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THE EFFECT OF NUTRITIONAL STATUS AND TNF ALPHA TO LUNG FUNCTION ON MARBLE CRAFTSMAN

Noeroel Widajati[a]*, Nisrina Tiara[a], Tri Martiana[a], Saliza Mohd Elias[b], Yuni Priyandani[c]

[a]Department of Occupational Health and Safety, Public Health Faculty, Universitas Airlangga, Surabaya
[b]Department of Enviromental and Occupational Health, Faculty of Medicine and Health Science, Universiti Putra Malaysia, Malaysia
[c]Faculty of Pharmacy, Universitas Airlangga, Surabaya, Indonesia

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

Graphical abstract

FEV_1			
Nutritional Status	Mean ± SD	Min.	Max
Normal	2.04±0,39	1.20	2.64
Obese	1.61±0,47	0.86	2.52
	p = 0.018		
FVC			
Nutritional Status	Mean ± SD	Min.	Max
Normal	2.55±0,49	1.51	1.13
Obese	1.98±0,52	3.28	2.83
	p = 0,009		
FEV_1/FVC			
Nutritional Status	Mean ± SD	Min.	Max
Normal	71.00±1.90	67.90	74.30
Obese	70.9±3,67	64.20	78.90
	p = 0.943		

Abstract

Marble craftsmen are potentially exposed to marble dust which contains about 60% silica resulting in marble craftsmen facing this hazard and possibly physiological lung disorders. This study aims to analyze the effect of working period, nutritional status, and TNF-a on physiological lung disorders. study is a quantitative study with observational research type and cross sectional research design In this study, the data collection techniques used were: (1) measurement of personal dust levels using a personal CCZG2A type; (2) TNF-a levels using the ELISA technique, (3) lung function with MIR spirolab III; (4) collection of data on respiratory complaints using the ATS standard questionnaire. (5) measurement of nutritional status by weighing body weight and measuring height. The subjects of this study were all marble craftsmen who worked in the marble household industry in Tulungagung Regency as many as 30 people with the number of samples taken as many as 26 craftsmen. The average value of %FVC in obese respondents was lower than that of respondents with normal nutritional status. The results of linear regression analysis showed that the respondents' working period had a significant effect (p=0.003) on serum TNF-a levels, with a value of p≤0.05. Serum TNF-a levels also had a significant effect on FEV1 and FVC (FEV1 p=0.007; FVC p=0.008), and nutritional status also had a significant effect on FVC (p=0.05, β=0.02). The greater a person's body weight, the faster the breathing frequency, so that more dust enters the respiratory air.
Keywords: Nutritional status, TNF-a serum levels, pulmonary function disorders

1.0 INTRODUCTION

One type of dust that causes occupational related diseases is silica dust, that is originating from marble stone with a SiO2 content of around 28.35% - 45% [1]. The type of dust that can cause lung disease in work environment is dust with a particle size of less than 2.5 microns, including silica dust produced from industrial activities using river stone as raw material [2]. The chronic exposure of silica dust could decrease the

pulmonary function and increase the pulmonary disorders. Based on research results presented at the NIOSH conference, it was stated that 88% of 260 stone dust samples, one of which was sandstone dust, more than 30% could be inhaled by workers when they worked [3].

The agent that is often considered as a cause of respiratory system disease and the most influencing of occupational disease incidence is respirable dust. Respirable dust is dust measuring 0.5 µm to 4 µm which can be inhaled by workers while working and can enter the respiratory tract (SNI 7325, 2009). The respirable dust with 2,5 microns size could trigger any respiratory infections.

Marble is one of sedimentary rock in the sandstone group that is formed by the deposition of material on the earth's surface and the rivers [2]. A study conducted on sandstone workers in Thailand showed that workers in the stone cutting group and stone carving group had been exposed to silica dust that exceeded the threshold limit for inhalable silica dust levels according to OSHA PEL (>0.05 mg/m3) [4]. Surface silica dust particles that injure lung tissue will activate macrophages and neutrophils and then release a number of cytokines and oxidants. Cytokines secreted by macrophages then cause fibroblast proliferation and deposits of connective tissue matrix material in large quantities [5]. Oxidant secretion induced by neutrophils will cause genotoxicity or damage to the DNA chain which ultimately manifests as lung cancer [6].

Research at CV Adhi Jembatan Batoe, Tulungagung, East Java, Indonesia that marble craftsmen in the study that several factors including age, nutritional status, and working period, have a significant influence on lung function disorders. Another influential factor, levels, including inhaled dust levels and duration of exposure in the workplace, also had a significant effect on the impaired lung function of marble craftsmen. However, IL-13 did not affect lung function, and dust exposure did not affect IL (interleukin)-13 [7]. Workers should consistently utilize appropriate personal protective gear, including masks tailored to the specific conditions of their workplace, and ensure their usage across all workstations. Furthermore, it is recommended for workers to uphold their physical well-being by prioritizing sufficient rest, consuming nourishing meals, and engaging in consistent physical activity [24].

One of the cytokines or mediators in the pneumoconiosis' pathogenesis, that is most widely studied, is Tumor Necrosis Factor-a (TNF-a). TNF-a is secreted by activated macrophages. Several studies stated that TNF-a is a potential biomarker that takes it role as an indicator of exposure to respirable dust containing crystalline silica [8]. The results of a study by Lee *et al.,* (2009)on subjects exposed to inorganic respirable dust, especially silica dust, showed a significant relationship between radiological findings and TNF-a serum levels (*rho*= 0.306, *p*< 0.01) [9].

Another study stated that after exposure for 4-8 hours to crystalline silica there was a significant increase in blood serum TNF-a levels [10]. A case control study on workers in China who were exposed to respiratory dust with high levels of silica showed that the cytokine TNF-a was associated with the risk of silicosis [11]. Serum TNF-a and Matrix metalloproteinase (MMP-9) levels increased in individuals exposed to silica dust ($p<0.05$), and there was a significant relationship between serum TNF-a and MMP-9 levels in individuals exposed to silica dust ($r=0.696$, $p<0.01$) and patients with silicosis ($r=0.768$, $p<0.01$) [12].

In Indonesia, the impact of silica dust levels on marble home industry workers is least to be studied. Therefore, this study needs to be done through examining lung function and biomarkers of inflammatory also fibrogenic responses in the body, such as interleukin-13. Gamping Village, Campurdarat, Tulungagung Regency has many home industry locations for river stone crafts. Data recorded in the Campurdarat Health Center area recorded 8 people who contracted lung disease with a background as river stone workers. The purpose of this study was to analyze the correlation between silica dust exposure and serum interleukin-13 (IL-13) levels and lung function in marble home industry workers in Tulungagung Regency, East Java, Indonesia.

2.0 METHODOLOGY

This research is a quantitative study with the type of observational research where researchers observe variables without intervening in the variables studied. Observing the variables of study, namely the characteristics of the respondents, measuring the levels of inhaled dust, and examining the condition of the marble craftsmen's lung function.

This study also uses a cross sectional design where measurements and observations in this study are made simultaneously at one time when conducting research in the field.

This research was conducted in one of the marble household industries located in Tulungagung Regency. This research was conducted from January 2020 to December 2020. The population of this study were 30 workers in the Tulungagung marble home industry. The sampling technique was carried out by simple random sampling By using the Lemeshow sample formula.

The research sample taken was 26 workers out of a total of 30 workers. The population of this study were taken with several inclusion factors such as willingness to participate expressed in informed consent, and never had a history of tuberculosis, asthma, allergies, and heart disease. The independent variable of this study was the nutritional status of workers, while the dependent variables were serum TNF-a levels and impaired lung function.

Data collection techniques were carried out by measuring workers' body mass index, serum TNF-a levels and lung function. Nutritional status was measured by measuring workers' height and weight, resulting in the correct body mass index. Referring to the 2022 Minister of Health Regulation concerning.

Measurement of TNF-a serum levels was carried out by taking worker blood samples which were then analyzed using the ELISA technique. The ELISA technique originated from Peter Permann and Eva Engvall from Stockholm in 1971. Lung physiology was measured using spirometry. Interviews and questionnaires were also used to collect worker data regarding individual characteristics, use of personal protective equipment (masks), and smoking habits.

Data were analyzed using descriptive analysis, correlation analysis, and comparative analysis. Descriptive analysis was aimed at calculating the frequency distribution of each variable. Spearman and Pearson correlation analysis was used to analyze the correlation between variables. Finally, comparative analysis was analyzed by free sample t-test. Ethical clearance number 163/EA/KEPK/2019 at FKM Universitas Airlangga.

3.0 RESULTS AND DISCUSSION

The respondents of this study who fall into the inclusion criteria were 26 people who work in the marble home industry at Tulungagung Regency, East Java, Indonesia.

Table 1 Age Distribution, Nutritional Status, Working Period, Length of Work, Smoking Habits, and Suitability of the Use of PPE for Marble Home Industry Workers in Tulungagung

Age (years)	Total	
	N	%
<49	12	46.2
≥ 49	14	53.8
Total	26	100
Nutritional Status (BMI)	**Total**	
	N	%
Thin	0	0.0
Normal	15	57.7
Obese	11	42.3
Total	26	100
Working Period (years)	**Total**	
	N	%
<16 years	13	50.0
≥ 16 years	13	50.0
Total	26	100
Length of work (hours / day)	**Total**	
	N	%
< 8 hours / day	10	38.5
> 8 hours / day	16	61.5
Total	26	100
Smoking habits	**Total**	
	N	%
Mild (IB = 0-200)	24	92.3
Moderate (IB = 201-600)	2	7.7
Severe (IB> 600)	0	0.0
Total	26	100
Suitability for the use of PPE	**Total**	
	N	%
In accordance with	15	57.7
Not suitable	11	42.3
Total	26	100

Table 1 shows that mostly, the age of the respondents are ≥49 years old (53.8%), while the rest are under 49 years old (46.2%). The majority of workers' nutritional status is the workers who have normal nutritional status (57.7%). Furthermore, 11 workers (42.3%) have obese nutritional status. The working period of the respondents is equally divided into two categories, namely <16 years (50%) and ≥16 years (50%). Most of workers work> 8 hours per day (61.5%). Moreover, most of workers are classified as having a mild smoking habit (92.3%) and the rest have a moderate smoking habit (7.7%). Most of the workers have worn PPE in accordance with the workplace requirements (57.7%).

Lung Physiology and TNF-a Serum

Physiological conditions and TNF-a serum levels of marble industry workers in Tulungagung are shown in Table 2.

Table 2 The Distribution of Respiratory Complaints, Physiological Pulmonary Function Status, Physiological Pulmonary Profile, and TNF-a Serum Levels in Marble Home Industry Workers in Tulungagung

Respiratory Complaints	Total	
	N	%
None	11	42,3
Exist	15	57,7
Total	26	100
Physiological Pulmonary Function Status	**Total**	
	N	%
Normal	19	73.1
Abnormal	7	26.9
Total	26	100

Physiogical Pulmonary Profile	Mean ± SD	Min.	Max
FEV_1 (litre)	1.86±0.47	0.86	2.64
FVC (litre)	2.31±0.57	1.13	3.28
FEV_1/FVC (%)	70.9±2.72	64.2	78.9

TNF-a Serum	Mean ± SD	Min.	Max
TNF-a Serum (ng/L)	62,3±52,4	25,04	253,11

Table 2 shows that most of the respondents had respiratory complaints (57.7%). The physiological pulmonary function status of most workers was still in normal condition (73.1%). The pulmonary function capacity profile of workers is shown by the values of FEV1, FVC, and FEV1/ FVC, which respectively show the mean values of 1.86 liters, 2.31 liters and 70.9%.

The TNF-a serum level in workers was averaged in 62.3 ng / L. Respiratory complaints in workers exposed to dust include coughing, phlegm, wheezing, shortness of breath and chest pain.

Correlation between Individual Characteristics, Physical Pulmonary Condition, TNF-a Serum and Nutritional Status

Individual Characteristics with the Nutritional Status

The analysis of the relationship strength between individual characteristics and nutritional status is shown in Table 3.

Table 3 Relationship between Individual Characteristics and Physiological Pulmonary Status

			Physiological Pulmonary Status
Spear-man's rho	Age	Correlation Coefficient	0,012
		Sig (2-tailed)	1,00
	Working Period	Correlation Coefficient	0,227
		Sig (2-tailed)	0,42
	Working Duration	Correlation Coefficient	0,405
		Sig (2-tailed)	0,04
	Smoking Habits	Correlation Coefficient	0,240
		Sig (2-tailed)	0,49

Spearman correlation test between individual characteristics andphysiological pulmonary function status shows that only the working duration variable has a significant value of 0.04 (sig. = 0.04 < α = 0.05) with a correlation coefficient of 0.405. Then, the other variables such as age, working period, and smoking habits did not have a significant result (sig.> α= 0.05). This indicates that the length of time spent for working is related to the physiological pulmonary function status of workers. Additionally, this has a strong positive relationship.

Correlation between Physiological Pulmonary Conditions and TNF-a Serum and Nutritional Status

1. Physiological Pulmonary Status

The analysis of the correlation between physiological pulmonary status and nutritional status is presented in Table 4.

Table 4 The Correlation between individual Characteristics and NutritionalSstatus

			Nutritional Status
Spear-man's rho	Pulmonary Complaints	Correlation Coefficient	0,386
		Sig (2-tailed)	0,05
	Physiological Pulmonary Function Status	Correlation Coefficient	0,168
		Sig (2-tailed)	0,65

The Spearman correlation test shows a significant value in the pulmonary complaints variable (sig. = 0.05 ≤ α = 0.05). This indicates a strong positive relationship between pulmonary complaints and the nutritional status of workers (coef. = 0.386). Meanwhile, there is no corellation between physiological pulmonary function status with nutritional status.

2. TNF- a Serum

The analysis of the correlation between TNF-a serum levels and nutritional status is presented in Table 5.

Table 5 The Correlation between TNF-a serum levels and nutritional status (Table does not exist)

			Nutritional Status
Pearson	TNF-a serum level	Correlation Coefficient	-0,042
		Sig (2-tailed)	0,83

Pearson correlation test shows insignificant value (sig. = 0.83 > α = 0.05). This indicates that there is no relationship between serum TNF-a levels and nutritional status.

TNF-a Serum and Pulmonary Physiological Profile Differences in Workers with Normal and Obese Nutritional Status

The comparative analysis was conducted to compare whether there were differences in TNF-a serum levels and pulmonary function profiles between groups of workers with normal and obese nutritional status.

1. TNF-a Serum Levels

The differences in TNF-a serum levels between workers with normal and obese nutritional status are presented in Table 6.

Table 6 The Differences in TNF-a serum levels between workers with normal and obese nutritional status

Nutritional Status	Mean ± SD	Min.	Max
Normal	59.40±45.13	25.043	212.069
Obese	63.16±19.04	29.004	253.110
	α = 0,745		

The data shows that the results of the analysis of differences in TNF-a serum levels obtained a p value of 0.745, where sig. > α = 0.05, which means there is no difference in levels TNF-a serum among workers with normal nutritional status and obesity. However, the mean of TNF-aserum levels in obese respondents were higher than workers with normal nutritional status. The mean of TNF-a serum level in obese workers is 63.16 ng / L, with the TNF-a level serum obtained at least 29,004 ng / L, and the highest TNF-a serum level is 253,110 ng / L. Whereas, for workers with normal nutritional status, the mean of TNF-a serum level is 59.40 ng / L, with the TNF-a serum level obtained at least 25,043 ng / L, and the highest TNF-a serum level of 212,069 ng. / L.

2. Pulmonary Capacity Profiles

Differences in physiological pulmonary capacity profiles between workers with normal and obese nutritional status are presented in Table 7.

Table 7 Differences in Physical Capacity Profiles of Workers Nutritional Status

FEV_1			
Nutritional Status	Mean ± SD	Min.	Max
Normal	2,04±0,39	1,20	2,64
Obese	1,61±0,47	0,86	2,52
	α = 0,018		
FVC			
Nutritional Status	Mean ± SD	Min.	Max
Normal	2,55±0,49	1,51	1,13
Obese	1,98±0,52	3,28	2,83
	α = 0,009		
FEV_1/FVC			
Nutritional Status	Mean ± SD	Min.	Max
Normal	71,00±1,90	67,90	74,30
Obese	70,9±3,67	64,20	78,90
	α = 0,943		

The data obtained shows that the results of the analysis of differences in FEV_1 obtained a significant of 0.018, which means that there is a difference in FEV_1 between workers with normal and obese nutritional status. The average %FEV_1 among obese respondents was lower than normal nutritional status workers.

The results of the analysis of FVC differences obtained a significant p value of 0.009, which means that there is a difference in FVC between workers with normal nutritional status and obese. The FVC mean in obese respondents was lower than respondents with normal nutritional status.

The results of the analysis of differences in FEV_1/ FVC values obtained p value of 0.943, where the p value > a = 0.05, which means that there is no difference in FEV_1 / FVC values between workers with normal nutritional status and obese. However, the average FEV_1 / FVC value in obese respondents was lower than respondents with normal nutritional status.

The research results showed that age, working duration, and smoking habits were not associated with physiological pulmonary function status, but the working period had a strong positive relationship with physiological pulmonary function status. This shows that age is not fully an independent variable, but there are other factors that also contribute to lung function conditions. Research in line shows that there is a negative relationship between age with lung function capacity, where the older a person gets, the more their lung function capacity decreases [13]. As in this research, most of the ages of both river stone craftsmen and non-craftsmen are above 36 years.

Factors such as age, race, gender and body posture, other factors that influence the vital capacity of the lungs are the physiological capacity of the lungs themselves, lung elasticity, exercise, and the size of the inside of the lungs [14]. Apart from influencing lung function values, the age factor can also influence TNF-a levels. Dust exposure with a duration of several years but if it is within a day.

Workers who are exposed every day to dust containing silica have the potential to experience silicosis lung disease in the long term. This type of accelerated silicosis can occur after exposure to dust for weeks, but usually occurs 5-10 years after the start of exposure [15]. Working period tends to be a risk factor for lung function disorders in workers who work in dusty areas for more than 10 years. Asthma and acute respiratory tract obstruction are the result of short-term exposure to dust. If exposure to inorganic dust lasts long enough, an initial inflammatory reaction will arise [16]. This can happen because the time spent by workers in a day is vary and even the workers with less working time also have the potential to have a lung function disorders.

Smoking triggers degenerative diseases. Smoking often impacts the respiratory system. The results of this study indicate that there is no correlation between workers' smoking behavior and workers' pulmonary function status. These results are in line with research conducted in India on mine area workers [17]. Basically, cigarettes have substances that can cause any lungs damage. Therefore, with only frequent smoking a person possible to have a bad pulmonary function. In this research, the causes that trigger any

pulmonary disorders is still ambiguous, whether it is caused by dust or by smoking habits. Several studies conducted in places with similar conditions showed a certain pattern. There is a positive correlation between smoking and physiological pulmonary conditions plus a long work period, which means that workers have long been exposed to the dust [18], [19]. Moreover, smoking can be only a cumulative effect that triggers lung function disorders in workers, but not as the main cause.

Correlation between Physical Pulmonary Condition and Nutritional Status

The nutritional status was indicated by body mass index (BMI). The results of the analysis showed a positive relationship between nutritional status and pulmonary function condition. This result is in line with research conducted in Pakistan which states that there is a relationship between body mass index and lung function parameters [20].

Lung volume and capacity become larger with the increasing of BMI when the BMI is below 24 kg / m^2. Otherwise, when the BMI is above 24 kg / m^2, lung volume and capacity become smaller as BMI increases above 24 kg / m^2. There are several reasons regarding these phenomena. The increase position of the diaphragm near the chest cavity causes a decreasing lungs ability to expand when the air enters. Obesity also causes the accumulation of fat on the chest wall, causing abnormalities in the intercoastal muscles system, which help the chest move to breathe. In addition, excess body weight triggers an excessive inflammatory response which affects the lung tissue and reduces the diameter of the respiratory tract [20].

Correlation between TNF-a Serum and Nutritional Status.

The results showed there is no relationship between TNF-a serum levels and the nutritional status. Since TNF-a serum is a biological marker of inflammation, the presence of inflammation in workers' lungs is not always due to excessive nutritional status, but also due to dust exposure during work.

Differences in TNF-a Serum and Pulmonary Physiological Profile with The Workers' Nutritional Status

The research results did not show any difference in TNF-a serum levels in workers with normal and obese nutritional status. Nevertheless, the mean of TNF-a serum levels of obese workers is higher. Meanwhile, the lung function capacity profile showed a significant difference between workers with normal and obese nutritional status.

TNF-a serum is a pro-inflammatory cytokine that is released when macrophages are being activated. TNF-a serum plays an important role in various cellular response processes such as inflammation, apoptosis, differentiation, and others. Since TNF-a serum has an important role in the inflammatory response, TNF-a serum becomes a biological marker. Accordingly, when the body's cells are inflamed, either due to pathogenic infection or due to other foreign particles such as dust, TNF-a serum is found in many places where macrophages are abundant in lungs tissues. Therefore, TNF-a serum is also a biological marker of pulmonary physiological conditions.

Research states that TNF-a is a potential biomarker as an indicator of exposure to respiratory dust containing crystalline silica [8], [10]. stated that after exposure for 4-8 hours to dust containing crystalline silica there was a significant increase in blood serum TNF-a levels. The results of the study are in line with artificial stone workers who were exposed to stone dust containing particles below 1 micron, that exposure to stone dust with a particle size < 1 µm can influence the increase in serum TNF-a ($p = 0.007$), and this increase in serum TNF-a can affect occurrence of respiratory complaints ($p = 0.021$) [21].

The temperature in the work environment which ranges between 31-36 0C, makes stone dust containing silica particles drier and lighter so it is easily carried by air currents, thereby expanding the distribution of the dust [22]. A hot work environment will cause the body to experience an increase in metabolism to maintain a stable temperature, so the body has to sweat more to reduce body temperature.

People with obesity tend to experience inflammation more easily because of there is inadequate regulation of their immune system. Thus, high TNF-a serum levels are associated with the decreasing of pulmonary function capacity. In addition, physiologically, the accumulation of fat tissue due to obesity also affects the structure of the respiratory system. Body weight affects a person's oxygen uptake in the respiration and oxidation processes [23].

The greater a person's body weight, the faster the breathing frequency, so that more dust enters the respiratory air. The amount of intake or intake of a substance is directly proportional to the value of chemical concentration, inhalation rate, frequency of exposure and duration of exposure, where the greater the chemical, inhalation rate, frequency of exposure and duration of exposure, where the greater the value, the greater the intake of chemicals a person receives. Researchers recommend a healthy diet for respondents with obese nutritional status through portion control at each meal.

4.0 CONCLUSION

There is a difference in TNF-a serum levels and physiological pulmonary disorders between the workers with normal nutritional status and the workers with obese. Workers with an obese nutritional status

have a tendency for experiencing high TNF-a serum levels and decreased pulmonary function conditions. Working period is the most simultaneously influencing variable on the TNF-a serum levels of workers. TNF-a serum significantly affected the lung function conditions of marble home industry workers. Future research can conduct more detailed dust analysis to nano size in order to know the actual content of river stone that can have an impact on the lung health of workers and added by involving other more specialized biomarkers such as TGF-β which plays a direct role in the formation of myofibroblasts forming fibrotic tissue in the lungs.

Conflicts of Interest

The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

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