Confirmatory Factor Analysis Immune Response (TNF-α) to Dust Exposure on Tulungagung Marble Craftsmen

Noeroel Widajati[1*], Tri Martiana[2], Tri Niswati Utami[3], Hadi Prayitno[4]

[1]Department of Occupational Safety and Health, Faculty of Public Health, Universitas Airlangga, Surabaya, Indonesia

[2]Department of Occupational Safety and Health, Faculty of Public Health, Universitas Airlangga, Surabaya, Indonesia

[3]Department of Occupational Safety and Health, Faculty of Public Health, Universitas Islam Negeri Sumatera Utara, Indonesia

[4]Program Study Magister Ilmu Kesehatan, Universitas Jember

*Corresponding author: noeroel.widajati@fkm.unair.ac.id

Potential Reviewer:

Ng Yee Guan

Departement of Community Health, Faculty of Medicine and Health Sciences, University Putra Malaysia.

Email: shah86zam@gmail.com

ABSTRACT

Background: As marble craftsmen, marble dust which may contain high levels of silica potentially exposed to the job, so workers have a risk of danger and can cause health problems. The purpose of this study is to determine the immune response of workers in order to identify complaints of respiratory disorders, measure the condition of workers' lung function, specifically FEV1 using an autospirometer, and measure levels of TNF-α.

Objective: This study aims to build a model of the immunological response (TNF-α) to dust exposure using CFA (confirmatory factor analysis) and route analysis (Path Analysis).

Materials and Methods: This type of study used a cross-sectional, observational methodology. This study focuses on all 26 marble craftsmen in the marble house industry in the Tulungagung area. Dust levels were sampled using a type 500 high volume dust sampler for 10 minutes at each measurement location as one of the factors examined. TNF-α levels were extracted from blood serum samples and tested using the ELISA technique. Lung function was examined using a spirometer, and respiratory symptoms were assessed using an interview questionnaire.

Results: According to the findings of the path analysis test, the immunological response is influenced by the following variables: 1) the characteristic has a T statistic value of 2.750, which is more than 1.96. 2) The T statistic for dust exposure is 2.155, which is more than 1.96. The T statistic score of 3.102 for smoking habit is larger than 1.96.

Conclusion: The three criteria and the suggested hypothesis are accepted in conclusion. There is an influence of age and nutritional state on the immunological response, as well as an effect of dust exposure and smoking habit on the immune response.

Keywords: Individual characteristics, Dust exposure, Immune response
DOI Number: 10.48047/nq.2022.20.19.NQ99192 **NeuroQuantology2022;20(19): 2278-2290**

INTRODUCTION

Marble is a sedimentary rock from the sandstone group generated through material deposition on the earth's surface and in rivers (1). Marble is composed primarily of silica minerals (64.18–92.68%), along with CaO (0.002%–0.005%), Al2O3 (11.65-25.04%), and muck content (>15.0%). Marble has exceptionally high levels of crystalline silica, 95% (2). which can induce occupational illnesses. According to Ministry of Manpower and Transmigration No.5/MEN/2018, the threshold value for silica dust in the workplace is 0.05 mg/m^3 (3). Chronic exposure can result in a decline in lung function that exacerbates anomalies in lung function. Air pollutants induce respiratory tract disorders, specifically inhaled pollutants from ambient air, such as SO_2, O_3, NO_2, and dust particles (3).

Tumor Necrosis Factor (TNF-α) is one of the most investigated cytokines or mediators in the pathophysiology of pneumoconiosis. TNF-α is released by activated macrophages; this cytokine has been linked to the inflammatory response and fibrogenesis in pneumoconiosis and silicosis (4). Mischeler et al. (2016) reported that blood serum TNF-α levels increased significantly after 4–8 hours of exposure to crystalline silica. In addition, a person's dietary situation significantly influences the increase of TNF-α levels and lung function disorders (5). Obese individuals have excessive non-essential fat reserves, including subcutaneous and visceral fat. These diseases can impact the mechanical properties of the chest and diaphragm and signal a change in respiratory function, namely a reduction in lung function and alterations in the ventilation pattern in each respiration (6).

The research result Sahri et al., 2019 showed that 42.6% of respondents have an unsafe risk level of exposure to c-silica dust and potential health concerns as a result of c-silica dust exposure. According to the estimated calculation of chronic exposure risk, the degree of risk is expected to rise over the next 20 years. Silicosis is still evident in employees who die after exposure to between 0.05 and 0.1 mg/m^3 of silica dust. Each respondent's sampler for measuring c-silica dust in the workplace exceeded the limit value established by Indonesian regulation (Ministry of Manpower and Transmigration No. PER.13/MEN/X/2011), which was 55.3%. The value of concentration has a significant effect on the value of intake in employees; the greater the concentration of dust c-silica in the workplace, the higher the value of intake, and thus, the value of risk will also grow. Based on Minister of Manpower Regulation Number 5/MEN/2018, the Indonesian government sets the silica dust threshold value in the workplace at 3 mg/m^3 (3).

The research hypotheses were determined as follows: 1) an individual's characteristics (age and nutritional status); 2) dust exposure affects lung function; 3) smoking behavior, and 4) immune response (respiratory complaints and TNF-α levels). Proving the research hypothesis, improving the immune response of in-home industry workers, and recommendations for improving the work environment.

MATERIALS AND METHODS

Research Design

This observational study used a cross-sectional design. The study was conducted on three workers in the marble industry in the Tulungagung Regency. Data were collected at three locations/work units: location 1: packaging and finishing; location 2: lathe and scrub polishing; and location 3: cutting and craft operators. The population is composed of 26 workers. The total population technique determined the sample.

Measurement

A questionnaire was used to collect data on age, years of work, duration of dust exposure, and nutritional status as measured by anthropometry (height and weight). Serum TNF-α data was measured using a sample of the respondent's blood serum, as much as 1 mL of blood serum. The level of TNF Alpha was measured using the ELISA (Enzyme-Linked Immunosorbent Assay) test technique. The condition of lung ventilation was assessed using FVC (Forced Vital Capacity) and FEV1 (forced expiratory volume in one second) parameters. Normal if FVC is greater than 80%; FEV1 is greater than 70%; restriction if FVC is greater than 80%; FEV1 is greater than 70%; obstruction if FVC is greater than 80%; FEV1 is greater than 70%. Dust measurement was carried out using a high volume dust sampler type 500 for 10 minutes. Respiratory complaints data was measured using a questionnaire containing respiratory complaints felt by workers.

Ethical consideration

The study was reviewed and approved by the ethics committee of Faculty of Dental Medicine, Universitas Airlangga with reference number 244/HRECC.FODM/V/2019.

Data Analysis

The analysis of the data using confirmatory factor analysis (CFA) aims at generating constructs and identify the routes between variables utilizing path analysis. Primary data is derived from surveys and observations given directly to study participants. Using a questionnaire, the following four factors were measured: 1) Characteristic indicators (X1), such as age (X1.1), gender (X1.2), service years (X1.3), and nutritional status (X1.4). 2) Dust exposure variable (X2): the dust exposure indicator consists of the extended working period (X2.1), the use of personal protective equipment (X2.2), and the use of personal protective equipment (X2.2). 3) Smoking indicators (X3.1), smoking while at work (X3.2), and smoking frequency (X3) (X3.3) are all part of the smoking habit variable (X3). 4) The respiratory complaint indicator quantifies the immune response variable (Y) (Y1).

Observation data researchers conducted direct observations. There are three observational data: dust content (X2.3) is an indicator of dust exposure variable (X2). Measurement of dust quality in the workspace using a portable high volume sampler type 100. Other observational data are the results of lung function examination using an autospirometer (Y2) indicator of the immune response (Y). Forced Expiratory Volume 1 was measured using spirometry. Other observational data is that the level of TNF-α (Y3) is an indicator of the immune response variable (Y). TNF-α levels took samples from respondents' blood serum, and serum concentrations were measured using the ELISA method.

Data were analyzed using Confirmatory Factor Analysis (CFA)–SEM combined factor analysis and path analysis using Partial Least Square software version 3.3.8. Considerations using CFA-SEM can be used on small samples and are relevant to the research objective of testing the indicators that make up the variable construct, the validity, and reliability of each indicator as well as knowing the path of the relationship between exogenous variables and endogenous variables (inner model). The indicator validity is declared valid if the loading factor value is more significant than 0.7. The Cronbach alpha value is more significant than 0.6, and the AVE value is more significant than 0.5. The path of the relationship between exogenous and endogenous variables was stated to be significant based on a significant T value greater than 1.96.

RESULTS

In the tables below, it provides the results of an investigation of the frequency distribution of the distinctive indicators, dust exposure, smoking habit, and immunological response.

Table 1. Distribution of Frequency for Characteristic Indicators

Indicators	Frequency (f)	Percentage (%)
Age		
25 – 39	3	11.5
40 – 54	19	73.1
55 – 69	4	15.4
Gender		
Male	17	65.4
Female	9	34.6
Length of Work		
6 – 12 years	5	19.2
13 – 19 years	15	57.7
20 – 26 years	6	23.1
Nutritional status		
Normal (BMI < 23)	12	46.2

Obesity (BMI ≥ 23)	14	53.8

Source: primary data processed, (2022)

According to table 1, 19 employees (73.1%) are aged 40 to 54. Age is one of the most influential elements on a person's physical and mental health, and in this situation, lung function will improve with age. The bulk of workers are male, consisting of 17 (65.4%) of the total workforce. The average length of employment for marble employees is 19 to 20 years, with 15 people (57.7%) having this length of employment. Dust exposure's enhanced risk is also influenced by the duration of employment. As many as 14 workers (53.8%) had a BMI of 23 or above, indicating that they were obese. Oxygen intake during the processes of respiration and oxidation is affected by a person's body mass (Habibah et al., 2017). The bigger a person's weight, the faster their respiratory rate, and the greater the amount of dust inhaled.

Table 2. Frequency Distribution of Dust Exposure Indicators, Smoking Behavior, and Immune Response

Variables and Indicators	Frequency (f)	Percentage (%)
Dust exposure		
Length of Work		
< 8 hours or 8 hours	14	53.8
>8 hours	12	46.2
PPE		
Yes	10	38.5
No	16	61.5
Dust level (mg/m^3)		
≤ 3	14	53.8
> 3	12	46.2
Smoking behavior		
Smoking		
Never	10	38.5
Sometimes	12	46.2
Always	4	15.4
Smoking while working		
Never	11	42.3
Sometimes	7	26.9
Always	8	30.8
Smoking frequency		
No	10	38.5
< 15 cigarettes/day	12	46.2
≥ 15 cigarettes/day	4	15.4

Immune response		
Respiratory complaints		
No	14	53.8
Yes	12	46.2
Autospirometer results		
Abnormal	12	46.2
Normal	14	53.8
TNF-α		
Normal	22	84.6
Abnormal	2	5.4

Source: primary data processed, (2022)

The majority of workers in the marble home industry, or 14 workers (53.8%), work less than eight hours per day, while the majority of them use PPE (masks) that are not in accordance with dust dangers in the work environment, or 16 workers (61.5%). The observed dust level in the workplace is compared to the NAV dust level of 3 mg/m3. The majority of workers smoked less than 15 cigarettes per day, 12 workers (46.2%), while the majority of them never smoked at work, 11 workers (42.3%). The majority of workers smoked less than 15 cigarettes per day, 12 workers (46.2%).

Indicators of respiratory complaints, autospirometer examination results, and TNF Alpha levels suggest the immunological response. This is confirmed by the findings of pulmonary function examination using an autospirometer, which revealed that 14 employees (53.8%) had normal lung function and 12 workers did not have respiratory problems (46 workers), 2%) autospirometer values are not normal.

In the figure below, the outcomes of the model's preparation using CFA are shown (confirmatory factor analysis and to determine the path of the relationship used Path Analysis test).

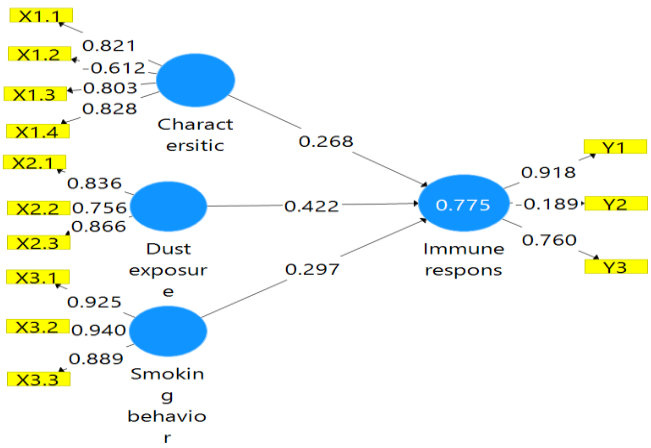

Figure 1. Outer Model Analysis

Figure 1 shows that the characteristic variable has two indicators with a loading factor value of less than 0.7, one invalid indication (X1.2) with a loading factor value of 0.612, and the autospirometer result indicator for the immune response variable (Y2). 0.189 loading factor Therefore, these two indicators must be omitted from the study.

After eliminating two indications with a loading factor value of less than 0.70, the results of the analysis are shown in the following table:

Table 3. Validity and Reliability of Variable-Construct Variables

Variable	Cronbach's Alpha	rho_A	Composite reliability	AVE
Characteristics	0.718	0.730	0.876	0.779
Dust exposure	0.782	0.904	0.860	0.672
Smoking behavior	0.907	0.911	0.942	0.843
Immune response	0.637	0.721	0.840	0.726

Source: primary data processed, (2022)

Table 3 shows that Cronbach's Alpha is 0.718, dust exposure is 0.782, smoking habit is 0.907, and immunological response is 0.637, all of which are more than 0.6. Since the composite reliability value for all variables is greater than 0.60 and the AVE value is greater than 0.50, it can be concluded that the indicators that comprise the variable constructs of the Confirmatory Factor Analysis test the indicators of the measured latent variables that represent a factor. Since latent variables cannot be measured directly, an indicator is required. when the size increases

The subsequent stage is to examine the route analysis of the examination of components that influence the immune response using boostrapping so that the t-significance value can be determined. The findings of the boostrapping study of the elements that affect the immunological response are displayed in Table 2 below.

Table 4. Path Analysis Significant Value

Path analysis	Original sample	Mean	STD	T-statistic	P-value
Characteristics ➔ immune response	0.326	0.338	0.119	2.750	0.006
Dust exposure ➔ immune response	0.308	0.301	0.143	2.155	0.032
Smoking behavior ➔ immune response	0.393	0.396	0.127	3.102	0.002

Source: primary data processed (2022)

Table 4 shows that the immune response is influenced by the following factors: 1) the presence of a T statistic value larger than 1.96. 2) The T statistic for dust exposure is 2.155, which is more than 1.96. The T statistic score of 3.102 for smoking habits is larger than 1.96. The three criteria and the suggested hypothesis are accepted in conclusion. The immune response is affected by age, nutrition, dust exposure, and smoking.

Table 5. R-square immune response

	R-square	R Square Adjusted
Immune response	0.795	0.767

Source: primary data processed, (2022)

Table 5 shows that the magnitude of the contribution of characteristic characteristics, dust exposure, and smoking habit to the immune response is 0.795, which is near to 1, showing that the impact of these factors is favorable. The categories for r square are mild, moderate, and strong. The conclusion is that the value of 0.795% has a considerable impact, or that 79.5% of the immune response is influenced by distinctive characteristics, such as dust exposure and smoking habit, and that 21.5% of the immunological response is controlled by factors other than those analyzed.

DISCUSSIONS

Stanojevic et al. (2008) found a substantial correlation between age and lung function. Maximum muscular strength drops by 20% between 20 and 40 years old, while the requirement for energy substances rises until age 40. The diminished desire for energy is a result of a weakened physical condition (7). According to Budiono (2007), as a person ages, organ performance usually declines, and lung function is no exception. Employees' lung function will deteriorate due to dusty environmental circumstances and other variables, such as smoking habits, mask unavailability, exposure duration, and illness history. Humans between the ages of 30 and 40 typically see a decline in lung function, although the prevalence of lung problems increases with age (8). Suyono (1995) also reported that the likelihood of a deterioration in lung function increases with a person's age. Numerous anatomical and functional alterations occur in the thorax and lungs of aged individuals. At this age, the alveoli become less elastic and more fibrous, and they contain fewer functional capillaries, resulting in a decline in their use. Due to the lungs' oxygen diffusion capacity to meet the body's needs (9).

Oxygen intake during respiration and oxidation is affected by an individual's weight. The bigger a person's weight, the faster their respiratory rate, and the greater the amount of dust inhaled. According to the Department of Nutrition and Public Health (2007), a persistent shortage of meals will disrupt the body's physiological composition. A person with a lower or higher nutritional status may suffer a drop in Forced Vital Capacity (FVC), which might influence the incidence of pulmonary function problems. Good nutritional status influences the body's food intake, which is used as an energy source; the body's primary energy source is sourced from energy intake and carbs, protein, and fat. If the diet is healthy, the digestive system and circulation throughout the body will be healthy as well (10). Exposure to silica dust that can cause lung fibrosis takes between 5 and 30 years; this is also significantly influenced by the health status of the craftsmen, lifestyle, nutrition, PPE (masks) that are in accordance with the exposure used by craftsmen, and numerous other factors (Jasminarti and Winariani, 2016). Length of time worked can represent the amount of daily exposure time experienced by workers. This study's findings were negative; there was no correlation between length of employment and the lung function of workers. This study's findings contradict research completed in Malaysia, Iran, and Indonesia. As well as earlier research findings about the length of service of employees. This is possible since workers in the marble home industry spend varying amounts of time every day on the job, and those who spend even less hours at work have the potential to experience a decrease in their lung function (11–13).

Marble dust containing silica in marble craftsmen with levels that continue to increase can cause pneumoconiosis and silicosis. The main factors that play a role in the pathogenesis of this lung disease are the composition of dust particles inhaled by workers, physical properties, levels and duration of exposure and the response of the respiratory tract to these dust particles. Host factors play an important role in the tissue response to inhaled agents or substances (14).

According to Susanto (2011), dust particles will stimulate macrophages to release products which are mediators of an inflammatory response and start the process of fibroblast proliferation and collagen deposition. Important macrophage mediators responsible for tissue damage, cell collection and stimulation of fibroblast growth are:

1. Leukotriene LTB4 and IL-8 which are chemotaxis against leukocytes.
2. Cytokines IL-1, TNF-α, eutrophil, and PDGF play a role in fibrogenesis.

The most important mediators in the pathogenesis of silicosis pneumoconiosis are Tumor Necrosis Factor (TNF)-α, Interleukin (IL)-6, IL-8, Platelet-Derived Growth Factor (PDGF) and Transforming Growth Factor (TGF)-β. Most of these mediators are very important for the process of fibrogenesis (4). Exposure to inhaled respiratory dust by workers such as rock dust containing silica crystals which are chronic in nature is associated with chronic inflammatory changes in the alveoli. The condition of chronic alveolitis causes pulmonary fibrosis.

Respiratory protection equipment is the final measure taken to mitigate the effects of dust exposure. Most workers utilize slayers or T-shirts as respiratory protection equipment. According to the findings of interviews with river stone craftsmen, the use of respiratory protective equipment that meets the standards interferes with work and is uncomfortable, resulting in air containing dust entering the respiratory tract directly, and if this condition is allowed to persist, there is a risk of impaired function lungs.

The amount of TNF-α in human blood serum is one of the biological indicators employed in this investigation. According to the results of this study's analysis, there is a correlation between blood TNF-α levels and lung function problems. This is consistent with research conducted in India regarding the association between blood TNF-α levels and the occurrence of lung illness (15). If the body's cells become inflamed due to a pathogenic infection or other external particles such as dust, serum TNF-α becomes a biological marker. Serum TNF-α is plentiful in areas where macrophages are prevalent, such as the lungs, where macrophages are abundant. Consequently, serum TNF-α is also a biological marker of lung physiology.

The WHO survey (2011) that around 70% of men in Indonesia are smokers, and of them are workers. Cigarettes can cause a decrease in lung function in the long term because one cigarette contains various types of substances that are harmful to the health of the body. Toxic substances in cigarettes will accumulate in number in the body, especially in the lungs (15). The presence of this toxin will inhibit the process of gas exchange of O_2 with CO_2 in the alveolus. This condition will get worse as the number of cigarettes smoked increases. Damage to the alveoli is also very likely to occur due to smoking habits. This will certainly reduce the number of functional alveoli that play a role in the respiration process. As a result, there will be a decrease in the function of the lungs.

Beginning with one or more cigarettes per day, smoking is a habitual behavior that is performed repeatedly. The structure and function of the respiratory tract and lung tissue can be affected by smoking. The deterioration of lung function is accelerated by smoking. Compared to other workplace health risks, smoking can also decrease vital lung capacity (9).

Prevention of occupational diseases was aimed at diagnosing the disease at an early stage and preventing complications. Workers exposed to inhaled silica should be followed in a health monitoring program, with periodic assessment of the clinical history, spirometry and chest X-ray, at intervals determined by accumulated years of exposure. When complicated pneumoconiosis is diagnosed, the diffusion capacity and static lung volume are determined. Routine examinations are performed every 1-3 years, depending on the clinical form, functional involvement, and radiology

(16). The role of silica in cancer and the possible synergies with tobacco in the development of COPD in exposed subjects make smoking cessation a very important goal in this group of patients (consistent level of recommendation). As sufferers of chronic respiratory disease, patients with silicosis are candidates for *Streptococcus pneumoniae* and annual influenza vaccination (high-quality evidence, consistent recommendation) (17).

Workers who are more than 30 years old are at risk of occupational diseases such as silicosis. This is because physiologically with age there will be a decrease in lung function such as reduced effectiveness of ciliary function, increased diameter of the trachea and respiratory tract, reduced elasticity of lung parenchymal supports, decreased mass lung tissue, decreased maximum inspiratory and expiratory pressures, chest wall stiffness, reduced cough effectiveness, increased residual volume, and decreased FEV and FVC, in addition to the increasing age of workers the longer the exposure time to the dust. But this must be adjusted to the number of particles and the level of dust concentration in the air. This is following the theory according to Suma'mur (2013), the effect of health problems on workers due to exposure to dust particles, and individual factors from the workers themselves. Factors from the workers themselves include age, adjustment, body resistance to disease, and the degree of health of the worker's body (17).

CONCLUSION

The contribution of characteristic factors, such as dust exposure and smoking behavior, to the immune response is depicted in Table 5 as 0.795, which is approaching 1, indicating that the contribution of these factors is positive. The categories for r square are mild, moderate, and strong. The conclusion is that the value of 0.795% has a considerable influence, or that 79.5% of the immune response is influenced by distinctive characteristics, such as dust exposure and smoking behavior, and that 21.5% of the immunological response is controlled by factors other than those analyzed.

REFERENCES

1. Noor D. Program studi teknik geologi. Pengantar Geol. 2009;279.
2. Ojakangas RW. Sand and sandstone [book review]. Vol. 275, American Journal of Science. 1975. 607–608 p.
3. Permenaker. Peraturan Menteri Ketenagakerjaan Republik Indonesia Nomor 5 Tahun 2018 Tentang Keselamatan Dan Kesehatan Kerja Lingkungan Kerja, Menteri Ketenagakerjaan. 2018.
4. Verleden, GM, Demedts MG, Westhovens R, Thomeer M, editors. Pulmonary Manifestations of Systemic Diseases [Internet]. European Respiratory Society; 2005. Available from: http://erspublications.com/lookup/doi/10.1183/1025448x.erm3405

5. Mischler SE, Cauda EG, Di Giuseppe M, McWilliams LJ, St Croix C, Sun M, et al. Differential activation of RAW 264.7 macrophages by size-segregated crystalline silica. J Occup Med Toxicol. 2016;11:57.
6. Collins LC, Hoberty PD, Walker JF, Fletcher EC, Peiris AN. The effect of body fat distribution on pulmonary function tests. Chest. 1995;107(5):1298–302.
7. Stanojevic S, Wade A, Stocks J, Hankinson J, Coates AL, Pan H, et al. Reference Ranges for Spirometry Across All Ages. Am J Respir Crit Care Med [Internet]. 2008 Feb 1;177(3):253–60. Available from: https://www.atsjournals.org/doi/10.1164/rccm.200708-1248OC
8. I B. Faktor Risiko Gangguan Fungsi Paru pada Pekerja Pengecatan Mobil. Universitas Diponegoro; 2007.
9. Suyono. Buku Ajar Ilmu Penyakit Dalam Jilid II. In Jakarta: Jakarta Balai Penerbit FKUI; 2001.
10. R.T A. Pengaruh Pemakaian APD Terhadap Kejadian Kecelakan Kerja Pada Perajin Batu Marmer di Desa Gamping Kabupaten Tulungagung. Str J Ilm Kesehat. 2013;
11. Dinda Sekar Mentari, Taufik Ashar, Nurmaini Nurmaini. The Relationship between Work Period and Dust Level with Disruption of Lung Capacity in Asphalt Mixing Plant Production Workers (AMP) Medan in Public Works Office 2019. Britain Int Exact Sci J. 2020;2(1):115–9.
12. Hashemi Habybabady R, Nasibi Sis H, Paridokht F, Ramrudinasab F, Behmadi A, Khosravi B, et al. Effects of dust exposure on the respiratory health symptoms and pulmonary functions of street sweepers. Malaysian J Med Sci. 2018;25(6):76–84.
13. Neghab M, Alipour A. Evaluation of respiratory toxicity of fiberglass dust. Iran Occup Heal. 2009;6(2):19–25.
14. Habybabady RH, Nasibi Sis H, Paridokht F, Ramrudinasab F, Behmadi A, Khosravi B, et al. Effects of Dust Exposure on the Respiratory Health Symptoms and Pulmonary Functions of Street Sweepers. Malaysian J Med Sci [Internet]. 2018;25(6):76–84. Available from: http://www.mjms.usm.my/MJMS25062018/08MJMS25062018_OA5.pdf
15. Mir H, Koul PA, Bhat D, Shah ZA. A case–control study of tumor necrosis factor‐alpha promoter polymorphism and its serum levels in patients with chronic obstructive pulmonary disease in Kashmir, North India. Lung India. 2020;37(3):204–9.
16. OSHA-REPORT. Occupational Exposure to Respirable Crystalline Silica -- Review of Health Effects Literature and Preliminary Quantitative Risk Assessment. Vol. 34, Docket OSHA'. 2010.
17. Suma'mur. Higiene Perusahaan dan

Kesehatan Kerja. XII. Jakarta: PT. Toko Gunung Agung; 2013.