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To cite this article: T K Intan *et al* 2019 *IOP Conf. Ser.: Earth Environ. Sci.* **245** 012013

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The correlation of sulfur dioxide length of exposure to c-reactive protein level of gas station employees in Medan Amplas District, Medan

T K Intan^{1,2}, A P Tarigan³ and Hidayati⁴

¹Master Program in Biomedical Sciences, Faculty of Medical, Jl. Dr. Mansyur No.1 University Sumatera Utara, Medan 20155, Indonesia

²Department of Anatomic Pathology, Faculty of Medical, Jl. Dr. Mansyur No.1 University Sumatera Utara, Medan, 20155, Indonesia, 20155

³Department of Pulmonology and Respiratory Medicine, Faculty of Medical, J. Dr. Mansyur No.1 University Sumatera Utara, Medan, 20155, Indonesia

⁴Bureau of Environment North Sumatera Utara Province, Jalan T. Daud No.5, Medan, Indonesia

Email: tengkukemalaintan@usu.ac.id

Abstract. As part of air contaminants, sulfur dioxide (SO₂) affects the lung functions including decreasing breathing ability, infection, and inflammation reaction which is indicated by the presence of C - reactive protein (CRP). This research is conducted to investigate the length of exposure of SO₂ in gas station employees located in Medan Amplas District. The samples were collected by total sampling method, while the data were analyzed by using the cross sectional design, while the hypothetical analysis were conducted by implementing the Spearman method, and Pearson statistical method. It was found that the working hours showed positive correlation, which was accounted 0.0628875 ± 0.04437757 mg/L for insignificant level of CRP. This shows a correlation between the work duration of exposure on SO₂.

1. Introduction

Formed sulfur dioxide is released to the atmosphere due to several processes like sulfuric acid production in chemical industries. It is released as organic matter, hydrogen sulfide (H₂S), and in the nature which will be oxidized by radical hydroxyl (HO[•]) (Jettawana, 2005). Sulfur dioxide is heavier than the air, and it is known as sulfurous anhydride, or sulfurous acid anhydride which have O=S chemical structure. Another physicochemical properties are colourless gases and soluble in organic solvent. While in the atmosphere, this gas reacts to form sulphuric acid. According to the data by EPA National Air Pollutant, the source of sulfur dioxide is the emissions from industries that related to steel, oil and motor vehicles process (International Agency for Research on Cancer, 1992; Riordan and Adeeb., 2004).

SO₂ with a 10-day lifetime oxidize rapidly in either homogenous and heterogeneous reactions then will vanish in the air due to precipitation process and air deposits in the surface with humidity level especially in the form of sulfuric acid. People who live nearby to industrial area or in a dense community, then crowded motor vehicles traffic are prone to sulfur dioxide inhalation. This is also valid for workers whose work close to motor vehicle emissions such as petrol station. It has been reported that epidemiology data showed the effect of air pollution to health causing chronic lungs impaired and cardiovascular diseases to deaths (Pope et. al., 2004; Brook et. al., 2004; Clancy et. al., 2002; Hoek et. al., 2002).



S-sulfonate metabolite is formed from the reaction between sulfur dioxide metabolite with sulfite and proteins. In human body, after inhalation, the SO_2 is absorbed at the surface of humid respiratory tract, producing sulfite metabolite, bisulfite and hydrogen ions. This sulfite then is oxidized by sulfite oxidase, which is found in mitochondria in the liver. Several studies have found that an increase of sulfite oxidase is found in the liver, kidneys and heart but not in the lungs (Gunnison and Jacobsen, 1987). This implies to the excretion process conducted by kidneys is affected by the contamination of sulfur dioxide in the lungs

Subsequently, if unknown matter is presence, then the human body enables protein plasma and leukocyte to leave the circulation and finally emigration from microcirculation to remove the infective agents (Kumar, 2010). As the results, blood circulation is disturbed which can lead to cardiac disease, and the inflammation is occurred. In this study, the investigation lies on the inflammation which is based on the reaction of C - reactive protein.

Particulate matter such as SO_2 in long term exposure will cause the increase of plasma endothelin-1 concentration and blood pressure in pulmonary artery. This causes inflammation reaction repetitively and produces chemokines and cytokines inflammatory by macrophage alveolar and dendritic pulmonary cells. The total inflammation molecules affect lungs and endothelium vascularization systemic directly, causing changes in vascular permeability, trigger on fibrinolysis and coagulation as the addition of inflammation adhesion cells in endothelial vascular (Barnes et al., 2012; Calderon-Garciduenas et al., 2007). And CRP level which is a protein synthesized in acute phase inflammation, especially by hepatocyte as a response to tissue wounds, implying that this protein is a systemic signal indicating an infection and maginancy (Black, 2004).

CRP has roles in body defense system. It can increase the production of cytokines which is a proinflammatory, so it can increase the development of leukocyte adhesion in endothelial blood vessel to strengthen inflammatory reaction in blood vessel. On the other hand, CRP also interacts with endothelial cells to trigger the production of IL-6, MCP-1 and endothelin-1 which alter the functions of endothelial blood vessel. As a result, CRP activates NFkB in endothelial and mononuclear cells to induce protease and proinflammatory cytokines like IL-1b, IL-6, IL-8, and IL-18 which have parts in triggering macrophage to absorb LDL (Kao, 2006; Khafaie, 2013). In healthy human blood, the CRP level is $<0.15\text{mg/L}$ (Kushner, 1978).

Therefore, CRP level in the circulation of most diseases shows more of inflammation compared to parameter in other acute phase laboratory response like plasma viscosity and erythrocyte sedimentation level. The most important value of acute phase CRP does not show diurnal variation and does not affect by food. The condition of liver failure destroys CRP production but medicines have little impact to CRP. The concentration of CRP is very helpful as a sign of nonspecific biochemistry like inflammation and gives a contribution in screening for organic disease, observing medicinal responses towards inflammation and infection treatment and detecting infection relapse in immunocompromised patients (Pepys, 2003).

2. Experimental

2.1 Research Design

This is a correlation test research with cross sectional design to know if there is a correlation between the duration of sulfur dioxide exposure to C-reactive protein level of employees in the gas station. The research was conducted in gas station in Medan Amplas sub-district, Medan City and the research time was conducted for 12-20 weeks.

2.2 Research Respondents and Research Samples

The research respondents are the employees in public gas station located in Medan Amplas sub-district, Medan city who meet the criteria set. There are two types of criteria which are inclusion and exclusion criteria. The inclusion criteria include male and female employees ages are between 18 to 40 years old, 1-year minimum of work duration, and 8 hours a day minimum of work hours. While the exclusion criteria are suffering from any obstructive lungs impaired or diseases history, smoking, obese, and pregnant.

The research samples were the gas stations which are located in Medan Amplas Sub-District, Medan City. Table 1 below shows the research samples of each gas station.

Table 1. Research samples of each gas station

No	Gas Station Number	Total Pump Operator	Total Sample
1.	14.202.126	6	5
2.	14.201.127	20	5
3.	14.202.185	21	7
4.	14.202.141	8	3
5.	14.202.1151	15	5
6.	14.201.1159	16	5
7.	14.202.1162	15	5
8.	14.201.114	20	6
9.	14.202.137	21	7
Total		152	49

2.3 Materials and Tools

Materials and tools in this research involved from preparation which is data sample needed as research variables. The tool used to support research variable was 0.04M tetrachloromercurate (TCM) absorbing reagent Impringer based on SNI (Indonesia National Standard) 19-7119-7-2005 to determine SO₂ concentration which was done in the field together with Environmental Agency Laboratory team, North Sumatera. Then, CRP measurement with ELISA method was conducted in Integrated Laboratory of Medical Faculty of University of Sumatera Utara together with other researches and laboratory technicians.

2.4 Research Framework

The research framework was firstly started by collecting the samples of population of workers who work in gas stations in region of Medan Amplas, Medan City, and this was conducted to obtain the demographical data. Then, the gas stations profiles were collected.

Afterward, the research was divided into two steps. The first step is the measurement of concentration of sulfur dioxide, while the other step is obtaining the value of C-Reactive Protein (CRP). The concentration of sulfur dioxide was obtained by collecting the air samples with instrument Impringer. After collecting, the samples then were taken to the laboratory of environmental bureau of Sumatera Utara province. Then, the samples were tested with Pararosaniline, and the concentration of sulfur dioxide was obtained.

Meanwhile, the population of workers was instructed to fill the questionnaire. After filing the questionnaire, the workers' serum was taken with ELISA methods. And the C-Reactive Protein level was obtained.

During the research, the normality test was conducted by using Kolmogorov-Smirnov against age, and work duration to see if the data is distributed normally. To determine the homogeneity of variance test, the Levene test was conducted. So, both of IF Kolmogorov-Smirnov and Levene tests were used to show that the distributed normally data meet the homogeneity of variance resulting to bivariate analysis. This was used to analyze the difference in mean with T test and to see the mean difference of CRP. If the previous tests showed different results, which are not distributed normally, then multivariate analysis was conducted. It is a correlation test with Spearman and Pearson method to see the correlation between work duration and CRP level.

3. Results and Discussion

3.1 Respondents Characteristics based on Age

In this research, respondents are the operators in public gas station. There are 71 people from 5 public gas stations in Medan Amplas sub-district, Medan. 12 out of 71 respondents did not meet the inclusion criteria and therefore were not included in selected respondents. Respondents who met inclusion criteria were 59 people in total from the planning of 48 respondents based on the calculation of sample size. Table 2 below shows the characteristic of the selected respondents based on Age.

Table 2. Respondents Distribution Based on Age

No.	Age (Years Old)	Total	Percentage
1.	15 – 24	29	49.2%
2.	25 – 34	19	32.2%
3.	35 – 44	7	11.9%
4.	45 – 54	3	5.1%
5.	55 – 64	1	1.7%
Total		59	100%

From the Table 2, we can see that almost half of the total respondents are under 25 years of age (49.2%). And it is followed by the group of age 25 – 34 with 19 people accounted for just above 30%. Whereas the least number of respondent was 1 who has age from 55 to 64 years old.

3.2 Respondents Characteristics based on Gender

Respondents based on gender are mostly male workers with over 60%. The distribution of worker can be seen on Table 3 below.

Table 3. Respondents Distribution Based on Gender

No.	Gender	Total	Percentage
1.	Male	37	62.7%
2.	Female	22	37.3%
Total		59	100%

The table 3 shows that male respondents are more than females, and the female workers are over a third of the total population.

3.3 Respondents Characteristics based on Work Duration

Work location distribution from the respondents is represented on Table 4. Below

Table 4. Distribution of workers based on Work Location

No.	Work Duration	Total	Percentage
1.	<5 years	30	50.8%
2.	≥5 years	29	49.2%
Total		59	100%

From the work duration distribution, the number of workers who has worked for less than five (5) years are similar (50.8%) to the number of those who has worked for 5 or more than 5 years (49.2%).

3.4 Air Ambient SO₂ Test Analysis

Based on the air testing in the laboratory with pararosaniline method to sulfur dioxide which has been converted to normal condition (N), with temperature of 25°C, atmospheric pressure (76

mmHg), also referring to standard quality of government regulation PP No. 41 year 199 about air pollution control, Ministry of Environment Regulation No. 50 year 1996 about standard ash level, No. 48 year 1996 about standard noise level as well as accredited parameters KAN No. LP-692-IDN, then the distribution of air ambient with sulfur dioxide parameter can be seen on Table 5 below.

Table. 5 Data analysis of Sulfur Dioxide Parameter Air Ambient

No.	Gas Station	Mean \pm SD ($\mu\text{g}/\text{m}^3$)	Total Vehicles (Unit)
1.	SPBU No. 14.201.127	241.40 \pm 26.197	1,291
2.	SPBU No. 14.201.126	216.53 \pm 37.683	578
3.	SPBU No. 14.202.141	230.40 \pm 32.369	1,562
4.	SPBU No. 14.201.185	253.40 \pm 19.909	1,143
5.	SPBU No. 14.202.162	235.27 \pm 34.605	1,111
Mean Total		237.03 \pm 12.090	5,685

It can be seen from Table 5 above, that the mean concentration of sulfur dioxide in this study is $237.03 \pm 12.090 \mu\text{g}/\text{m}^3$ with the highest level in SPBU No. 14.202.185 with mean level of $253.40 \pm 19.909 \mu\text{g}/\text{m}^3$. While the lowest mean concentration of SO_2 is SPBU No. 14.201.126 with mean level for $216.53 \pm 37.683 \mu\text{g}/\text{m}^3$.

3.5 Variable Characteristics based on Work Duration

Assessment to h-CRP test was conducted as dependent variable and work duration; age as independent variable. The dependent variable characteristics are as follow:

Table 6. Dependent Variables Characteristics

Variable	Work Duration	Mean \pm SD
Sulfur Dioxide Concentration	< 5 years	236.32447 \pm 11.019267
	\geq 5 years	237.75859 \pm 13.263173
CRP	< 5 years	0.0650490 \pm 0.05017814
	\geq 5 years	0.0606514 \pm 0.03822895

Next, normality and variance homogeneity tests using Kolmogorov-Smirnov and Levene methods respectively were conducted as assumption tests to do parametric statistic test.

Table 7. Normality Test with Kolmogorov-Smirnov Method Result

Variable	Work Duration	KS Value	p value
Sulfur Dioxide Concentration	< 5 years	0.195	0.005
	\geq 5 years	0.191	0.008
CRP	< 5 years	0.184	0.011
	\geq 5 years	0.128	0.200*

*p>0.05; it can be considered as normal data

Table 8. Variance Homogeneity with Levene Method Result

Variable	Levene Value	p value
Sulfur Dioxide Concentration	2.647	0109*
h-CRP	1.577	0.214*

*p>0.05; it means data meet variance homogeneity

From Kolmogorov-Smirnov and Levene tests above, we can see that the data meet variance homogeneity assumption, but it is not in normality assumption. Therefore, parametric statistic cannot be used in this case. Thus, the hypothesis test in this study is using correlation with Spearman and Pearson statistic test.

3.6 Correlation Tests between Work Duration with CRP value

The correlation tests between work duration with CRP value were with Spearman correlation test.

The table 9 shows the correlation of this variable.

Table 9. Correlation between Work Duration with CRP Value

Variables	Correlation Test	CRP Value
Work Duration	Spearman value	0.01
	<i>p</i> value	0.94

**p* < 0.05

From the table above, we can find that work duration has a positive correlation to CRP value which shows that the group with longer work duration has higher CRP value. While in Table 10, the Pearson Correlation test, there is positive significant correlations which are shown in sulfur dioxide concentration against total number of vehicles coming into the gas stations.

Table 10. Pearson Correlation Test Variables

Variable	Age	SO ₂ Level	CRP	Total number of Vehicles
Age	1	0.007	0.103	0.110
SO ₂ Level		1	-0.101	0.469*
CRP			1	-0.044
Total number of vehicles				1

**p* < 0.05; correlation is significant

For CRP variables, this research gets the correlation with $r = 0.01$ and $p = 0.94$. This result shows a small and significant positive correlation. The result obtained is similar to the study done in 2007 by Ruckerl et al., in studying Air Pollution and Inflammatory Response in Myocardial Infarction Survivors: Gene-environment Interaction in a High-risk Group) which see the relationship between pollutants and inflammation responses in patients with myocardial infarction medical history. There was no relationship between pollutant and CRP value. But, this study shows the relationship between pollutant with IL-6 value and fibrinogen.

CRP, IL-6 and fibrinogen are acute phase reactants, but there is no relationship between CRP to pollutant. This might due to 2 factors which are CRP level in younger respondents are relatively lower, and the second is due to bias which is statin consumptions in the research subjects. Statin has the effect to decrease CRP value. In this research age might be the main factors that lead to the result which shows no relationship between work duration and CRP value (Ruckerl et. al., 2007).

Research done by Routledge et al in 2006 also shows an insignificant relationship between gas pollutant, sulfur dioxide and carbon dioxide against CRP acute reactant phase. He did a random research, double blind and experimental to patients with angina medical history. Then, he found the reasons for a no relationship between gas pollutant and inflammation parameter (in this case is CRP). Due to the inflammation occurring did not happen systematically and its response depends on pollutant which is the transitional metal composition, which is different in emissions by vehicles powered by fossil fuel. This is the reason why inflammation response does not occur if the exposure of sulfur dioxide is not pure. Another probability is the inflammation effect which only occurs locally in respiratory tissue and non-systemic inflammation. Therefore, the CRP level examined from blood sample does not show an accurate result. It is expected that the next study for CRP level examination can be done with samples from tissue under respiratory tract to give a more representative data.

Several limitations in this study is control group and smoking history in research samples. This is due to the limitation in technical aspects to obtain sample which had always been constrained by workers' working hours and technician schedule to do emission measurement also the problem in funding and research duration. Second, this study is an analytical study with a cross sectional design. Therefore this study cannot be used to track either the difference in CRP value or lung function due to sulfur dioxide exposure. Research using cohort prospective design is more capable to be used to track the exposure risk factors against effect assessed. Third is the calculation for sulfur dioxide emission which was done in 10 hours while observation for 24 hours will reduce bias due to diurnal variation. These happened due to the limited instrument.

4. Conclusion

This research is assessing the correlation between work duration with CRP level to employees in the gas station in Medan Amplas area. There is insignificant positive between CRP with work duration. The measurement of sulfur dioxide which was conducted by calculating the mean concentration level accounted for $237.03 \pm 12.090 \mu\text{g}/\text{m}^3$. While the mean C-Reactive Protein (CRP) level in gas station employees in Medan Amplas was $0.0628875 \pm 0.04437757 \text{ mg/L}$, which indicated the insignificant positive correlation between work duration in public gas station and the CRP value. While SO_2 level with total number of vehicles coming into the gas station provided positive correlation.

The results obtained are in accordance with previous study by Bhide et al., (2014) which compared spirometry test result between employees in public gas station and work duration above 5 years, less than 5 years and control group. In the study, Bhide found significant difference parameters which were in lung function parameters.

5. Acknowledgement

I would like to express my deepest grateful to two teams: the first is for team of scientists from the North Sumatera Environmental Department whom collaborate research on Sulfur Dioxide with me to be completed accordingly. Secondly goes to the team of Intergrated Laboratory Faculty of Medical University of North Sumatera whom assisted me on "the Elisa Method of C-Reactive Protein"

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