Original Article

Surfactant Protein A Serum Level in Cement Worker

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Abstract

Background: Pneumoconiosis occurs almost in entire worldwide. Pneumoconiosis had threatened cement workers. Serologic abnormalities had found in pneumoconiosis. Surfactant Protein A (SP-A) levels increased in silica-exposed workers. Surfactant Protein A (SP-A) may be a helpful biomarker for the early diagnosis of pneumoconiosis, but it has not yet been studied in Indonesia.

Methods: The design of this study was observational with cross-sectional. A sampling of cement-exposed workers was done by consecutive sampling. The subjects were 88, approach population of 67 cement exposed workers from September 2017 – March 2018 and 17 healthy people as control. The serum level of SP-A was measured by the ELISA method. Cement exposed workers is a worker in the production area and workers in the quarry area.

Results: The total number of research subjects met the criteria was 67, and the control subjects were 21. The mean serum SP-A level in the study subject group or the exposed group was 6.02 ng/ml, and the mean SP-A level in the control group was 4.50 ng/ml. The difference in SP-A levels between the exposed and control groups was different but not significant, with value of *P*=0.084.

Conclusion: SP-A levels in the exposed and control groups were different but not statistically significant.

Keywords: Cement workers, Serum surfactant A, Silica exposure

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INTRODUCTION

The negative impact of the cement industry is air pollution by dust; the cement industry has the potential to cause air contamination in the form of dust. The dust was produced from procurement of raw materials, combustion process, transportation of raw materials to the factory, and finished materials out of the factory, including their packaging. It should be realized that the development of industrial activities, in general, is also a sector with great potential as a source of air pollution that will be detrimental to health and the environment.[1]

Lung disease caused by harmful dust is called pneumoconiosis. The cement factory is one of the industries that produce dust. An epidemiological study at a cement factory in Tanzania measured levels of dust exposure and found high levels of dust exposure in cranes (38.64 mg/m^3), packing (21.30 mg/m^3), crushers (13.48 mg/m^3), low dust exposure in cement mill (3.23 mg/m^3), kiln (2.87 mg/m^3), raw mill (1.85 mg/m^3), maintenance (1.16 mg/m^3) and administration (0.29 mg/m^3).[2] Based on lung function measurements, 31.6% of respondents had normal lung function, and the remaining 64.4% had impaired lung function. Based on reports of disease patterns from the PT. Semen Tonasa for five years in a row, respiratory disease ranks first.[3]

Data from the World Health Organization (WHO) and The World Labor Organization (ILO) in 2003 reported that about 1.7 million workers were exposed to silica dust. About 10% of workers are at risk of suffering from silicosis in the United States. This finding was also found in Germany, with around 3000 cases of silicosis each year since the 1990s. Furthermore, Japan reports 1,000 new cases yearly, and Australia reports more than 1,000 predicted cases yearly. Every year France reports about 300 new patients diagnosed with silicosis, while China reports 10 million people diagnosed with silicosis, and 5,000 deaths occurred from 1991-1995.[4]

A study found that surfactant A (SP-A) and surfactant D (SP-D) levels increased in patients with Idiopathic Pulmonary Fibrosis (IPF) with Progressive Systemic Sclerosis (PSS).[5] In contrast, Shi Xin et al found that SP-A protein levels were increased in workers exposed to silica. Serum SP-A levels may be used as a biomarker for the early diagnosis of silicosis.[6]

This study aimed to compare the serum SP-A levels of cement factory workers with the average population and the risk factors that affect serum SP-A levels.

METHODS

The research design is a cross-sectional study. This research was conducted at PT. X Pangkep Regency, South Sulawesi Province, and was carried out in September-October 2019. Data collection for control subjects was carried out at the Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Hasanuddin University, in November 2019.

The target population is all factory workers at PT. X. The affordable population is the entire target population that works in the raw material and production areas and has worked for five years compared to the control subjects. The control subjects were those who did not work in the cement factory and did not live in the cement factory environment. Samples were taken in September–October 2019.

Sampling was done by consecutive sampling. The subjects studied worked in the raw material area and the production area. The criteria for acceptance of the case subject are factory workers of PT. X in the work area of raw materials and production who has worked for at least five years, male gender, normal BMI, agreed to participate in research, sign approval letters, and take blood samples.

The criteria for acceptance of control subjects were not working in a cement factory, not living in a cement factory environment, did not agree to participate in research and sign a letter of approval, taking blood samples, having normal BMI, and routine chest X-ray.

Respondents' exclusion criteria were refusing to be research subjects, having a history of pulmonary TB, asthma, COPD, and lung tumors.

RESULTS

This study was cross-sectional to determine the difference in serum SP-A levels of cement workers with the normal population. Sampling is done by consecutive sampling. The number of subjects in this study was 67 research subjects and 21 control subjects. Drop-out subjects were two research subjects, 4 study subjects were excluded because of damage to serum labeling.

In this study, SP-A levels were found in the research subject group, the exposed group with an average of 6.02 ng/ml, and the control group with an average of 4.50 ng/ml. Box plot graph describes SP-A levels in the exposed and the control groups. The difference in SP-A levels between the exposed and control groups was different but not significant, with *P*=0.084.

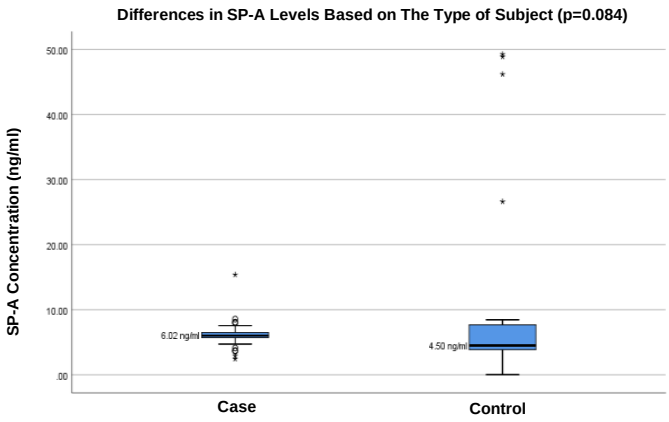

Figure 1. Box plot graphic of serum SP-A levels by age group

Differences in SP-A levels based on respiratory complaints in the exposed group; this study found SP-A levels in two groups, the group with respiratory complaints with an average of 11.97 ng/ml and the group had no respiratory complaints with a mean of 6.02 ng/ml. The difference in SP-A levels between the two groups was significantly different, with *P*=0.017.

Table 1. Characteristics of Research Subjects

Variable	Exposed (n=67)		Control (n=21)		Total (n=88)	
	n	%	n	%	n	%
Gender						
Men	67	100	21	100	88	100
Women	0	0	0	0	0	0
Age						
≥40 years	49	73,1	0	0	49	55,7
<40 years	18	26,9	21	100	39	44,3
Education level						
Low	6	9	0	0	6	6,8
Middle	51	76,1	0	0	51	58
High	10	14,9	21	100	31	35,2
Length of work						
≥10 years	50	74,6	0	0	50	56,8
<10 years	17	25,4	0	0	17	19,3
Smoking history						
Smokers	18	26,9	0	0	18	20,5
Ex-Smokers	7	10,4	0	0	7	8
Non-Smokers	42	62,7	21	100	63	71,6
Brinkman Index						
Mild	12	48	0	0	12	13,6
Moderate	13	52	0	0	13	14,8
Severe	0	0	0	0	0	0
Use of PPE						
Poor	3	4,5	0	0	3	3,4
Moderate	57	85,1	0	0	57	64,8
Good	7	10,4	0	0	7	8
Respiratory complaints						
Exist	2	3	0	0	2	2,3
There is no exist	65	97	21	100	86	97,7
History of inflammation of the respiratory tract						
Exist	2	3	0	0	2	2,3
Did not exist	65	97	0	0	65	73,9
Work Area						
Cement packer	8	11,9	0	0	8	9,1
Kiln	5	7,5	0	0	5	5,7
Crusher	14	20,9	0	0	14	15,9
Finish mill	10	14,9	0	0	10	11,4
Quarry	5	7,5	0	0	5	5,7
Raw mill	8	11,9	0	0	8	9,1
Silica crusher	9	13,4	0	0	9	10,2
Other sites	8	11,9	0	0	8	9,1

Differences in SP-A levels based on a history of respiratory tract inflammation in this study found SP-A levels in two groups, the group with a history of respiratory tract inflammation with an average of 6.51 ng/ml and the group without a history of respiratory tract inflammation with an average of 6.02 ng/ml. The difference in SP-A levels between the two groups showed that the results were not significantly different, with *P*=0.418.

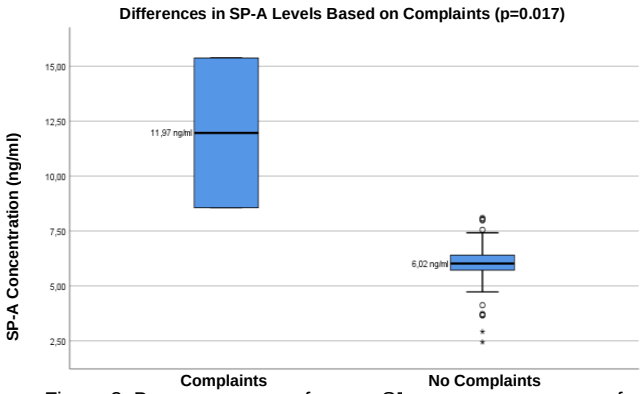

Figure 2. Box plot graphic of serum SP-A levels by a group of respiratory complaints

Differences in SP-A levels based on education level were grouped into low, middle, and high. Groups with low education levels with an average of 6.34 ng/ml, groups with moderate levels of education with an average of 5.96 ng/ml, and groups with high education levels with an average of 5.91 ng/ml. The difference in SP-A levels between the three groups showed that the results were not significantly different, with *P*=0.695.

The difference in SP-A levels based on the length of work in this study found SP-A levels in two groups. The group with an average length of work above ten years with an average of 6.06 ng/ml and a group with an average length of work <10 years with an average of 5.66 ng/ml. The difference in SP-A levels between the two groups of the length of work obtained significantly different results with value of *P*=0.008.

Differences in SP-A levels based on smoking history in this study found SP-A levels in three groups, the smoking group with an average of 6.07 ng/ml, the ex-smoker group with an average of 5.84 ng/ml, and the non-smoker group with an average of 6.01 ng/ml. The difference in SP-A levels between the three smoking history groups showed that the results were not significantly different, with *P*=0.819.

The difference in SP-A levels was based on the Brinkman Index in the three groups. However, there was no sample for severe IB; the group with moderate IB had an average of 5.98 ng/ml, and the group with mild IB had an average of 5.91 ng/ml. The difference in SP-A levels between the two groups based on IB showed that the results were not significantly different, with *P*=0.480.

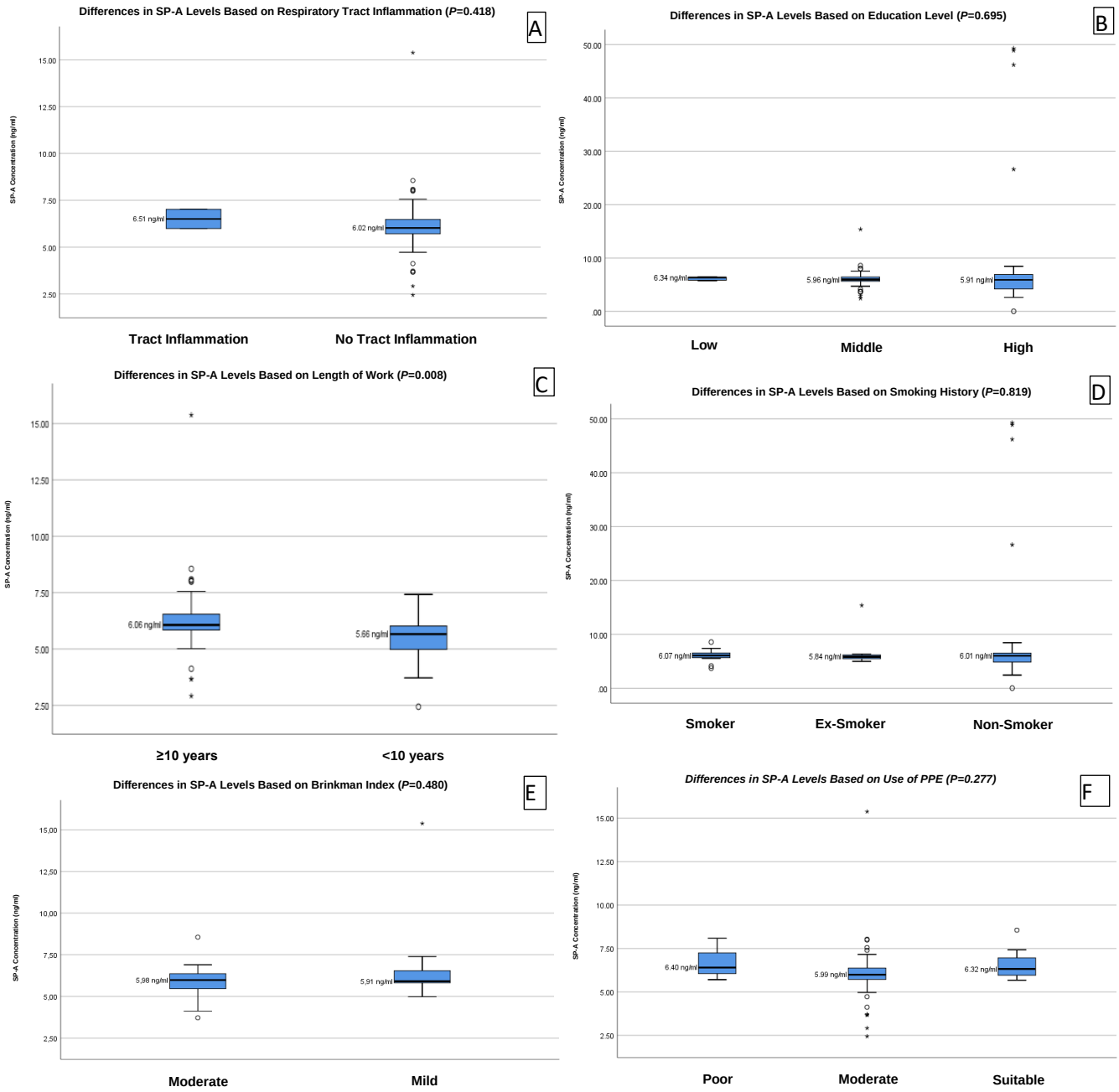

Figure 3. Graphic box plot of serum SP-A levels based on A) history of respiratory tract inflammation in the exposed group; B) education level; C) length of work; D) Smoking History; E) the Brinkman Index; F) use of PPE

Differences in SP-A levels based on the use of PPE, this study found SP-A levels in three groups, the group with poor PPE with an average of 6.40 ng/ml, the group with moderate PPE with an average of 5.99 ng/ml, and the group with suitable PPE with an average of 6.32 ng/ml. The difference in SP-A levels between the three groups using PPE was not significantly different, with *P*=0.277.

Differences in SP-A levels based on the work area with the results of SP-A serum levels in eight groups. The group of cement packer working area with an average of 6.13 ng/ml, the group of kiln working area with an average of 5.82 ng/ml, the group of crusher working area with an average of 6.20 ng/ml, a group of finish mill working area with an average of 5.72 ng/ml, the group of quarry working area with an average of 5.71 ng/ml, the group of raw mill working area with an average of 5.60 ng/ ml, the group of silica crusher working area with an average of 6.37 ng/ml, the group of other working sites with an average of 6.38 ng/ml. The differences in SP-A levels between the eight groups based on the work area were not significantly different.

In this study, the highest dust content was

found in the cement packer area of 31.45 mg/m^3, followed by the crusher area of 9.78 mg/m^3, the finish mill area of 4.41 mg/m^3, and the raw mill area of 0.52 mg/m^3.

Table 2. Total dust content of the working environment by work area

Working Area	Dust Content (mg/m^3)
Crusher	9.78
Finish mill 2/3	4.41
Raw mill 2/3	0.52
Cement packer	31.45

DISCUSSION

The study investigating SP-A serum as a marker of occupational lung disease in cement workers is rare in Indonesia. SP-A has been researched as a marker for various lung diseases, including examining serum levels of SP-A against interstitial lung disease, interstitial pneumonia, sarcoidosis of pulmonary fibrosis disease, ARDS, pulmonary TB, pneumonia, bronchiectasis, COPD, and silicosis.[7]

Another study reported increased SP-A and age associated with slower mucociliary clearance rates compared to young adults and decreased lung function. A decrease in the quality of humoral immunity, which is characterized by loss of high affinity blocking antibodies and an increase in self-reactive antibodies, has been reported in the elderly, resulting in decreased levels of IL-13 that trigger transcription of matrix metalloproteinases (MMP)-2, 9, 12, and 14, reducing MMP-1 synthesis, and synergistically with TGF-β increase fibroblast TIMP-1 which is a pro-fibrotic mechanism. [7]

In this study, based on respiratory complaints, the group with respiratory complaints had an average of 11.97 ng/ml, and the group without respiratory complaints had an average of 6.02 ng/ml. The difference in SP-A levels between the two groups was significantly different, with *P*=0.017. The results of this study are different from the study of Hideo Kobayashi et al in 2008 in patients with COPD who had respiratory complaints; serum SP-A levels increased significantly (*P*=0.01),[8] Study of Yoshio Kuroki's in 1998, with the results of SP-A levels were quite different between patients with respiratory complaints and controls (*P*<0.001).[9]

According to Akella study in 2013 in patients with COPD, asthma, bronchiectasis or other respiratory disorders, the surfactant function decreased due to alveolar macrophage activity, and released proteins, proteolytic enzymes, inflammatory mediators, reactive oxygen and nitrogen species, all of these chemical agents can reduce the availability of decreased functional capacity synthesis.[10]

Differences in SP-A levels based on smoking history in this study found SP-A levels in three groups, the smokers' group with an average of 6.07 ng/ml, the ex-smokers group with an average of 5.84 ng/ml, and the non-smokers' group with an average of 6.01 ng/ml. The results were not significantly different (*P*=0.819).

This study's results differ from the research conducted by Hideo et al in 2008 with the same variables: groups of active smokers, ex-smokers, and non-smokers. The results were significantly different between active smokers and ex-smokers (*P*<0.05), the results of the comparison between groups of active smokers and non-smokers (*P*=<0.01), and the comparison between a history of smoking and never smoking were not significantly different.[8] In the study of Fernandez-Real et al, which linked Sp-A levels with metabolite variables, the same results were obtained in the smoking and non-smoking groups.[11]

The difference in SP-A levels was based on the Brinkman Index in the three groups. However, there was no sample for severe IB, and the group with moderate IB had an average of 5.98 ng/ml, and the group with mild IB had an average of 5.91 ng/ml. The difference in SP-A levels between the two groups based on Brinkman Index showed that the results were not significantly different, with *P*=0.480

The study by Hideo et al in 2008 found that the relationship between serum levels of SP-A and the Brinkman Index in active smokers was significantly different (r=0.39; *P*<0.01).[8] In addition, Nomori et al concluded that there was a relationship but not related considerably between SP-A serum and the Brinkman index (r=0.53).[12]

Differences in SP-A levels based on the use of PPE, this study found SP-A levels in three groups, the group with poor PPE with an average of 6.40 ng/ml, the group with middle PPE with an average of 5.99 ng/ml, and the group with suitable PPE with an average of 6.32 ng/ml. The difference in SP-A levels between the three groups using PPE was not significantly different, with *P*=0.277. The Mengkidi study in 2006 reported no significant relationship between the use of PPE and impaired lung function in cement workers.[3] Another study said that the use of PPE depends on the high concentration of dust exposure; in this study, dust <5 microns in size is required and used when working in the factory area.[13]

The research subjects were grouped into workers >10 years with an average of 6.06 ng/ml and groups of workers <10 years with an average of 5.66 ng/ml. The difference in SP-A levels between the two groups obtained significantly different results with *P*=0.008. This study is in line with the research of Dutt et al in 2015, which found that workers who were directly or indirectly involved in mining activities were mainly exposed to silica dust after working for more than 20 years because the percentage of T cells that produced IL-13 showed a decrease. Along with increasing age, this causes a decrease in neutrophil function in chemotaxis.[14]

Differences in SP-A levels based on the work area with the results of SP-A serum levels in eight groups, the group in the cement packer working area with an average of 6.13 ng/ml, the group in the kiln working area with an average of 5.82 ng/ml, the group in the crusher working area with an average of 6.85 ng/ml, the group in the finish millwork area with an average of 5.72 ng/ml, the group in the quarry work area with an average of 5.71 ng/ml, the group in the raw mill working area with an average of 5.60 ng/ml, the group in silica crusher working area with an average of 6.37 ng/ml, the group in other areas with an average of 6.38 ng/ml.

The difference in SP-A levels between the eight groups based on the work area obtained results that were not significantly different from the value. The manufacture of cement uses a mixture of silica sand which contains free silica at varying levels, so that silicosis can occur in workers in the raw material area, cleaners, closed rooms, and slag milling.[15]

This study found SP-A levels in the research subject group or the exposed group, with an average of 6.02 ng/ml, and control subjects with an average of 4.50 ng/ml. The difference in SP-A levels between the exposed and control groups was different but not significant (*P*=0.084). In contrast, Spech et al identified a substantial relationship between silica exposure and the incidence of increased SP-A (*P*=0.001).[16]

Lesur et al performed a different study in 1993 with sheep exposed to silica as a subject with controls; there was a significant twofold increase in the silica-exposed group; based on this study, experimental animals can represent what happens to humans, but further research is still needed.[17] Another study showed an increase in SP-A in the blood serum in workers exposed to silica dust, starting from the occurrence of fibrosis, which resulted in alveolar damage and an increase in alveolar vasculature, which then resulted in vascular leakage that serum A was found in blood serum.[16]

In this study, the highest dust content was found in the cement packer area of 31.45 mg/m^3, followed by the crusher area of 9.78 mg/m^3, the finish mill area of 4.41 mg/m^3, and the raw mill area of 0.52 mg/m^3. Previous research in Indonesia found that the dust content in the cement packer area was 18.47

mg/m^3, the mining area was 20.23 mg/m^3, and the crusher was 14.98 mg/m^3, while the raw mill and finish mill areas were <10 mg/m^3. In the cement packer area, there is an increase in dust content. In the Tungu AM study, it was found that there was a decrease in total dust levels as well as a decrease in the prevalence of COPD and an increase in lung function among cement workers.[12]

According to Akella's research in 2013. Inhaled silica dust can inhibit surfactant secretion in AT-II cells, thereby increasing the intracellular phosphatidylcholine content. The threshold value (NAV) is the standard of environmental work factors recommended in the workplace so that workers can still deal with them without causing illness or health problems in their daily work for no more than 8 hours a day or 40 hours a day week. This NAV uses to replace the adverse effects of chemicals in the workplace. The unit of NAV of chemicals in the workplace air can be expressed in mg/m^3 of air. NAV for silica dust content based on the Circular Letter of the Minister of Manpower No. 01/MENNAKER/1997 is 0.05 mg/m^3 for silica cristobalite and tridymite, and 0.1 mg/m^3 for silica quartz and tripoli.[12,13,18]

LIMITATION

This study has several limitations. Sampling according to the inclusion criteria is difficult and the process of sending serum samples takes a long time so it is feared that it will interfere with the quality of the serum. The terrain used in sampling the dust content is difficult. Furthermore, some of the labels on the serum samples could not be identified. The lack of respondents and the limitations of related references are also limitations in this study.

CONCLUSION

SP-A levels in the research subject group or the exposed group compared with the control group were statistically different but insignificant. The relationship between serum SP-A levels with respiratory complaints, history of the respiratory tract, length of work, and age in the research subjects obtained statistically significant different results. The relationship between SP-A levels and the smoking history group and the IB group is different but statistically not significant. The relationship between SP-A levels and the PPE use group was statistically insignificant.

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CONFLICT OF INTEREST

None.

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