalambe H. Open Fractures and Incidence of Infection in Tertiary Care Government Hospital. Inj J Sci Stud. 2017;5(5):24-8.
12. Guerra MTE, Gregio FM, Castro CC. Infection rate in adult patiens with open fractures treated at the emergency hospital and at the ULBRA university hospital in Canoas, Rio Grande do Sul, Brazil. Rev Bras Ortop. 2017;52(5): 544-8.
13. Asia Pacific Society Of Infection Control. The APSIC Guidelines For The Prevention Of Surgical Site Infection. Forthcoming 2018.
14. Cross WW, Swiontkowski MF. Treatment principles

in the management of open fractures. Indian J Orthop. 2008;42(4):377-86

15. Zalavraz CG, Marcus RE, Levin LS, Patzakis MJ. Management of Open Fractures and Subsequent Complications. J Bone Joint Surg Am. 2007; 89:883-95
16. Deviandri R, Ismiarto YD, Singh A. Dilution of Open Fracture Grade IIIA of the Lower Leg Using Normal Saline 0,9% Mixed with Honey Compared With Normal Saline 0,9% to the Bacterial Growth. Ortho Res Online J. 2018; 2(5): 175-8.
17. Patzakis MJ, Wilkins J. Factors influencing infection rate in open fracture wounds. Clin Orthop Relat Res. 1989;(243): 36-40
18. Hoff WS, Bonadies JA, Cachecho R, Dorlac WC. East Practice Management Guidelines Work Group: Update to Practice Management Guidelines for Prophylactic Antibiotic Use in Open Fractures. The Journal of TRAUMA Injury, Infection and Critical Care. 2011;70(3): 751-4
19. Viscarra LF, Lozano L, Rios J, Forga MT, Soriano A. Preoperative Nutritional Status and Post-operative Infection in Total Knee Replacements: A Prospective Study of 213 Patients. Int J Artif Organs 2011; 34 (9): 876-881
20. Bohl DD, Shen MR, Kayupov E, Della Valle CJ. Hypoalbunemia independently Preduct Surgical Site Infection, Pneumonia, Length os Stay, and Readmission After Total Joint Arthroplasty. The Journal of Arthroplasty 31 (2016) 15–21
21. Singh J, Rambani R, Hashim Z, Raman R, Sharma HM. The Relationship Between Time to Surgical Debridement and Incidence of Infection in Grade III Open Fracture. Strat Traum Limb Recon (2012) 7:33–37
22. Diwan A, Eberlin KR, Smith RM. The Principles and Practice of Open Fracture Care, Chinese Journal of Traumatology xxx (2018) 1-6
23. Doshi P, Gopalan H, Pradhan C, Kurkani S, Bhandari M. Incidence of infection following internal fixation of open and closed tibia fractures in India (INFINITI): a multi-centre observational cohort study. BMC Musculoskeletal Disorders. 2017;18:156
24. Gosselin RA, Robert I, Gillespie WJ. Antibiotics for preventing infection in open limb fractures. Cochrane database syst rev. 2004; (1): CD003764
25. Brown KV, Walker JA, Cortez DS, Murray KC, Wenke JC. Earlier Debridement and Antibiotic Administration Decrease Infection. J Surg Orthop Adv. 2010; 19(1): 18-22.
26. Das R, Singh A, Srivastava P, Pradhan S, Murthy R. Microbial Profile and Antibiotic Susceptibility Pattern of Sugical Site Infection in Orthopedic Patients at a Tertiary Hospital in Bilaspur. Int J Sci Stud. 2015;3(3):43-7
27. Oliveira PR, Carvalho VC, Felix CS, Paula AP, Santos-Silva J, Lima ALLM. The incidence and microbiological profile of surgical site infections following internal fixation of closed and open fractures. Rev Bras Ortop. 2016;41(4):396-9.
28. Amaradeep G, Prakah S, Manjappa. Surgical site infections in orthopedic implant surgery and its risk factors: A prospective study in teaching hospital. Int J Orthop Sci. 2017;3(3): 169-72
29. Brooks, G. F., K. C. Carroll, J. S. Butel, S. A. Morse, dan T. A. Mietzner, *Jawetz, Melnick, & Adelberg's Medical Microbiology 26th Edition.* America. The McGraw-Hill Companies, Inc. 2013.
30. Kalmeijer MD, Coertjens H, Nieuwland-Bollen PM, Bogaers-Hofman D, Baere GAJ, Stuurman A, et al. Surgical Site Infections in Orthopedic Surgery: The Effect of Mupirocin Nasal Ointment in a Double-Blind, Randomized, Placebo Controlled Study. Clinical Infectious Diseases. 2002;35:353-8.