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Official Journal of The Indonesian Society of Respiriology



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No.715/SK/DitjenPPG/SST/1980 Tanggal 9 Mei 1980

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PDPI Jl. Cipinang Bunder, No. 19, Cipinang Pulo Gadung
Jakarta Timur 13240 Telp: 02122474845
Email : editor@jurnalrespirologi.org
Website : <http://www.jurnalrespirologi.org>

Publisher

The Indonesia Society of Respiriology (ISR)
Published every 3 months (January, April, July & October)

Jurnal Respirologi Indonesia

2nd Rank Accreditation
According to the Decree of the Minister of Research and
Technology/Head of the National Research and Innovation
Agency of the Republic of Indonesia Number: 200/M/KPT/2020
December 23, 2020

JURNAL RESPIROLOGI INDONESIA

Majalah Resmi Perhimpunan Dokter Paru Indonesia
Official Journal of The Indonesian Society of Respiriology

VOLUME 42, NUMBER 2, April 2022

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Surfactant Protein D (SP-D) Serum Levels In Limestone Mining Worker

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Abstract

Background: Limestone is sedimentary rocks consisting of the minerals calcite and aragonite, often containing silica and fossils, and commonly used in building materials. Limestone mining workers are at high risk of developing pneumoconiosis. Surfactant protein D (SP-D) is part of the collectin family, and functions as the innate immune system pathogen recognition receptor (PRR). The SP-D levels are usually elevated in fibrotic lung disease. In this study, we looked for serum levels of SP-D as a marker of early pneumoconiosis in limestone worker in Indonesia.

Method: This study was cross-sectional observational study. Study subjects were 65 limestone workers, willing to participate in this study by signing informed consent, were interviewed, and their blood samples were collected to measure SP-D level using ELISA.

Results: The study subjects were dominated by male with a median age of 42 years and had low education level. The majority had worked <6 years and worked >8 hours per day, did not wear personal protective equipment, had normal weight and had smoked. The mean SP-D level among study subjects was 66.3±5.5 ng/mL, slightly higher than normal subjects. Smoking status, gender, and working hour were correlated with higher SP-D levels.

Conclusion: Serum SP-D levels in limestone mining workers could be used as monitoring for early screening for pneumoconiosis although it was not statistically significant. (*J Respirol Indones 2022; 42 (2): 151–5*)

Keywords: Biomarkers; levels; limestone miners; pneumoconiosis; serum surfactant protein D (SP-D)

Kadar Serum Protein Surfaktan-D (SP-D) Pada Pekerja Tambang Batu Kapur

Abstrak

Latar belakang: Batu kapur (limestone) merupakan batuan sedimentasi terdiri dari mineral kalsit dan aragonit, sering mengandung silika dan fosil, dan biasa digunakan dalam bahan bangunan. Pekerja tambang batu kapur berisiko tinggi terkena pneumokoniosis. Protein Surfaktan-D (SP-D) merupakan bagian dari rumpun collectin, dan berfungsi sebagai reseptor pengenalan patogen dari sistem imun bawaan. Kadar SP-D sering didapatkan meningkat pada penyakit paru fibrotik. Pada penelitian ini, kami mencari kadar SP-D serum sebagai penanda awal pneumokoniosis pada pekerja tambang batu kapur di Indonesia.

Metode: Penelitian ini bersifat observasional potong lintang. Subjek penelitian adalah 65 pekerja tambang batu kapur yang bersedia berpartisipasi dalam penelitian ini dengan menandatangani informed consent, lalu diwawancarai dan diambil sampel darahnya untuk diukur kadar SP-D menggunakan metode ELISA.

Hasil: Subjek penelitian didominasi laki-laki dengan nilai tengah usia 42 tahun dan tingkat pendidikan rendah. Mayoritas telah bekerja <6 tahun dan waktu bekerja dalam sehari >8 jam per hari, tidak memakai alat pelindung diri, memiliki berat badan normal, dan pernah merokok. Rerata kadar SP-D pada subjek penelitian adalah 66,3±5,5 ng/mL, sedikit lebih tinggi dari subjek normal. Status merokok, jenis kelamin dan jam kerja berkorelasi dengan kadar SP-D yang lebih tinggi.

Kesimpulan: Kadar SP-D serum pada pekerja tambang batu kapur dapat digunakan sebagai pemantauan untuk penapisan awal pneumokoniosis meskipun secara statistik tidak bermakna. (*J Respirol Indones 2022; 42 (2): 151–5*)

Kata kunci: penanda hayati, kadar, penambang batu kapur, pneumokoniosis, protein surfaktan-D serum

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INTRODUCTION

Pneumoconiosis is a disorder that occurs due to the accumulation of dust in the lungs, which causes a reaction of the tissues to the dust.¹ Pneumoconiosis can be caused by a variety of mineral dust. Asbestos, silica, and coal dust are the main causes of pneumoconiosis. Classification of dust causing pneumoconiosis includes inorganic dust such as silica, asbestos, and lead; coal mine dust; as well as organic dust such as cotton. Silicosis is a pneumoconiosis caused by chronic exposure to silica dust will later manifest into progressive pulmonary fibrosis even after exposure has ceased. Limestone is a sedimentary rock consisting of the minerals calcite and aragonite, often containing silica and fossils, which are commonly used in building materials.¹

Surfactant-D (SP-D) is part of the innate immune system, as a pattern-recognition receptor from the collectin family (collagen-containing C-type lectins), which functions to bind, opsonize and cleanse bacteria, viruses, fungi, and parasites.² SP-D also binds to other biological particles, allergens, genomic DNA, apoptotic materials, and particulate matter cleared from the airways.³

Surfactant-D is a hydrophilic molecule, its level in BAL or circulating blood⁴ may be associated with the development, progression, and severity of lung diseases, such as idiopathic pulmonary fibrosis, interstitial lung diseases, ARDS, tuberculosis, and COPD.^{5,6} Data regarding the diagnosis of pneumoconiosis such as ILO chest X-ray, and SP-D as possible biomarker of pneumoconiosis have been mentioned.⁷⁻¹⁰ In this study we tried to find out whether serum SP-D levels might be a candidate of biomarker to diagnose early lung disease in limestone workers.

METHODS

This was a cross-sectional study using total sampling to determine the serum SP-D levels of limestone mining workers in Citatah Village, West Bandung Regency. Since the prevalence of pneumoconiosis in West Bandung Regency was

unknown, we calculated a sample size of at least 90 subjects. The inclusion criteria in this study were limestone mining workers and were willing to participate by signing informed consent form. Exclusion criteria were subjects with history of chronic lung diseases (asthma, COPD, pulmonary TB) or history of thoracic surgery. This study was conducted with the approval of the Research Ethics Committee of the Faculty of Medicine, Universitas Indonesia. After obtaining informed consent, the subjects were interviewed and the blood samples were collected.

Serum SP-D was measured using the ELISA method at the Laboratory of Respiratory Immunology, Department of Pulmonology and Respiratory Medicine, Faculty of Medicine Universitas Indonesia-Persahabatan Hospital, Jakarta. A total of 5 mL of blood was taken from one arm of the subject, then put into a vacutainer tube, centrifuged at 3000 rpm for 10 minutes. Serum was then diluted 11 times, and serum SP-D levels were determined by ELISA method using the Human Surfactant Protein D catalog kit ELISA Number RD194059101 (BioVendor). SP-D levels were read on a microplate reader (iMark® BioRad) at 450 nm, and measured using the provided control SP-D concentration.⁴⁻⁶

RESULTS

A total of 80 subjects participated in this study, 7 subjects were excluded due to treatment for pulmonary TB, 2 subjects had chest injuries, another 2 subjects refused to participate, while 4 samples were damaged during serum preparation.

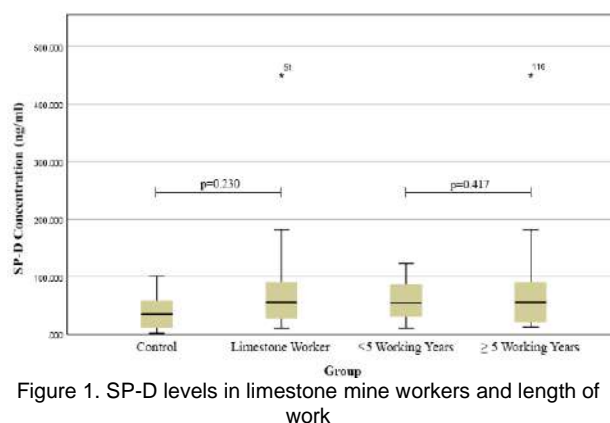


Figure 1. SP-D levels in limestone mine workers and length of work

A total of 65 participants met the study criteria, conducted a questionnaire study, and underwent blood sampling for SP-D measurement. Previously, we had measured serum SP-D concentration in ten healthy subjects, as SP-D measurements have not been carried out in Indonesia. Among these healthy subjects, the mean concentration was 40.2±5.5 ng/ml (data in file). Seventy limestone workers were mostly male (89.2%), with a median age of 42.2±16.5 (18–85) years.

Table 1. Limestone mining workers characteristics

Variables	Subjects (n=65)	
	N	%
Sex		
Male	58	89.2
Female	7	10.8
Former Education		
Elementary School	42	64.6
Junior High School	10	15.4
Senior High School	13	20.0
Smoking History		
Yes	47	72.3
No	18	27.7
Brinkman Index		
Mild	22	33.8
Moderate	23	35.4
Severe	2	3.1
Non-smoker	18	27.7
Work Duration per Day		
<8 Hours per day	13	20.0
≥8 Hours per day	52	80.0
Body Mass Index		
Underweight	4	6.2
Normal	36	55.4
Overweight	11	16.9
Obese grade I	12	18.5
Obese grade II	2	3.1
Age		
<40 years	28	43.1
≥40 Years	37	56.9
Use of PPE (mask)		
Yes	14	21.5
No	51	78.5
Length of Work		
<5 years	24	36.9
≥5 years	41	63.1

Duration of working was 7.8±1.2 hours per day and the mean length of work was 7.8±1.2 years. Most subjects had low education level (64.6% had former education of elementary school), were smokers (72.3%) and did not use personal protective equipment/PPE (78.5%), as shown in

Table 1 and Table 2. Mean serum level of SP-D in limestone workers was 66.3±5.5 ng/mL.

Table 2. Subjects' characteristics

Variables	Data distribution (mean)	Control Subjects (n=9)
Age (years)	42.2±16.5	31.±2.5
Length of work (years)	7.7±7.9	n/a
Height (cm)	162.9±8.3	166.7±10.4
Weight (kg)	60.3±12.2	74.2±19.6
BMI (kg/m ²)	21±1.4	26.7±7.1
Work duration per day (hours)	7.8±1.2	n/a
SP-D level (ng/ml)	66.3±5.5*	40.2±5.6*

Note: *P=0.230

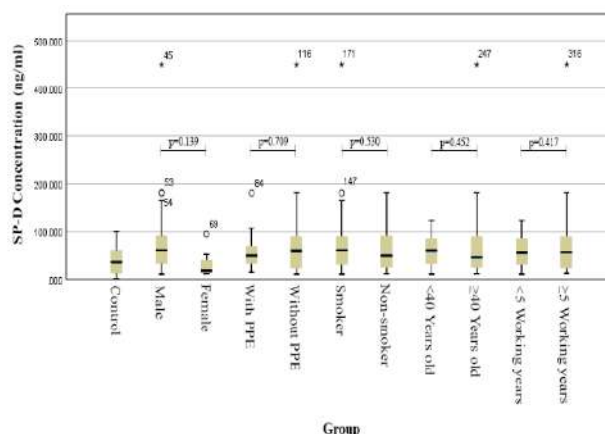


Figure 2. SP-D level in subgroup subjects

Table 3. Correlation of SP-D values with several study variables

Variables	N	SP-D±SE (ng/mL)	P
Sex			
Female	7	32.8±8.5	0.139
Male	58	70.4±11.7	
PPE Use			
No	51	67.9±9.5	0.709
Yes	14	60.7±11.6	
Smoking History			
No	18	45.1±10.7	0.530
Yes	47	69.0±10.1	
Working time (hour)			
<8	13	94.9±32.1	0.293
>8	52	59.2±5.5	
Age (years)			
<40	28	59.5±6.3	0.452
>40	37	71.5±12.9	
Length of Work (years)			
<5	24	57.9± 6.6	0.417
>5	41	75.6±11.8	

DISCUSSION

This was the first study to evaluate serum SP-D levels in limestone miners in Indonesia. Serum level of SP-D in limestone workers was 66.3±5.5 ng/mL, slightly higher than normal controls based on

our previous data (40.2 ± 5.5 ng/mL) although this was not a comparative study. This might be due to the limited number of subjects and duration of occupational exposure. Honda et al stated that normal SP-D levels were 66.3 ± 3 ng/ml in serum and 880 ± 130 ng/ml in BAL.⁴ The normal cut-off value of SP-D in Indonesian population still have to be determined.

In this study, although limestone miners were mostly male, probably due to the economic burden, female miners accounted for 10% of workers. The median age of the subjects was 42 years with the youngest of 18 years old and the oldest of 85 years old. SP-D levels in male workers (70.4 ± 11.7 ng/mL) were higher than female workers (32.8 ± 8.5 ng/mL), although this difference was not statistically significant.

SP-D levels were slightly higher in the older age group (>40 years) of 71.5 ± 12.9 ng/mL. This was in accordance with our previous study which stated that there were no significant difference between serum SP-D levels and age.⁷⁻¹⁰ In this study, 47 subjects had a history of smoking and 18 subjects had never smoked. SP-D concentrations were higher in individuals with smoking history, although not statistically significant.

Length of work >5 years showed a higher level of SP-D compared to <5 years, although it was not statistically significant. This suggested that SP-D levels might be useful in monitoring disease progression/disease detection in limestone workers. Wang et al found that SP-D levels in workers exposed to silica for 21 years were higher (47.26 ng/ml) compared to the unexposed control group (29.16 ng/ml).⁷ In another study, Xue et al observed a mean SP-D of 9.9 ng/ml.⁷ This data showed higher levels of SP-D in limestone workers compared to previous studies.

As an innate immune receptor, SP-D is capable of binding to silica, thereby enhancing direct phagocytosis of alveolar macrophages, regulating ROS production and alveolar macrophage clearance. Silica-exposed population had higher serum SP-D level, the reasons were thought to be caused by low clearance of alveolar macrophage,

effect of silica to AT-II and Clara cells which increased level SP-D in the alveolar fluid, and leakage of SP-D level in the alveolar fluid into circulation. Chronic silica exposure will result in proliferation of AT-II cells thus increased SP-D level.²⁻⁴

The SP-D levels were inversely related with PPE (masks) use, this possibly due to the low adherence to PPE, although further study is needed for confirmation.⁵⁻¹² Kondo et al reported that mean serum SP-D level on 8 patients with pneumoconiosis was 121.9 ± 92.8 ng/ml and it was not statistically different with control group (57.6 ± 38.4 ng/mL), and several lung diseases.

Part of this study has been published as a thesis for pulmonology residency program of Anna Yusrika, MD. We are indebted for the assistance of Mrs. Refniwita in sample preparation. Sita Laksmi Andarini, MD was designed, funded, did the sampling and laboratory works, did data analysis and wrote the manuscript. Anna Yusrika, MD did the sampling and laboratory works. Ahmad Hudoyo, MD designed and funded the study. Sri Wening Pamungkasningsih, MD and Widhy Yudistira Nalapraya, MD did the sampling and prepared the manuscript. Sri Wening Pamungkasningsih, MD; Widhy Yudistira Nalapraya, MD; Farhan Hilmi Taufikulhakim, MD; Agus Dwi Susanto, MD helped with data processing and manuscripts preparation. The Authors would like to give appreciation to Pramita Laboratory for on-site serum preparation.

CONCLUSION

The mean SP-D level in limestone workers in West Java was 66.3 ± 5.5 ng/mL. Although this study was not designed to be compared with normal subjects, SP-D level in limestone workers were slightly higher than in normal subjects. Smoking status, male, length of work were associated with higher concentrations of SP-D in limestone workers. Serum SP-D examination might be important as a biomarker for screening of early pneumoconiosis in limestone workers.

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