INTRODUCTION

One of the factors causing increased blood pressure is the workplace and the uncovered environment. Workers in different industries are regular exposure to heavy metals. Those metals enter their physical structure through various routes (inhalation, food contamination, etc.) and accumulate in the tissues and induce generation of reactive oxygen species (ROS) leading to oxidative damages. Chronic, regular exposures result in a health risk. Certain physiological, biochemical, and behavioral dysfunctions cumulate to pathological conditions. Many of the symptoms complained by those industry workers are hardly known to be related to occupational exposure to heavy metals, often unidentified as occupational health hazards with a story of metal-induced oxidative stress beneath their etiology [1], it's evidenced by a study that included 105 people with arterial hypertension divided into occupational history groups with lead exposure and the group having no work history with lead exposure. This study concluded that lead concentrations were higher in Group I compared with Group II [2].

The workplace or high environment of lead exposure in addition to refueling is the final disposal (FD). In 2011, Chu conducted a survey on heavy metals found in the FD Vietnam that lead metal is more dominant than chromium and cadmium [3]. The various negative impacts arise from FD, from infrastructure damage to environment pollution. The impact of environmental pollution will be very influential in the communities around the FD such as employees and residents. According to Hygiene officials of Medan City Government, stated that every day, the residents are in the FD location, while employees still have a period of leave each month [4]. Exposure prolonged and continuous exposure will have more severe toxic effects [5].

Based on the experience of an observer of lead poisoning in Indonesia states that many lead sources have not been identified or studied, especially lead in contaminated waste in human blood [6]. The lead content in earthworms taken from FD, it was found that the lead content in earthworms was above the threshold [7]. It's very closely related to the FD that is categorized as a source of lead exposure.

Approximately 90-95% of lead is stored in the bone, while only a small part is found in the blood. The half-life of lead in the blood is only about 30 days [8], whereas according to the WHO (1995) the half-life of lead in blood is approximately 36 days, in soft tissue 40 days, while in bone over 25 years. A researcher stated that lead levels in the blood of volunteers as many as 1052 people experienced of decreasing 40% in men over 11 years and 30% in women after 5 years [9]. However, from the bone, lead is demobilized and put into the bloodstream [10], so with the bad effects of lead, lead is a risk factor for hypertensive disease [11].

MATERIALS AND METHODS

Materials

Materials were used are pro-quality analysis of E. Merck if not stated otherwise is demineralized water, concentrated HCl, concentrated HNO₃, concentrated HClO₄, concentrated H₂SO₄, volunteers blood, cotton (Bratachem), standard solution of calcium nitrate, the standard solution of lead nitrate, and Na₂EDTA.

The study was conducted using a comparative causal method. Data were collected by interview using a structured questionnaire, including measurement of blood pressure, weight, height, and fill out a questionnaire regarding working time, age, family history, and physical health as well as laboratory analysis; while the approach in this study is cross-sectional. Each volunteer is measured 3 times at intervals for 1 week at 1-21th days. In the previous month should measure the concentration of lead and calcium to see and confirm whether there is a decrease in the concentration of lead and calcium after 1 month.

This study was conducted on FD (Group I) employees; scavengers who move in FD, and control. Confounding variables in this study are the working period, age, and body mass index. Determining calcium content performed acetylene flame atomic absorption spectrophotometry-air while the lead is done by atomic absorption spectrophotometry graphite furnace method.

RESULTS

The results of the study showed differences of concentration lead of each group. In Group II on day 30 it contained a lead level of 29.9141 μg/DL. This level has exceeded the threshold set by the WHO. Statistical test results using Rank Spearman correlation showed no relationship between lead and calcium to hypertension, the p value of each group was 0.187, 0.819, and 1.00.

Conclusion: The results of this study can be concluded that the lead and calcium does not affect blood pressure on employees and scavengers in the FD Medan-Marelan.

Keywords: Hypertension, Lead, Calcium, Final disposal.

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ABSTRACT

Objective: The aim of this study was to determine the relationship between lead and calcium to hypertension.

Methods: This study uses causal comparative cross-sectional study, which subjects of study as many as 31 people consisting of 10 people in Group I (employees of final disposal [FD]), 17 people in Group II (scavengers who move in FD), and 4 people in Group III (control). Confounding variables in this study are the working period, age, and body mass index. Determining calcium content performed acetylene flame atomic absorption spectrophotometry-air while the lead is done by atomic absorption spectrophotometry graphite furnace method.

Results: The results of the study showed differences of concentration lead of each group. In Group II on day 30 it contained a lead level of 29.9141 μg/DL. This level has exceeded the threshold set by the WHO. Statistical test results using Rank Spearman correlation showed no relationship between lead and calcium to hypertension, the p value of each group was 0.187, 0.819, and 1.00.

Conclusion: The results of this study can be concluded that the lead and calcium does not affect blood pressure on employees and scavengers in the FD Medan-Marelan.

Keywords: Hypertension, Lead, Calcium, Final disposal.
were active in FD (Group II) and control (Group III) were 10, 17, and 4 persons, respectively. The total sample is 31 people.

The study was conducted on FD Medan city Palu Nibung Street, Paya Pasir sub-district, Medan Marelan sub-district and four villages (Jl Marelan Raya Pasar V, Medan Marelan sub-district, Paloh Maran, Del Serdang sub-district, Hamparan Perak district; Titi Pahlawan Pekan Labuhan Street, Medan-Labuhan and Kampung Lama, Deli Serdang district, Hamparan Perak sub-district).

Sample preparation
Prepare vial previously been given powdered Na$_2$EDTA as much as ±500 mg, then wipe the arm veins radial of volunteers with cotton previously moistened with alcohol 70% (v/v), take a syringe the size of 5 ml, then take the blood through the veins radial, then insert it into the vial which already contains Na$_2$EDTA and transported to the laboratory Pharmacy University of North Sumatra for dry destruction.

Process of sample destruction
Putting blood in a crucible porcelain, put into 5 ml of concentrated nitric acid, heat with digital hot plate in a fume hood for 30 min at a temperature of 150°C, add 0.2 ml of perchloric acid 50% (v/v) and 0.4 ml of concentrated sulfuric acid and continue heating with the beginning of the heating temperature 150°C followed by increasing temperature to 200°C and 250°C for 15 min. Then ashing followed using a furnace at a temperature of 400°C for 48 h. To obtained a perfect ashing can be followed by dissolving with 6N HNO$_3$ as much as 10 ml and heated at a temperature 90°C for 30 min. A 20 ml puts into a volumetric flask quantitatively and added with demineralized water to the mark line, and then filtered with Whatman filter paper No. 42. Dilute 1 ml of sample solvent and put into 10 ml volumetric flask and heated on quantitative and complete with demineralized water, to the mark line for lead metal and added 5 ml in a 25 ml tin-shaped flask for calcium metal and 2.3% lanthanum oxide solution added 2.5 ml [12,13].

Laboratory analysis
The solution samples obtained from the destruction process in measuring using an AAS method with graphite furnace atomic at a wavelength of 283.3 nm for lead and 422.7 nm for calcium with spectrophotometry flame atomization.

RESULTS AND DISCUSSION
Lead and calcium calibration curves
The lead and calcium calibration curves were obtained by measuring the absorbance of lead and calcium standard solution with various concentrations at wavelength 283.3 nm for lead and 422.7 nm for calcium. The results of measurements of lead and calcium calibration curves can be seen in Figs. 1 and 2.

The calibration obtained for both lead and calcium (lead = 0.9990 and calcium = 0.9986), both of it within acceptable ranges of r≥0.95. This shows that there is a linear correlation of the relationship between concentration (X) and absorbance (Y) which means, the increasing of concentration comparable increased observance [14].

Recapitulation of lead level in blood
The result of measurements recapitulation in blood can be seen in Table 1.

| Group | Lead levels in the blood (mg/dl) |
|-------|---------------------------------|
|       | 0 days  | 30 days | 37 days | 51 days |
| I     | 13.3221 | 22.3606 | 11.4673 | 16.2635 |
| II    | 15.2584 | 29.9141 | 12.0791 | 22.0720 |
| III   | 1.0072  | 5.4340  | 1.1300  | 4.1318  |

| Description: Group I: FD employee, Group II: Scavengers that are active in FD, Group III: Controls living in the 4-way region of the wind, FD: Final disposal |

Fig. 1: Calibration curve of lead

Fig. 2: Calibration curve of calcium

Fig. 3: Percentage diagram of high lead concentration relationship of calcium, blood pressure, and confounding variables
blood lead level between 20 and 29 µg/dl in 1976 s/d 1980 showed that increased mortality due to circulatory and cardiac disorder [16].

Levels of calcium in the blood
The result of measurement recapitulation of blood calcium level in all volunteers can be seen in Table 2.

The results of recapitulation of blood calcium levels in Table 2 showed that the Groups I and III on the 37th day contained calcium levels of 8.2673 and 7.6586 mg/dl. The level is below the threshold set by Mayus (2013). The amount of normal calcium in the blood is about 9-11 mg/dl for adults. Based on these criteria, in Group I, there were 36.36% of respondents had moderate blood calcium level (9-11 mg/dl) which is still within normal criteria, 18.18% had low calcium levels (<9 mg/dl), and 45.45% or 5 people who have high levels of calcium in the blood.

Increased calcium concentration is not related to lead concentration, but there is a tendency that the higher the concentration of lead, the higher the concentration of calcium. This can be seen in Table 3.

There is a linear relationship between lead and calcium. It's because lead pushes the calcium to the intracellular magnitude and can regulate the inclusion of calcium or calcium release from the sarcoplasmic reticulum. This affects the bond with the sodium-potassium-adenosine triphosphate pump. The excess calcium ion will cause the heart undergoes spastic contraction. This is due to the direct influence of calcium ions in initiating the process of cardiac contraction. This instability of calcium will cause increasing arterioles of smooth muscle contractility thus increasing blood pressure [17].

### Table 2: Recapitulation of measurement of blood calcium level in all volunteers

| Group | Calcium levels in the blood (mg/dl) |
|-------|-------------------------------------|
|       | 0 days | 30 days | 37 days | 51 days |
| I     | 11.3715 | 13.5117 | 8.2673 | 8.7255 |
| II    | 14.1066 | 14.4211 | 11.8521 | 11.8716 |
| III   | 9.3090  | 11.9458 | 7.6585 | 8.5748 |

Description: Group I: FD employee, Group II: Scavengers that are active in FD, Group III: Controls living in the 4-wind direction, FD: Final disposal

### Table 3: Recapitulation of volunteers with high lead and calcium content

| Day    | Volunteers | Pb  | Ca  |
|--------|------------|-----|-----|
| 0 days | G.1        | 27.63 | 24.22 |
|        | G.2.5      | 44.85 | 30.79 |
|        | G.2.6      | 28.80 | 24.68 |
|        | G.2.12     | 53.08 | 35.41 |
|        | G.2.13     | 46.03 | 29.96 |
| 30 days| G.1.4      | 33.11 | 27.75 |
|        | G.2.5      | 57.98 | 32.36 |
|        | G.2.6      | 34.68 | 41.25 |
|        | G.2.12     | 56.79 | 41.95 |
|        | G.2.13     | 38.91 | 13.47 |
| 37 days| G.1.4      | 17.45 | 16.37 |
|        | G.2.5      | 5.31  | 24.25 |
|        | G.2.6      | 4.92  | 18.02 |
|        | G.2.12     | 14.71 | 28.99 |
|        | G.2.13     | 11.96 | 18.39 |
| 51 days| G.1.4      | 27.13 | 17.68 |
|        | G.2.5      | 13.68 | 28.92 |
|        | G.2.6      | 14.11 | 29.70 |
|        | G.2.12     | 29.42 | 32.44 |
|        | G.2.13     | 21.85 | 21.19 |

Description: G.1: Group I=FD employee, G.2: Group II=Scavengers that are active in FD, Pb: Lead, Ca: Calcium

The relationship between lead, calcium and blood pressure based on time
The test used to determine the relationship between lead to calcium and blood pressure is Rank Spearman. From rank, Spearman Correlation test showed no relation between lead to calcium and blood pressure. The result of the Rank Spearman correlation test in each group can be seen in Table 4.

Table 5 summarizes that lead, calcium, and blood pressure show an increase from the 30th day, decreasing on the 37th day, and increasing again on the 51st day.

Recapitulation of volunteers with high lead content related to calcium, blood pressure, age, body mass index (BMI) and years of service
Recapitulation of volunteers with high lead content related to calcium, blood pressure, age, BMI, and years of service can be seen in Table 6.

Based on data, it can be concluded that, of 5 people who have high lead concentrations, only 3 people have a relationship with calcium, hypertension, and confounding variables, while 2 others have no relationship between lead concentration with calcium, hypertension, and confounding variables, so the percentages can be shown as Fig. 3.

Based on Table 6 and Fig. 3, the percent increase is greater than the decrease, it suggests that the lead in the blood has put into the bone so that it can induce osteoporosis. The half-life of lead in blood is about 36 days, in soft tissue 40 days, while in the bone is more than 25 years. On the 51st day, there was an increase in the lead concentration of around 40%; this is due to continuous exposure to lead metal through burning waste, especially plastic which is one of the factors of lead exposure. The basic components in plastic manufacture are lead type support and stearate [18].

Heavy metal enters the cell through various interactions between metal ions and a functional group present at the cell surface and causes toxicity. Heavy metals also cause oxidative stress by generating ROS, including superoxide, hydrogen peroxide, and hydroxyl radical which are highly reactive and toxic and cause damage to a nucleic acid, protein, and lipid [19].

Lead that put into the bloodstream can cause hypertension. Lead can cause increased production of ROS. ROS is a derivative form of oxygen that occurs when reacting with electrons. The main source of ROS is the result of cellular respiration and metabolic processes. In addition, ROS can also occur from radiation. ROS has a crucial role in human physiology and pathophysiological processes. ROS plays a role in the function of immune, thyroid, cognitive, and nutrient sensor modulation and age. In relation to ROS health, it is associated with the implications of several diseases such as cancer, cardiovascular disease (including hypertension), neurological diseases, emotional disorders, and illnesses [20].

CONCLUSION
Based on the of Rank Spearman's statistical test result, there is no relationship between lead and calcium concentration to increase blood pressure, but visually there is a correlation between lead and calcium to increase individual blood pressure so that the concentration of lead in the blood is one of the factors causing hypertension.

### Table 4: The relationship between lead to calcium and blood pressure

| Variable | Ex. I | Ex. II | Ex. III |
|----------|-------|--------|---------|
| Calcium  | 0.187 | 0.819  | 1.00    |
| Systole  | 0.256 | 0.130  | 0.742   |
| Diastole | 0.053 | 0.157  | 0.684   |
Table 5: Distribution of lead, calcium and blood pressure

| Category against lead | Average group (K) | Criteria | Time   | 0 days | 30 days | 37 days | 51 days |
|-----------------------|-------------------|----------|--------|--------|---------|---------|---------|
| High                  | G.1 (1 Person)    | Pb       | 27.63  | 33.11  | 17.13   | 27.30   |         |
|                       |                   | Ca       | 10.80  | 12.41  | 7.82    | 7.82    |         |
|                       |                   | BP       | 140/95 | 160/100| 140/90  | 140/90  | 140/90  |
|                       | G.2 (4 Persons)   | Pb       | 43.19  | 47.09  | 9.23    | 19.77   | 12.90   |
|                       |                   | Ca       | 13.53  | 14.47  | 9.98    | 9.98    | 9.98    |
|                       |                   | BP       | 143/90 | 140/89 | 139/89  | 145/93  | 145/93  |
| Medium                | G.1 (5 People)    | Pb       | 19.17  | 27.34  | 9.63    | 15.02   |         |
|                       |                   | Ca       | 10.70  | 14.10  | 8.03    | 8.76    |         |
|                       |                   | BP       | 137/88 | 136/87 | 136/88  | 138/92  | 138/92  |
|                       | G.2 (6 People)    | Pb       | 9.78   | 20.84  | 7.77    | 15.50   |         |
|                       |                   | Ca       | 14.69  | 16.25  | 11.02   | 11.27   |         |
|                       |                   | BP       | 139/88 | 132/88 | 136/89  | 140/92  |         |
| Low                   | G.1 (4 Persons)   | Pb       | 5.41   | 13.44  | 12.26   | 15.09   |         |
|                       |                   | Ca       | 12.06  | 13.04  | 8.81    | 8.90    |         |
|                       |                   | BP       | 143/93 | 148/93 | 145/93  | 145/90  |         |
|                       | G.2 (7 People)    | Pb       | 4.75   | 20.84  | 17.44   | 29.28   |         |
|                       |                   | Ca       | 14.69  | 16.25  | 11.02   | 11.27   |         |
|                       |                   | BP       | 139/88 | 132/88 | 136/89  | 140/92  |         |
|                       | G.3 (4 Persons)   | Pb       | 1.00   | 5.43   | 1.13    | 4.13    |         |
|                       |                   | Ca       | 9.31   | 11.94  | 7.66    | 8.51    |         |
|                       |                   | BP       | 130/83 | 131/81 | 131/84  | 130/83  |         |

Description: G.1: Group I = FD employee, G.2: Group II = scavengers that are active in FD, G.3: Group III = controls living in the 4-way region of the wind, Pb: Lead, Ca: Calcium, BP: Blood pressure

Table 6: Recapitulation of volunteers with high lead content

| Day   | Volunteers | Pb    | Ca    | BP     | Age | BMI | Years of service |
|-------|------------|-------|-------|--------|-----|-----|-----------------|
| 0 days| G.1.4      | 27.63 | 24.22 | 140/95 | 44  | Normal | 13              |
|       | G.2.5      | 44.85 | 30.79 | 130/80 | 25  | Normal | 6               |
|       | G.2.6      | 28.80 | 24.68 | 140/90 | 42  | Normal | 20              |
|       | G.2.12     | 53.08 | 35.41 | 140/85 | 48  | <BW   | >20              |
| 30 days| G.1.4      | 33.11 | 27.55 | 160/100| 58  | Normal | 13              |
|       | G.2.5      | 57.98 | 32.36 | 130/90 | 25  | Normal | 6               |
|       | G.2.6      | 34.68 | 41.25 | 130/80 | 42  | Normal | 20              |
|       | G.2.12     | 56.79 | 41.95 | 130/80 | 48  | <BW   | >20              |
| 37 days| G.1.4      | 17.45 | 16.37 | 140/90 | 44  | Normal | 13              |
|       | G.2.5      | 5.31  | 24.25 | 135/85 | 25  | Normal | 6               |
|       | G.2.6      | 4.92  | 18.02 | 130/80 | 42  | Normal | 20              |
|       | G.2.12     | 14.71 | 28.99 | 130/90 | 48  | <BW   | >20              |
| 51 days| G.1.4      | 27.13 | 17.68 | 140/90 | 44  | Normal | 13              |
|       | G.2.5      | 13.68 | 28.92 | 140/90 | 58  | Normal | 6               |
|       | G.2.6      | 14.11 | 29.70 | 140/90 | 42  | Normal | 20              |
|       | G.2.12     | 29.42 | 32.44 | 140/90 | 48  | <BW   | >20              |
|       | G.2.13     | 21.85 | 21.19 | 160/100| 58  | >BW   | >20              |

Description: G.1: Group I = FD employee, G.2: Group II = scavengers that are active in FD, Pb: Lead, Ca: Calcium, BP: Blood pressure, BW: Body weight

CONFLICTS OF INTEREST

All author have none to declare.

AUTHOR CONTRIBUTION

Pharmaceutical Technology, Pharmaceutics, Novel Drug Delivery, Biopharmaceutics, Pharmacokinetics.

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