Biomarker Of Kidney Function In Electroplating Workers Exposed To Chromium

Katharina Oginawati, Septian Hadi Susetyo, Intan Pratiwi

Abstract: Chromium (Cr) is one of the substances used in the electroplating industry. Continuous exposure to chromium in a long time has the potential to cause renal function impairment. This study aimed to analyze the exposure of inhaled Cr from the electroplating process. This research used the cross-sectional method with The number of respondents of the electroplating workers was 40 people who conducted in three industry electroplating in Indonesia. Each respondent consists of 20 workers from automatic processing in Compony X and 20 workers from manual processing in industry Y (15 respondents) and Z (5 respondents). The Chromium exposure to the worker was measured by a personal sampler pump, which was equipped with a PVC filter, and it was placed on the collar of the worker shirt as a breathing zone. The analysis of Urinary Chromium (UCr) and urinary albumin (UAlb) were carried out using a glass bottle sample of 50 ml. UCr was analyzed using analyzed with Graphite Furnace Atomic Absorption Spectrophotometer (AAS), and UAlb was analyzed using the Immunoturbidimetry method. This study showed 40 samples had concentration values were 0.0031 mg/m3 in the automatic workers and 0.0034 mg/m3 in manual workers. The mean values of UCr were 168.93 µg/g creatinine in the automatic workers and 203.99 µg/g creatinine in the manual workers. While the mean values of UAlb were 7.032 µg/mg creatinine for the automatic workers and 9.52 µg /mg creatinine for the manual workers. Based on the statistic analysis, there were no significant differences between automatic workers and manual workers.

Index Terms: Biomarker, Urinary Chromium, Urinary albumin, Chromium Exposure, Electroplating industry

1. INTRODUCTION

THE Chromium (Cr) is a chemical element with the atomic number of 24 as heavy metals. Chromium is including metal, which has high toxicity. Chromium is widely used in metal plating or electroplating to create a metal surface that is hard and beautiful and prevent corrosion. Chromium used in the electroplating process is chronic acid (H_2CrO_4). The electroplating process will generate a chromium mist from the electroplating bath [1, 2]. Chromium (Cr) on the metal plating has the potency to contaminate the working environment and endanger the health of workers due to exposure to Cr (VI), which is primarily through of inhalation can cause effect such as impairment of respiratory, liver, kidney, and cancer [3, 4]. Inhaled chromium will go into the lungs and the bloodstream or absorbed through the blood, transported to the kidneys, and eventually excreted through the urine [5, 6]. Chromium in blood and urine has been used as a biomarker of environmental exposure [7]. Exposure to chromium can increase chromium concentration in the blood (whole blood, serum, and erythrocytes), urine, hair, and nails. Increased chromium in blood and urine is considered an indicator of the most reliable exposure [7]. Antelmi et al. (2007) state that chromium measurement in urine was measured as urinary chromium (µg/L) [8]. Research of Jyh al. (2002) showed a positive correlation between chromium exposure, inhaled, and chromium concentration in the urine [9]. The levels of chromium noted in urine, plasma, and organs reflect the body burden of chromium. The determination of urine chromium was considered an indicator of chromium exposure [10, 11]. Continuous exposure of chromium in a long time would have the potential to cause health problems in workers. Exposure of inhaled chromium can cause chronic and carcinogenic effects. In urine, the effects of chromium exposure can be measured through the N-acetyl-ß-glucosaminidase (NAG), ß2-microglobulin (ß2M), total protein, and microalbumin [12, 13]. Measurements of chromium levels, total protein, albumin, and retinol-binding chromium exposure [13]. Industry X, Y, and Z are the electroplating industry. The electroplating industry can generate waste containing heavy metals such as Cr, Zn, Cu, Co, and Fe [14]. In industry X the metal plating is done automatically using a machine while in industry Y and Z, metal plating is done manual processes or by hand. In their metal coating process in these industries, there is a chromium plating process. So this research aims to analysis of chromium (Cr) exposure to the electroplating workers who do chrome plating needs to be done to examine the relationship between exposure concentrations of chromium to urinary chromium levels in urine and albumin levels in the urine of workers which is one of the biomarkers for renal function impairment. The results can be used to determine and develop ways to effectively control the hazard of chromium exposure that can impact workers' health.

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2 METHODOLOGY

This research was conducted in three electroplating industries. Industry X Industry Y and industry Z is located in Indonesia. Industry X does the electroplating process using a machine while industry Y and Z do the electroplating process manually.

2.1 Equipment and Materials of Research

When sampling, the equipment includes anemometer, sling psychrometer, personal sampler pump, PVC filter, and container tube of urine. The materials used in the laboratory include concentrated nitric acid (HNO_3 of 65%), nitric acid of 10%, distilled water, perchloric acid ($HClO_4$), acid phosphate, and aquaregia. While the equipment used, include Graphite Furnace Atomic (GF-AAS) and flame Atomic Absorption Spectrometry (FAAS) [15, 16]. Erlenmeyer flask of 100 ml, glass beaker of 100 ml, a funnel of 40 mm, measuring pipette of 10 ml, hotplate with a surface temperature of 140-300º C, a volumetric flask of 10 mL, filter paper, furnace, platinum cup, OHAUS balance, films, and HDPE (High-Density Polyethylene) bottles. Data on the quantitative measurement of urinary albumin were analyzed using Siemens ADVIA 1800 [17].

2.2 Research Stages

This research is an epidemiological study with a cross-sectional method in which the agent (chromium exposure) and the response (UAlb and UCr) investigated simultaneously. Sampling consisted of 40 electroplating workers. The sample was selected adapted to the characteristics or inclusions as follows:

1. It has been working as a minimum of 2 years in electroplating industries
2. Male
3. Age 20-55 years
4. In a healthy state (not in the care of a doctor/taking medicine)

The sample in this study was electroplating workers who did the plating of chromium. The sample was divided into two groups: the first group was workers who did the electroplating process automatically by using machines. The second group was groups of workers who did the electroplating using manual process (by hand). Each group consisted of 20 workers. Information about the respondent's characteristics, the electroplating process, and the solution used, obtained from the questionnaire and interview. Before conducting the inhalation air sampling, it has to be done measurement of physical parameters environment: airspeed, air temperature, and humidity. According to NIOSH (National Institute of Occupational Safety and Health) 7600, issue 2 (1994), air sampling was conducted [18]. The measurement of inhaled chromium exposure was conducted using a personal sampler pump mounted PVC filter with a 5.0-μm and diameter of 37 mm. Measurement of chromium in the filter of sampling results was done using flame AAS. Inhaled chromium concentration obtained from laboratory analysis results is then calculated to determine the concentration for 8 hours. The calculation is performed by the guidelines IRRST (2013) for sampling less than 8 hours (less than fill-shift sampling). The chromium concentration can be calculated by Equation 1 below [19,].

$$\mathrm{C\ (8\ hours)} = \frac{[(480 - \mathrm{X})\ \mathrm{X}\ \mathrm{C}] + (\mathrm{x} \times 0)}{480\ \mathrm{minutes}} \qquad (\textbf{Equation 1})$$

Where C (8 hours) that the concentration of chemical exposure on workers who worked for 8 hours (mg/m3), C is the Cr concentration of results of laboratory analysis (mg/m3), and x is time less than 8 hours (minutes). After the concentration of Cr for 8 hours is gotten, it needs to be calculated exposure dose in the form of Chronic Daily Intake (CDI), which enters workers' body. CDI is calculated by Equation 2 [20, 21].

$$\mathrm{CDI} = \frac{\mathrm{C} \times \mathrm{IR} \times \mathrm{ET} \times \mathrm{EF} \times \mathrm{ED}}{\mathrm{BW} \times \mathrm{lifetime} \times \mathrm{AT}} \qquad (\textbf{Equation 2})$$

Where CDI is Chronic Daily Intake (mg/kg-day), C is Exposure Concentration (mg/ m3), IR is Inhalation Rate, 20 m3/day [6], ET is Exposure Time (hours/day), EF is Exposure Frequency (days/year), ED is Exposure Duration (years), BW is the Body Weight (kg), the AT is Averaging time (365 days/year). The long lifetime is 70 years, based on the average age of humans. After calculating CDI, the next step is the Hazard Index calculation to determine whether exposure to chromium is at risk of having harmful effects to humans exposed. HI, value is obtained by calculating the Hazard Quotient in advance, using Equation 3 [22].

$$\mathrm{HQ} = \frac{\mathrm{CDI}}{\mathrm{RfD}} \qquad (\textbf{Equation 3})$$

HQ is a Hazard Quotient, and RfD is chromium with a Reference Dose value in mg/kg- (ATSDR, 2012). In this study, HQ calculation is only done for chromium day exposure than the HI value = HQ. If HI > 1, then the dose of inhaled chromium has a risk to endanger human health, but if HI ≤ 1, then the dose of inhaled chromium is not harmful to human health [22]. Urine sampling was done at the end of the working shift (end of shift) amount of 30 ml. UCr examination was based on NIOSH 8310 issue 2 (1994). Urine extraction was conducted using GF-AAS. The Immunoturbidimetrimethod carried out UAlb examination. UAlb is examined while quantitative urinary albumin. Examination of UAlb level using a Siemens ADVIA 1800 [23]. The data of this study were analyzed and interpreted to hypothesis test using a statistical test. Statistical analysis was done in this study include the equivalence test of respondents with t-test, descriptive analysis, bivariate correlation test, logistic regression, and multivariate analysis—statistical analysis aided by using Statistical Product and Service Solutions (SPSS) series of 16.

3 RESULTS AND DISCUSSION

3.1 Working Environment Climate Measurement

The working climate results from a combination of temperature, humidity, air movement speed, and heat radiation from his worker [24]. Measurement of physical parameters of the environment carried out in each location of sampling of inhalation air both automatic workers group and manual workers group. Parameters measured include temperature, humidity, direction, and speed of air. Measurement of workplace climate was conducted to analyze the climatic conditions of work and calculate inhaled chromium concentration. The measurement results can be seen in Table 1 below.

Tabel 1. *Environmental physical parameter in research location*

Physical Parameter	Sampling Location		TLV*
	Worker Group (Automatic)	Worker Group (Manual)	
Temperature (ºC)	25,4±2,1	27,2±2,5	18-30
Humidity (%)	54,8±3,2	56,9±12,2	65-95
Air Speed (m/s)	0	0	0,15-0,25

*)KepMenKes No.1405/MENKES/SK/XI/2002

Based on data of measurement of physical environmental parameters in Table 1 above, shows that the air temperature both of groups still meet the TLV, while the air humidity parameter for both groups was below the range of TLV. The parameter of airspeed in the working environment in both groups was below the range of TLV. TLV reference taken for this based on Annex II requirements of the industry's workplace health, Kepmenkes No.1405/Menkes/SK/XI/2002

[25]. Statistical analysis of Mann Whitney unpaired t-test showed no significant differences between the working climate in the automatic worker's group and manual workers group.

3.2 Characteristics of Respondents

Respondents used as research objects were electroplating workers (automatic) and electroplating workers (manual). The respondent's equivalence test was conducted to determine automatic workers' equivalence and manual workers' various attributes. If the results of the statistical test (Mann-Whitney unpaired t-test) demonstrated the p-value <0.05, then the automatic electroplating workers and manual electroplating workers significantly different (unequal). Based on the statistical analysis results with the Mann-Whitney t-test was obtained p-value <0.05 to attributes of age, body mass index (BMI), working period, education, water consumption, and the consumption of milk and use of gloves. To attribute the exercise, smoking, consumption of fruit, vegetable consumption, use of masks, and a history of illness, the results of statistical analysis Mann-Whitney t-test showed that the value of p-value > 0.05, which means that the average value of these attributes was not significantly different (equivalent).

3.3 The Concentration of Inhaled Chromium

Inhaled chromium concentration was calculated based on the guidelines IRRST (2013) for sampling less than 8 hours (less than fill-shift) than the TLV of chromium for 8 hours/day 40 hours/week. TLV value of Cr based on Surat Edaran Menteri Tenaga Kerja Nomor: SE01/MENAKER/1997 is 0.05 mg/m3. TLV-TWA value Cr6+ by ACGIH (2010) is 0.05 mg/m3 and according to OSHA is 0.1 mg/m3 Cr6+ as CrO3. All samples, both automatic workers or manuals worker, had inhaled chromium concentration below the TLV of MENAKER and ACGIH [26, 27]. The chromium concentration in automatic workers was in the range of 0.0020 - 0.0050 mg/m3, with a mean value of 0.0031 ± 0.0008 mg/m3. The chromium concentration in manual workers was in the range of 0.0019 - 0.0053 mg/m3, with a mean value of 0.0034 ± 0.0009. Based on a statistical analysis of the Mann Whitney unpaired t-test, the p-value for the chromium concentration parameter was 0.176 (p-value > 0.05). The p-value indicated that the two groups' mean of chromium concentration was not significantly different (equivalent). The results of other studies indicate that the concentration of chromium (Cr 6+) in the electroplating industry is in the range of 0.0001-0.01 mg / m3 [28], 0.140 µg / m3 (Kuo et al., 1997) and 0.34-14 µg / m3 [9]. Chromium exposure can be influenced by physical environmental factors such as temperature and humidity as well as the presence of assistive devices that function as prevention of exposure to workers such as LEV (local exhortation ventilation) so that the concentration of exposure to workers is reduced [28]. There is a correlation with several references related to the same concentration of Cr exposure. Still, in Industry X, Y and Z are included in low Cr exposure, this is likely to be influenced by the work environment and the presence of LEV, thus reducing Cr exposure in workers.

3.4 Chronic Daily Intake (CDI) of Chromium

Chromium exposure may cause chronic effects, so it is necessary to find the value of CDI intake. CDI value for electroplating workers (automatic) was in the range of 0.0000155-0.000102 mg/kg-day with mean value of 0,0000588 ± 0.0000255 mg/kg-day, while electroplating workers group (manual) CDI values were in the range of 0.00000403-0.0000038 mg/kg-day with a mean value 0.0000269 ± 0.0000202 mg/kg-day. Statistical analysis by unpaired t-test showed that the p-value for CDI value in automatic workers group and manual worker groups was 0.000 (p-value <0.05). The p-value indicated that the two groups' CDI's mean value was significantly different (unequal). CDI values depend on the working period or exposure

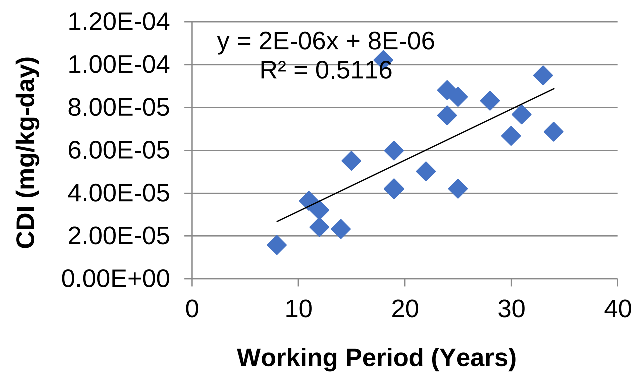


Figure 1a. Automatic workers

duration. The relationship between the working period and CDI value in electroplating workers (automatic) and electroplating workers (manual) can be seen in Figure 1a and 1b.

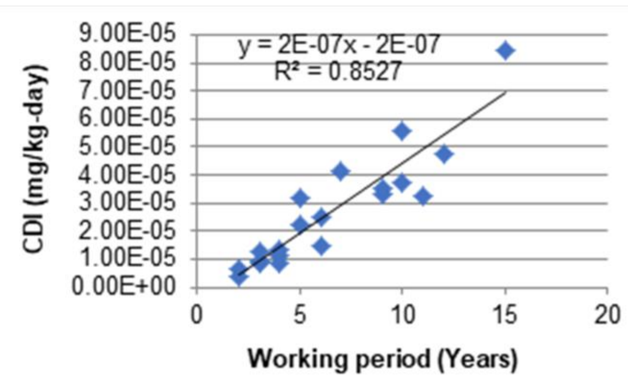


Figure 1b. Manual Workers

***Figure 1a** and 1b. Effect of working period to CDI*

The linear graphic in Figure 1 showed a positive relationship between the working period and the CDI. Spearman correlation test also showed the p-value of 0.002 ($p < 0.05$) in the automatic worker's group and the p-value of 0.000 ($p < 0.05$) in the manual worker's group, which means that there was a significant relationship between working period and CDI.

3.5 Evaluation of Chromium Exposure Dose to The Body Response

According to the Biological Exposure Indices standards set by ACGIH (2005), one of the indicators used to detect chromium exposure in humans is chromium levels in urine. BEI issued standards for chromium in urine (UCr) is ten µg/g creatinine at the end of the work (end of shift) and 25 µg/g creatinine at the end of the working day at the end of the week (end of a shift, end of the workweek). The value of urinary chromium (UCr) in each sample exceeded BEI value (10 µg/g creatinine). UCr value had variation from 30.26 to 790.21 µg/g creatinine in the automatic worker's group and 42.65 to 792.45 µg/g creatinine in the manual worker's group. The mean value of UCr in the automatic worker's group was 168.93 ± 190.43 µg/g creatinine, whereas the mean value of UCr in the manual worker's group was 203.99 ± 198.31 µg/g creatinine. The statistical test of the unpaired t-test showed a p-value of 0.267 (p> 0,05). It showed that the mean value of UCr in both groups was not significantly different (equivalent). The level of albumin in humans is one indicator to determine the presence of renal function impairment symptoms. The urinary microalbumin (mAlb) level has been used to evaluate renal's glomerular functions [13, 29, 34]. The urinary microalbumin excretion was also a functional predictor of glomerular [35, 36]. A screening for mAlb was even reported to predict the specific morphologic type of glomerular disease [30]. According to Consensus in Diabetes Mellitus 2011, albumin level in normal human urine is < 30 µg/mg creatinine. Urine samples from 20 automatic workers showed one urine sample with UAlb value (urinary albumin) exceeded the TLV of UAlb. Whereas in the manual worker's group, two urine samples had value exceeded TLV of UAlb. The range of automatic group albumin levels was 0 - 60.58 µg/mg creatinine, with an average of 7.032 ± 13.01 µg/mg creatinine. The range was from 0 to 78.18 µg/mg creatinine in the manual group with a mean value of 10.22 ± 18.09 µg/mg creatinine. Based on statistical analysis, Mann Whitney unpaired t-test, a p-value obtained by 0.8600 (p > 0.05), it means that the mean of UAlb value of two groups was not significantly different (equivalent). The urinary mAlb level did not significantly elevate in the chronic and low-level occupational Cr-exposed workers [30]. The cumulative Cr exposed is based on personal Cr exposure concentration and exposure duration. The workers' cumulative dose can only be calculated based on currently available data because of lacking the exposure's history record. The worker's Cr exposure may be different year by year over the period exposure. The cumulative dose for each subject may not be accurately calculated. It could be a reason why there was no significant correlation between the cumulative doses of Cr and kidney injury biomarkers [30]. The summary data is shown in Table 2.

Tabel 2.*Summary of research data*

Parameters	Automatic (n=20)	Manual (n=20)	p-value
	Mean	Mean	
Cr Concentration (mg/m^3)	3.10E^{-3}± 8,0E^{-4}	3.4E^{-4}± 9.0 E^{-4}	0.262
CDI (mg/kg-day)	5.88E^{-5}± 2.55E^{-5}	2.69E^{-5} ± 2,02E^{-5}	0.000
UCr (µg/g creatinine)	168.93 ± 190.43	203.,99 ± 198.31	0.267
UAlb (µg/mg creatinine)	7.032 ± 13,01	9.52 ± 18,09	0.860

According to the EPA (2015), when the dose increases, the response also increases [31]. Chromium intake contributes to the increasing level of chromium in the urine. The relationship of chromium intake by inhalation and UCr (urinary chromium) can be seen in Figure 2a and 2b. The relationship between inhaled chromium intake and UAlb (urinary albumin) can be seen in Figure 3.

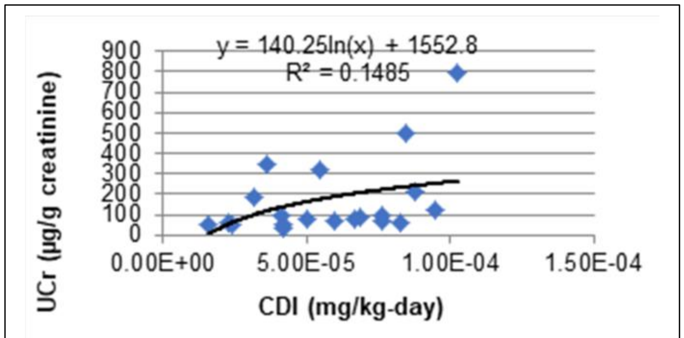


Figure 2a Automatic

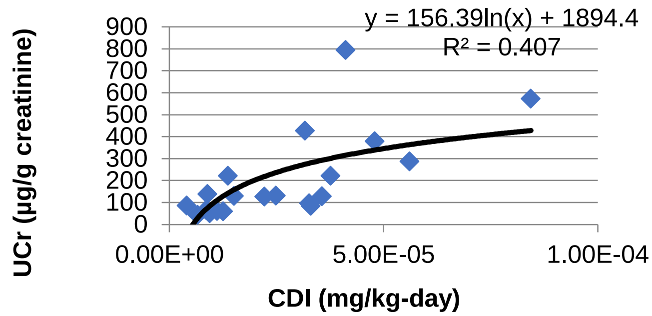


Figure 2b Manual

Figure 2a and *2b. Effect of intake chromium value to UCr response*

Figure 2 above shows that the R2 value of 0.154 in the automatic worker's group and R2 value of 0.407 in the manual worker's group means a correlation between CDI and UCr. Statistical analysis of Spearman bivariate correlation between CDI and UCr showed the p-value of 0.012 (p < 0.05) in the automatic group and the p-value of 0.000 (p < 0.05) in the manual group, it showed that there was a significant relationship between CDI and UCr.

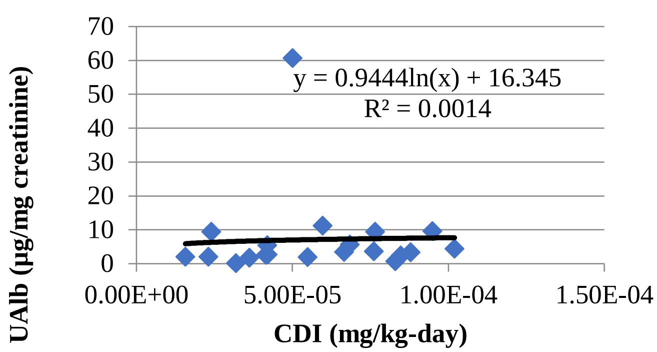


Figure 3a. Automatic

Figure 3a and *3b. Effect of intake chromium value to UAlb response*

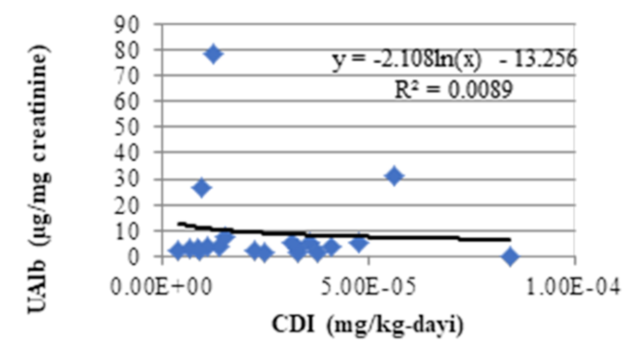


Figure 3b. Manual

Based on Figure 3 above, the R2 value of 0.0008 in the automatic worker's group and R2 value of 0.0089 in the manual worker's group means no relationship between CDI and UAlb. Statistical analysis of Spearman bivariate correlation between CDI and UAlb showed the p-value of 0.332 ($p > 0.05$) in the automatic group and p-value of 0.885 ($p > 0.05$) in the manual group, it showed that there is no relationship significantly between CDI and UAlb.

3.6 Hazard Index

Calculation of Hazard Index (HI) was done to determine whether the chromium substances in the body due to chromium exposure to electroplating workers in the workplace pose a risk in the form of non-carcinogenic effect or not. HI, the value of chromium exposure can be seen in Figure 4.

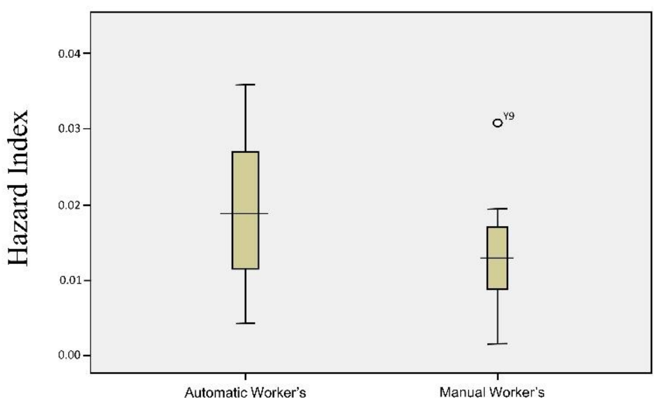
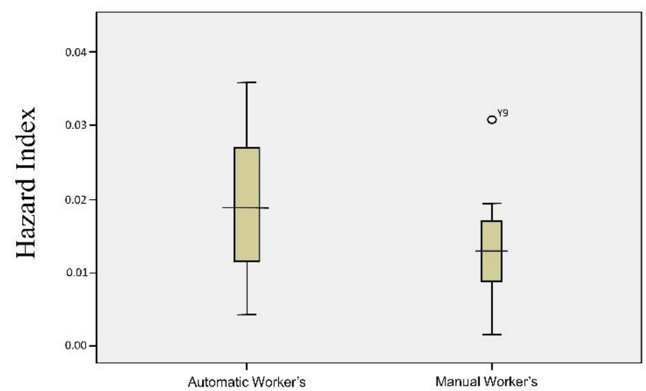


***Figure 4**. Hazard index*

The boxplot chart above showed the difference between the automatic worker's group and the manual worker's group. Statistical analysis of Mann Whitney unpaired t-test showed a p-value of 0.000 ($p < 0.05$), which means the mean value of HI both groups had a significant difference. HI, range in the automatic worker's group was 0.0052 - 0.034 with a mean value of 0.01966 ± 0.0085, and the HI range in the manual worker's group was 0.0013 - 0.028 with a mean value of 0.00904 ± 0.00678. Automatic workers have a higher HI value than manual workers. This can be influenced by work culture, where disciplined manual workers use PPE well. Workers who are directly involved with the electroplating process are given special clothes and complete PPE before carrying out the work process. Likewise, the electroplating process chamber is designed with good airflow, there are many hoods of the LEV (local exhaust ventilation) that are placed to suck the concentration of the resulting chemical. So that with adequate treatment can reduce Cr exposure in workers [32, 33]. All respondents between automatic and manual groups had a value of HI < 1, which means that the dose of chromium will not the risk of non-carcinogenic effects for human health. However, if the chromium exposure combined with other heavy metals exposure is also contained in the electroplating solution such as Ni, Zn, and others, then the HI value will increase and give the effect of non-carcinogenic, which endanger the health of workers.

4. CONCLUSION

The mean value of inhaled chromium concentration in the automatic electroplating workers group was 0.0031 mg/m3, while the mean value in the manual electroplating workers group was 0.0034 mg/m3. All respondents had chromium concentration below the TLV by the MENAKER and ACGIH. UCr concentration values for all respondents exceeded the BEI ACGIH standards. The mean value of UCr in the automatic group was 168.93 µg/g creatinine, while the mean value of UCr in the manual group was 203.99 µg/g creatinine. CDI's mean value in the automatic electroplating workers group was 0.0000588 mg/kg-day, while the mean value of CDI in the manual electroplating workers group was 0.0000269 mg/kg-day. The mean values of UAlb concentration were 7.032 µg/mg creatinine for the automatic group and 9.52 µg/mg creatinine for the manual group. In the automatic group, one respondent had UAlb value exceeded the TLV, while in the manual group, two respondents had UAlb value exceeded the TLV. Spearman correlation analysis showed a significant relationship between exposure dose of Cr and UCr response,



but there was no significant relationship between exposure dose of Cr and UAlb . The mean values of HI were 0.020 for the automatic group and 0.009 for the manual group. All respondents, both the automatic and manual groups, had a value of HI < 1. It means that the inhaled chromium dose has not given the risk of a non-carcinogenic effect on workers' health.

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