

## Effect Inhaling of Limestone Dust Exposure on Increased Level of IL-8 Serum and Pulmonary Function Decline to Workers of Limestone Mining Industry

Safrudin Tolinggi, Moh. Rivai Nakoe, Inne Ariane Gobel, James Sengke, Soedjajadi Keman, I Ketut Sudiana, Ririh Yudhastuti, Mukono, R. Azizah  
(Department Of Environmental Health, Airlangga University, Indonesia)

**Abstract:** This aim of this study were to analyze the effect of exposure by limestone dust for increasing of IL-8 serum and pulmonary function decline to workers of limestone mining industry in Wangun Village, Palang District, Tuban Regency after working for 8 hours (cross shift). The Method was analytical observation with prospective longitudinal study. Before and after works for measuring of IL-8 serum increase and pulmonary function decline between population exposed by limestone dust (study group) and population not exposure by limestone dust (comparison group). Data was collecting on 18 respondents consist of 9 study samples workers at mining industry in Wangun Village and 9 samples working at semending district office were taken randomly and inclusion criteria had been matched with the study group. Result showed inhaling of limestone dust exposure was significantly to increasing level of IL-8 serum ( $p = 0.026$ ) but it didn't cause decline on pulmonary function. Physical activity factors and differences of individual immunity can influence the symptoms of respiratory disease caused by increased IL-8 serum so. the decrease in pulmonary function after 8 hours of work (cross-shift) does not occur.

To require use of Personal Protective Equipment (PPE), Air Purifying Respirator Non power types and use a wet method on mining activities. Be required a regular monitoring for evaluate worker's pulmonary function changes by the owner of mining.

**Keywords:-** Limestone Dust, pulmonary function, IL-8 serum

### I. INTRODUCTION

The progress of mining industry in Indonesia has increased from year to year, the increase be accordance with economy development of the country. The mechanism of activity such crushing, grinding, cleaning, drying and to transform mineral mining become a valuable goods in the market will be produce dust with high intensity and it can be a negative impact on the respiratory tract in mining industrial workers. The composition of limestone containing 95%  $\text{CaCO}_3$  and 11%  $\text{MgCO}_3$ , crystalline silica by 1-20% when exposed in a long time (time and average weight measurement) with a weight up  $2\text{-}5 \text{ mg/m}^3$  can cause an inflammation reaction [2].

Lime particles are irritants but not classified as carcinogens [14]. The effects on the respiratory tract are the occurrence of respiratory tract irritation, increased mucus production, airway narrowing, loss of cilia and mucus membranes of cells lining as well as difficulty breathing. Early detection of the limestone mining industry workers should be earlier to prevent progression to Chronic Obstructive Pulmonary Disease (COPD) is irreversible [20].

Obstructive ventilation disorders affect to ability of expiration, and restrictive ventilation disorder affecting to ability of inspire [13].

The defense of pulmonary mechanisms for inhaled dust particles consisting of three interrelated system and work together mechanical air filtration, liquid mucus which serves as a physical and chemical defense contains material which has bactericidal and detoxifying properties, and specific defense lung are divided into two systems the primary humoral immunity (antibody production) and cellular immunity (T lymphocytes). *Macrophages* are a cellular defense system that cleans all the small particles. *Alveolar macrophages* to clean particles deposited by phagocytosis mechanism [25]. Therefore, we need a pulmonary function tests for supporting the diagnosis of obstructive lung disease. In addition, pulmonary function test can distinguish between obstructive and restrictive ventilation disorder.

Workers are exposed with high intensity of dust would have increased  $\text{TNF-}\alpha$  serum so, its risk of pneumoconiosis disease caused by mining activities CWP (Coal Worker's pneumoconiosis) [7].  $\text{TNF-}\alpha$  is a strong indicator in predicting the prognosis of the disease pneumoconiosis someone even after the end of occupational. While Interleukin-8 (IL-8) is a chemokine, that is released by various cell types including fibroblasts in response to IL-1 and  $\text{TNF-}\alpha$ . IL-8 is an important activator and chemo attractant for neutrophils,

and is involved in the process of inflammation. Interleukin-8 has an important role play on process inflammation in the lungs caused by crystalline silica [27].

International Labour Organization (ILO) defines *pneumoconiosis* as a disorder occurs causing by accumulation of dust in the lungs so that the tissue will be reaction because the dust. The main reactions because to exposure with dust in the lungs is called fibrosis. The term *pneumoconiosis* reaction is limited to non-neoplastic disorders caused by dust but not including asthma, *chronic obstructive pulmonary disease* (COPD) and hypersensitivity *pneumonitis*, although the disorder may occur because to expose with dust with long time [25].

Wangun Village in Palang District the regency of Tuban there are many locations of limestone mining industry because the soil type is red-yellow mediterranean sediments derived from limestone. According on The Central Statistics Agency of Tuban Regency, minerals are exploited in Tuban in 2012 included: limestone, clay, pedel, ballclay, dolomite, quartz sand and phosphate minerals but the most exploited is limestone, it's reaches 12.729. 758 tons Per Years [21].

The results of preliminary observations that, worker's activities such as quarry, crushing, and cutting stone into bricks they do without the use of Personal Protective Equipment (PPE) such as masks, gloves, boots and goggles. Subjective complaints obtained by author from interviews are such as cough, phlegm, and tightness cause by dust generating during the work. Besides discomfort feel and caused a respiratory diseases as a result of accumulation of dust in the lungs, it can also be effect to loss of material due to sagging of worker's productivity and affecting to their income. Aside from having a rest a few days they also have to spend money for reduce disruption to their breathing.

The aims of this study were to analyze the effect of exposure by limestone dust for increasing of IL-8 serum and pulmonary function decline to workers of limestone mining industry in Wangun Village, Palang District, Tuban Regency after working for 8 hours (cross shift).

## II. MATERIALS AND METHODS

The Method was analytical observation with prospective longitudinal study. Before and after works for measuring of IL-8 serum increase and pulmonary function decline between population exposed by limestone dust (study group) and population not exposed by limestone dust (comparison group). Inhaling by dust exposure is the independent variable. Elevating of IL-8 serum and pulmonary function decline are dependent variable. Age, period of working, BMI, and smoking are confounding variable.

Data was collecting on 18 respondents consist of 9 study samples workers at mining industry in Wangun Village and 9 samples working at semanding district office were taken randomly and inclusion criteria had been matched with the study group. Meanwhile, for measured inhaling of dust exposure used PDS, pulmonary function measurements (FVC and FEV1) used a spirometer (Spirolab III), and used ELISA technique for measurement levels of IL-8 serum.

Data of characteristic respondent such age, period of working, and smoking habits collected by questioner. Mikrotoa and bathroom scales for measured BMI. Data were analyzed with 2 independent samples t-test, paired t test, and multiple linear regression and the significance level of 5%.

## III. RESULTS

### III.1 Characteristics of Respondents

**Table 1. The Difference of Data Characteristics Respondents between the Exposed and Unexposed Groups**

Characteristics of Respondents	Workers of Mining Industry (Study Group) n= 9	Workers of Semanding District Office (Control Group) n = 9	p-values
Age	30.22 ± 5.82	37.56 ± 1.88	0.005*
Body Mass Indeks	21.4 ± 2.23	25.07 ± 4.61	0.045*
Period of working	5.78 ± 3.56	5.00 ± 2.87	0.617**
Smoking habits	218.89 ± 234.42	271.11 ± 261.08	0.885**

Values in mean ± SD

\*p < 0.05 (significant)

\*\*p > 0.05 (not significant)

Table shown the mean age of the respondents based on the different work sites. The youngest respondents in the location of the mining industry are 22 years and youngest respondents in the non-industrial location (Semanding District office workers) that is 34 years old. The results of statistical analysis with two

independent samples t test was obtained value of  $p = 0.005$ , so that is a significantly difference between age of limestone mining industry workers and employees in office Semanding districts.

### III.2 Level of Personal Dust

**Table 2. The Difference Level of Dust Between Respondents by Workplace.**

Level of Personal Dust (mg/m <sup>3</sup> )	Workers of Mining Industry (Study Group) n= 9	Workers of Semanding District Office (Control Group) n = 9
Average level of dust	4.81 ± 1.51	0.19 ± 0.09
Minimum level of dust	2.19	0.01
Maximum level of dust	6.71	0.32
<b>p = 0.000*</b>		

Values in mean ± SD

\*p < 0.05 (significant)

\*\*p > 0.05 (not significant)

The highest levels personal dust was in limestone mining industry workers (6.71 mg / m<sup>3</sup>) and the employees in Semanding districts office (0.32 mg/m<sup>3</sup>). Results of statistical analysis with 2 independent samples t-test  $p < 0.05$ . There are very significant differences between personal dust levels in limestone mining industry workers and personal dust levels employees in Semanding districts office.

### III.3 Interleukin-8 Serum

**Table 3. The Level of Interleukin-8 serum Differences Between Respondents by Workplace**

Level of Interleukin-8 Serum (pg /ml)	Workers of Mining Industry (Study Group) n= 9	Workers of Semanding District Office (Control Group) n = 9
Δ IL-8 average	15.00 ± 4.47	5.11 ± 4.96
Δ IL-8 minimum	7.00	-3.00
Δ IL-8 maximum	20.00	14.00
<b>p = 0.000*</b>		

Values in mean ± SD

\*p < 0.05 (significant)

\*\*p > 0.05 (not significant)

The difference in levels of IL-8 on workers in the mining industry is very possible influenced by the levels of dust inhaled by workers. Results of statistical analysis in 2 independent samples t-test ( $p < 0.05$ ). There are differences in increased serum levels of IL-8 were significant between the limestone mining industry workers and employees of districts.

From the statistical test results shown the increase of serum IL-8 is significantly between two groups of respondents after work, but more significant is the mining industry group its influenced by exposure with lime dust with high intensity of their workplace.

### III.4 Pulmonary Function

**Table 4. Differences of Pulmonary Function Decline Between Respondents by Workplace**

Pulmonary Function Parameters	Workers of Mining Industry (Study Group) n= 9	Workers of Semanding District Office (Control Group) n = 9	(p-values)
Δ FVC (L)	0.52 ± 0.32	0.14 ± 0.09	0.007*
Δ % FVC (%)	11.56 ± 7.00	3.44 ± 2.30	0.008*
Δ FEV <sub>1</sub> (L)	0.36 ± 0.30	0.14 ± 0.09	0.047*
Δ % FEV <sub>1</sub> (%)	9.79 ± 7.99	3.33 ± 2.45	0.034*
Δ FEV <sub>1</sub> / FVC (%)	-2.88 ± 11.78	1.42 ± 1.83	0.309**

Values in mean ± SD

\*p < 0.05 (significant)

\*\*p > 0.05 (not significant)

Pulmonary function decline values was analyze by 2 independent samples t test, that there is a difference between the pulmonary function decline on parameters FVC, FVC %, FEV1 and FEV1% among

respondents in the location of the limestone mining industry and Semanding Districts Officer. However, no significantly differences in parameters FEV1 / FVC of respondents.

### III.5 Effect of Dust Levels and Characteristics of respondents for Increasing Levels of IL-8 Serum on Respondents

Table 5. Results of Multiple Linear Regression to Independent Variable are Level of Personal Dust, Variable Dependent is Levels of IL-8 Serum and Confounding Variables are Age, Period of Working, Body Mass Index, and Smoking Habits.

Variables	Level of IL-8 (coefficient)	
	$\beta$	p
Age of Respondent	-0.185	0.440
Period of working	0.422	0.063
Body Mass Index	0.104	0.578
Smoking habits (Packyears)	-0.162	0.436
Level of Personal Dust	0.617	0.026*

\*p < 0.05 (significant)  
 \*\*p > 0.05 (not significant)

Table 5 shows that after a multiple linear regression to all variables simultaneously to increased levels of IL-8 serum, obtained level of personal dust will affect to increase levels of IL-8 serum. Direction of the relationship ( $\beta$  value) is positive, its means that the levels of personal dust is high the levels of interleukin-8 will be increase.

### III.6 Effect of Increased Levels of IL-8 Serum and Respondent Characteristics to Pulmonary Function Decline

Table 6. Effect of Increased Levels of IL-8 Serum, Age, Period of Working, Body Mass Index and smoking habits to Respondents Pulmonary Function Decline

Variables	p-values				
	$\Delta$ FVC	$\Delta$ %FVC	$\Delta$ FEV1	$\Delta$ %FEV1	$\Delta$ % FEV1/ FVC
Age of Respondent	0.909**	0.971**	0.351**	0.371**	0.359**
Period of working	0.680**	0.684**	0.864**	0.851**	0.696**
Body Mass Index	0.104**	0.150**	0.840**	0.735**	0.146**
Smoking habits (Packyears)	0.465**	0.424**	0.092**	0.166**	0.514**
Increased level of IL-8	0.239**	0.312**	0.069**	0.160**	0.641**

\*p < 0.05 (significant)  
 \*\*p > 0.05 (not significant)

Table 6 shows after multiple regression test for all variables with simultaneously to pulmonary function decline was obtained that was not a significant influence between smoking (packyears) and increased levels of IL-8 to pulmonary function decline. So did with age, years of service and body mass index does not affect to pulmonary function decline.

## IV. DISCUSSION

The age factor affects to physical conditions and associated with pulmonary function. Lung function capacity will continue to increase along with increasing age and will reach its maximum value is at the age of 19 to 21 years. After that age will experience the value of pulmonary function with age [6].

Besides factors likes age, race, gender, body mass index, another factors that can affect the lung vital capacity is the ability of the lungs, lungs elasticity, exercise and physical activity, and size of lungs inside. An athlete who trains regularly can improve lung vital capacity by 30-40% above normal [10].

Body Mass Index Between Respondents is difference with significantly. Results of statistical analysis with Mann Whitney test was obtained value of p = 0.045, so that is significantly difference between BMI of limestone mining industry workers and employees in Semanding districts office.

Nutritional status also affects in person's lung capacity. People has posture high skinny usually vital lung capacity power greater than those with stubby stature [10]. It can be concluded that the physiologically of

someone with less and more nutritional status has decreased in their lung vital capacity which may turn affect in the occurrence of pulmonary function impairment.

Period of working according on Suma'mur (2009) [24] one of the variables that potentially cause lungs problems if a person are expose for long time with these pollutants. The longer work in dusty, the more dust is inhaled more the pile of dust in the lungs of the person. Smoking habits will accelerate decline in lung function. Cigarette smoke can irritate and damage the respiratory tract, it's causing various respiratory problems such as difficulty for breathing and other diseases such as bronchitis and emphysema. Decreased force expiratory volume per year for current smokers was 41.7 mL, non-smokers was 28.7 mL, and 38.4 mL for former ex-smokers [3]. But for the period of working and smoking behavior was not a difference with significantly ( $p > 0.05$ ).

This material of dust contains crystalline silica 1-20% then, if silica dust in to the lungs it will be cause disorder in the lung tissue such as silicosis and pneumoconiosis. The toxicity of dust determines on tissue reactions in pneumoconiosis. Silica dust and asbestos have powerful biological effects. Form of nodular cystic parenchymal reaction is a classic example of silicosis [25].

Based on regulation the minister of labor and transmigration in Indonesia, 2011 about threshold values of physical and chemical factors in the workplace. The threshold limit values of dust on workplace must  $3 \text{ mg} / \text{m}^3$ . Average value obtained personal dust levels  $4.81 \pm 1.51 \text{ mg} / \text{m}^3$ . Based on TLV values are 8 samples that passes the value of TLV and only 1 sample that still meets the TLV is allowed. This is consistent with increased levels of IL-8 were experienced by workers in the mining industry limestone differs significantly from existing workers in Semanding District office.

Increased of IL-8 serum secretion, that is a pro inflammatory media can be affected by oxidant stress will be effected in the recruitment of inflammatory cells and the induction of oxidant stress mediators. In addition, there is a relationship between the levels of IL-8 production by a person's body mass index is associated with diseases caused by obesity, such as diabetes [23]. In addition, the increase in IL-8 sensitivity can be effecting by inflammation in coronary artery disease, [15] and the acute effects of consuming alcohol which can increase levels of IL-8 and TNF- $\alpha$  in the blood [4]. However, abnormalities of serum cytokine production may be suffered by the alcoholic to consider several aspects such as intake and consumption of ethanol (alcoholic liver disease) or liver disease in alcoholics [17].

The age factor may affecting in pulmonary function impairment due to aging affects lung elasticity as other organ tissues. It will be oldest a person, greater lung function decline will be occur to them. The decrease lung vital capacity generally occurs after the age of 30 years, but the decline will be fast after the age of 40 years. This can be seen from some of the sample with of 35-40 years, where the value of FVC and FEV1 before work has shown a lower value than the respondents who are still young. In addition, factors such as the characteristics of the respondent factors of race, sex, and body mass index may affect the quality of one's lung capacity [6].

According to the American Thoracic Society spirometer accuracy of measurement results for diagnosing the condition of pulmonary function disorders is affected by difficulties or tightness in the measurement process, unfamiliarity of the patients when given instructions, funnel deformation due bite during the measuring process has beginning [18].

From the regression test results that amount of respirable dust levels can increase IL-8 serum level ( $p = 0.026$ ). Because lime dust components has contained silica and including on type fibrosis dust, when exposed with high intensity can be increasing levels of IL-8. This is reinforced by the study of Schins and Borm in 1995 [22], and Kim et al., in 1999 [16], and Lee et al., in 2010 [19]. Their statement that increasing levels of IL-8 serum has a role for responding of crystalline silica compound into and will cause inflammation on lung tissue. With the characteristics of IL-8 is a neutrophil chemotactic factor which binding neutrophil for migration into inflamed tissue

For the more characteristics respondent such as age, years of service, body mass index, smoking habits does not affect in accumulation of interleukin-8 levels because its only acute sensitivity enhancement [11]. Effects of smoking habits on serum proinflammatory increase for response to free radical likes ROS, generated depending the brand of cigarettes because every cigarette brands usually has a different tar levels. High levels of ROS that influence to cell damage associated with the quality of tar any cigarette brand [12].

In addition cytokines and chemokines, some enzyme are composite by zinc and calcium and has a role on inflammatory reaction is MMP-9. This enzyme always called type IV of collagenase because it's ability for damage or break down a gelatin, has a specific substrate for various forms of Extracellular Matrix (ECM) likes collagen IV and V, gelatin, elastin and vitronectin according with research studies which having an important role for make fibrosis on lungs [1]

MMP-9 has function in providing potential effect of IL-8 for neutrophils migration so that MMP-9 it's more specific as an indicator of pulmonary function decline [26]. But keep in our mind is effect of inflammatory serum increase are depends with individual's immunity and work activity. It based on research by Ford in 2002

[9], Autenrieth et al., in 2009 [5], and Fell et al., in 2011[8]. Workers who work with high physical activity, increased of inflammatory serum effects such as IL-6 and IL-8 are not feel by them but even decreasing serum inflammatory during their work and rest so that it's not cause decline of lung function.

## V. CONCLUSION

Inhaled limestone dust can increase level of IL-8 serum of limestone mining workers after work. Has a differences on increase level of IL-8 serum between workers of mining industry and employees of semanding district office ( $p = 0.000$ ). Has a differences decline on pulmonary function between groups of respondent for parameter  $\Delta FVC$ ,  $\Delta\% FVC$ ,  $\Delta FEV_1$ , and  $\Delta\% FEV_1$  with a value of  $p < 0.05$ . For parameters  $\Delta FEV_1 / FVC$  hasn't difference because the value of  $p > 0.05$ . Based on multiple linear regression between elevated levels of IL-8 serum workers of mining industry and a decline on pulmonary function obtained values ( $p > 0.05$ ) so the increased level of IL-8 serum hasn't effect on pulmonary function decline in limestone mining industrial workers.

For suggestion use a Personal Protective Equipment (PPE), Air Purifying Respirator Non power types (NAPR) N Series (Not resistant to oil) to protection from dust produced by process likes crushing, quarrying, grinding, bricking and use a wet method on mining activities. Be required a regular monitoring for evaluate worker's pulmonary function changes by the owner of mining.

The Research has limitations such as research samples are less to able a diversity of data results of serum and lung capacity, people with diabetes are not controlled as samples on this research because people with diabetes can affecting for measure their IL-8 serum levels. The other factors has a causal in lung function decrease likes consuming alcohol is uncontrolled.

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