Relation Of Concentration And Risk Characterization Of Toluene With Malondialdehyde Cholesterol And Diabetes

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Abstract

Toluene is an organic compound which has high volatile property at room temperature and widely used as a solvent. Considering the side effects of toluene exposure in long term for humans which people may experience hepatotoxic effect. This study aims to determine the relationship between the concentration and characteristics of toluene with malondialdehyde, cholesterol and diabetes in five selected industry in Surabaya which uses toluene as an organic solvent in their industry. This is an observational study with cross sectional design conducted at 5 industry in Surabaya. The selected industry are Osowilangun, Ketintang, Jemursari, Kalijudan and AUP. The population in this study were all workers exposed to toluene in the industry which is 90 of them in total. The research sample of 77 people was taken using the accidental sampling method. The variables studied in this research are Risk Qoutient, Toluene concentration, level of cholesterol, diabetes and malondialdehyde. No correlation exist between toluene concentration and cholesterol ($p>1.0$) and diabetes ($p> 0.25$). Significant correlation is seen between toluene concentration and malondialdehyde (MDA) ($p<0.03$). **Conclusion:** High level of toluene concentration doesn't affect cholesterol and diabetes level. The level of malondialdehyde in RBC greatly influenced by the level of toluene exposure.

Keyword: RQ Toluene, Toluene concentration, Diabetes, Cholesterol, Malondialdehyde

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Introduction

Concentration of toluene in industry is higher than the threshold limit. Based on the research conducted by WHO in 2000, toluene ingestion approaches 780 ppm during routine work whereas 270 ppm during strenuous work. According to WHO, the accepted threshold limit for toluene is 1 mg/m3 for 30 minutes in an average range (WHO., 2000). Environmental fact sheet in 2005 reported that the lowest range of threshold limit for toluene in water is 0.04 parts per million (ppm) whereas in air is 8ppm (Environmental fact sheet. 2005). On the contrary, GEUS confirmed that 209 out of 908 underground water contains toluene which is breached the requirement of drinking water. (GEUS. 2013). It has been confirmed that, there is abnormalities occurs particularly in kids and pregnant ladies as a consequence of high level inhalation of toluene (Larsen et. al., 2016).

Inhalation of toluene above the limit range affects the cholesterol present in the human body. Based on the research conducted by Environmental Protection Agency high inhalation of toluene causes alteration in the membrane fluidity due to the solvent particles that exist in between the cholesterol contained interstices particularly in sphingolipids and phospholipids. This in turn leads to changes in normal interaction between cells and normal ion motions in the body (EPA. 2005). This statement supported by Unger et. al., in 1994 who stated that the hypo intensity can be attributable to the division of toluene into the lipid membranes of cells in a cerebral tissue (Unger et. al., 1994). On the other hand, a previous research conducted on toluene which oppose this statement indicates that there is no any correlation between toluene exposure and cholesterol level (Toluene. 2008).

Apart from that, high level of ingestion of toluene correlates with diabetes. This statement supported by Journal of Diabetes Research in 2016 as they confirmed that resistance towards insulin is greater in those consuming products containing monocyclic aromatic hydrocarbons (MAH). Monocyclic aromatic hydrocarbons inclusive of 3 main components which is namely toluene, xylene and styrene (Pressinger, R., 2016). This further supported by Airaksinen et. al., (2011) who conducted research on association between type 2 diabetes and exposure to persistent organic pollutants. He revealed that there is high possibility for to get diabetes if there is continuous exposure to organic pollutants for a longer period. In this case, a C-PCB 128 of toluene liquid was used as recovery standard (Airaksinen et. al., 2011).

On top of that, inhalation of toluene does increase malondialdehyde, a free radicals or commonly known as marker for oxidative stress. This statement supported by the Stajkovic et.al. In 2008 in the journal of Serbian Chemical Society. From her research, she concluded that toluene generally increases malondialdehyde in RBC in groups that has received toluene treatment intraperitoneally compared to group that has been controlled (Stajkovic et. al., 2008). This statement further clarified by Omur et. al., in 2016 who examines the oxidative stress among employee due to toluene exposure. In his study, he measured the intensity of malondialdehyde in the lipid peroxidation and carbonyl protein (PCO) test for protein oxidation (Omur et. al., 2016).

Based on the paragraph, there is no information on the relation of toluene concentration and risk characterization of toluene with malondialdehyde, cholesterol and diabetes in Indonesia especially in painting industry, motor workshops and shoe industry. There is research conducted in IRIS submission desk in the year of 2005, Korea occupational safety and health agency at Incheon, Korea in the year of 2011, Helsinki in the year of 1934 till 1944 and at Turkey in the year of 2016.

In this article, I will write about relation of concentration and risk characterization of toluene with malondialdehyde cholesterol and diabetes in industry exposed with toluene in Indonesia particularly in painting industry, motor workshop and shoe industry. The aim of this research is to describe and analyse the relation of concentration and risk characterization of toluene with malondialdehyde cholesterol and diabetes. The function of this research is to provide information to employee to prevent disease such as diabetes and cholesterol induced by toluene.

Method

This is a descriptive research with a cross sectional study design. This research was conducted at five different location at Surabaya. The location includes Ketintang, Jemursari, Airlangga University Press, and Kalijudan and

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show industry at Osowilagun. The study population varies among the location as follows. There was 12 respondent from Ketintang, 10 respondent from Jemursari, 11 respondent from Airlannga University press, 20 respondent from Kalijudan and 24 respondent from Osowilagun. The study population inclusive of all employee of the respective industry mentioned above. Research sample was obtained by accidental sampling method until it reaches 77 respondent. The variables of this research study can be divided into two, namely concentration and risk characterization of toluene as the independent variables whereas malondialdehyde, cholesterol and diabetes being the dependent variable.

The measurement of toluene concentration in the air done using vacuum and tube filled with active charcoal. This task was done by officers from laboratory unit of occupational safety health, Surabaya. Meanwhile, toluene concentration in the working environment done by Cincinnati in 1997 method by using activated carbon absorber which utilize gas chromatography. The intake of toluene dose was measured by determining the risk agent of toluene dose by using the following equation. I=C x R x tE x Dt / Wb x tavg. Measurement of non-carcinogenic toluene (Risk Qoutient (RQ)) was done by comparing intake (nk) and reference value (RfD or RfC). Data collection mainly was done by measuring toluene concentration whereas the effects was studied by distributing questionnaires and by conducting observation in the above mentioned location.

MDA was measured by modified spectrophotometric and GSH method of thiobarbituric acid (TBA) test (Tualeka et. al., 2019). A maximum of 400 µl of the specimen was exposed to 20 percent deprotein with 200 µl of trichloroacetic acid (TCA). Then it was centrifuged for 10 minutes at a rate of 5000 rpm. This extracted the supernatant and 0.67% of 400 µl TBA was added. The specimen was then vortexed and incubated at 96 ° C in a water heater, for 10 minutes. The absorption was read at 530nm of wavelength. While cholesterol level and blood glucose was measured by obtained venous blood which is then sent to laboratory for lipid profile and fasting blood glucose result.

Result And Discussion

Frequency Distribution of Respondent's Characteristics of toluene exposed Industry in Surabaya

Based on the research conducted, respondent's demographic profile was obtained. This includes the information such as age, sex, level of education and working area. The table below shows the characteristics of respondents who works in shoe industry at Surabaya.

Table 1. Frequency distribution of employee's characteristics who exposed to toluene in five industry in Surabaya

Respondent Characteristics	Frequency	Percentage
Age		
16-25	15	19.5%
26-35	13	16.8%
36-45	24	31.2%
46-55	16	20.8%
56-65	9	11.7%
Sex		
Male	61	79.2%
Female	16	20.8%
Level of education		
SD	14	18.2%
SMP	19	24.7%
SMA/SMK	43	55.8%
PT	1	1.3%
Workplace		
Osowilangun	24	31.2%
Ketintang	12	15.6%
Jemursari	10	13.0%
Kalijudan	20	26.0%
AUP	11	14.3%

Source: Primary Data

Based on table 1, it is known that the majority of industrial workers age ranges from 36 to 45 which includes a total of 24 (31.2%) people out of 77 people. In addition, the majority sex of workers are male which is 61 (79.2%) employee in total. Most of the employees have obtained a high school / vocational education level which inclusive of 43 (55.8%) of the total workers. Most of the respondent works at Osowilagun region as this included 24 (31.1%) people out of total workers.

Toluene Concentration

Table 2. Frequency Distribution of toluene concentration in five industry in Surabaya

Workplace	Measurement Point	Toluene concentration (NAB= 20 ppm)	
		< NAB	≥ NAB
Ketintang	Point 1	2.15 ppm	
	Point 2	0.42 ppm	
	Point 3	0.30 ppm	
Jemursari	Point 4	2.99 ppm	
	Point 5		40.27 ppm
	Point 6	1.91ppm	
AUP	Point 7	0.99 ppm	
	Point 8	0.04 ppm	
	Point 9	0.003 ppm	
Kalijudan	Point 10	0.43 ppm	
	Point 11		33.89 ppm
	Point 12		38.38 ppm
Osowilangun	Point 13		289.3 ppm
	Point 14		30.5 ppm
	Point 15		62.7 ppm
	Point 16		58.5 ppm
	Point 17	15 ppm	
	Point 18		137.5 ppm
	Point 19	9.3 ppm	

Source: Primary Data

Based on table 2, it is known that the largest concentration of toluene in the air is at point 13 with a value of 289.3 ppm and the lowest at point 9 with a value of 0.003 ppm with an average value of the measurement of toluene concentration of 32.9 ppm. Based on the measurement point, it is known that there are 8 measurement points that have toluene levels above the NAB issued by ACGIH (2011) which is 20 ppm and there are 11 measurement points that have toluene levels below the NAB. The average results of air toluene levels were below the NAB that was set by ACGIH (2011).

Table 3. Distribution of toluene concentration among employees in five Industry in Surabaya

Toluene Concentration	Total	
	N	%
>20 ppm	37	48
≤20 ppm	40	52
Total	77	100

Based on table 3, there are 37 respondents (48%) who are being exposed to toluene concentrations above the value issued by the American Conference of Governmental Industrial Hygienists (ACGIH) in 2007 which is 20 ppm, while 40 respondents (52%) are at concentrations below 20 ppm.

Non carcinogenic Risk

Table 4. Frequency distribution of risk characterization of Toluene towards employee in five Industry in Surabaya

Risk Characteristics	Total	
	N	%
Not Safe (≥1)	50	65
Safe (<1)	27	35
Total	77	100

Health risk characteristics are stated as Risk Quotient (RQ, Risk Level) calculated by dividing the intake (Ink) with reference (RfC). The calculation results of Risk Quotients (RQ) can show the level of health risk for workers due to exposure toluene in the work environment. If the RQ value is more than or equal to 1 (RQ> 1) it indicates that workers exposed to toluene and might encounter health risks due to toluene exposure. On the contrary, if the RQ value is less than 1 (RQ <1), it indicates that workers are safe from health risks although exposed to toluene (Kolluru. 1996). Based on the RQ calculation in

table 4, the results show that the majority of workers which is 50 (65%) out of 77 employee have an RQ value> 1. This indicates that the employee will facing negative impact on health due to toluene exposure.

Table 5. Frequency Distribution of cholesterol among employee exposed to toluene in five industry

Cholesterol Level	Total	
	N	%
>200 mg/dL	28	36
≤200 mg/dL	49	64
Total	77	100

Based on table 5, it shows that only 28 (36%) people out of 77 suffers from high cholesterol which is above 200mg/dL, whereas the majority of the employee which is another 49 (64%) of them are free from high level of cholesterol. In other words, there are having cholesterol level lesser than 200mg/dL.

Table 6. Frequency Distribution of diabetes among employee exposed to toluene in five industry

Glucose Level	Total	
	N	%
>110 mg/dL	11	14
60-110 mg/dL	66	86
Total	77	100

Based on table 6, it shows that only 11(14%) workers out of the total employees (77 workers) are having high level of glucose which is above 110mg/dL. The rest of the workers, which is 66 (86%) of them having a normal range of glucose level in blood which is between the range of 60 to 110 mg/dL.

Table 7. Frequency Distribution of MDA (µm) among employee exposed to toluene in five industry

MDA	Total	
		%
> 4.65µm	74	96
2.02-4.65µm	3	4
Total	77	100

Based on table 7, it shows that about 96% of the total employees having a very high level of malondialdehyde which is about 74 of the workers out of 77 workers. Meanwhile, only 3 of the workers which is equivalent to 4% of the total employee are in the safe zone in which they are having a normal range of malondialdehyde (<2.6 2.61 µmol/L).

Table 8. Relationship between toluene concentration and cholesterol

Toluene concentration	Cholesterol level				Total		Prevalence Ratio
	Abnormal		Normal				
>20 ppm	18	37%	31	63%	49	100%	1.03
< 20 ppm	10	36%	18	64%	28	100%	
Total	28	36%	49	64%	77	100%	

Based on the table 8, it shows that majority employees (63%) that has been exposed to high level of toluene concentration which is above NAB (>20ppm) having a cholesterol level within normal range. Meanwhile, majority workers (18%) that has been exposed to toluene concentration below NAB (<20ppm) shows cholesterol level within normal range in their body. Statistical analysis shows a prevalence ratio of 1.03. This means there is high risk to get cholesterol due to toluene exposure.

Table 9. Relationship between toluene concentration and diabetes

Toluene concentration	Glucose level				Total		Prevalence Ratio
	Abnormal		Normal				
>20 ppm	9	18%	40	82%	49	100%	2.57
< 20 ppm	2	7%	26	93%	28	100%	
Total	11	14%	66	86%	77	100%	

Based on table 9, it shows that majority of the workers that inhaling high level of toluene concentration (>20ppm) which is 82% of the workers having a normal glucose level in the body whereas 18% of the employee shows a high level of glucose in the body. On the contrary, 93% of the workers having a glucose level within range and 7% of the workers having a high level of glucose although has been exposed to a low level of toluene concentration (<20ppm). Statistical analysis shows a prevalence ratio of 2.57 indicating high risk to get diabetes due to toluene exposure.

Table 10. Relationship between toluene concentration and malondialdehyde

Toluene concentration	Malondialdehyde				Total		Prevalence Ratio
	Abnormal		Normal				
>20 ppm	48	98%	1	2%	49	100%	1.01
< 20 ppm	27	96%	1	4%	28	100%	
Total	75	97%	2	3%	77	100%	

Based on table 10, 2% of the employee shows a malondialdehyde within normal range while the rest of 98% shows a high level of malondi-aldehyde although has been exposed to high level of toluene concentration in the industry. Meanwhile, 4% of the workers shows malondiadehyde within normal range whereas 97% shows high level of malondialdehyde although all of them are being exposed to low level of toluene concentration in the industry. Statistical analysis Pearson correlation test shows a prevalence ratio of 1.01 indicating there is high risk of toluene exposure that leads to increase of malondialdehyde.

Table 11. Relationship between malondialdehyde and cholesterol

Malondialdehyde	Cholesterol				Total		P- Value
	Abnormal		Normal				
>2.6 µmol	28	36%	49	64%	77	100%	0.02
< 2.6 µmol	0	0%	0	0%	0	0%	
Total	28	36%	49	64%	77	100%	

Based on table 11, 28 (36%) of the employee is having an abnormal cholesterol level whereas 49 (64%) of the employee having a cholesterol level within normal range although being exposed to high level of toluene. The Pearson correlation test shows a value of 0.02 (<0.05), indicating there is a significant correlation exist between MDA level and cholesterol in the body.

Table 12. Relationship between malondialdehyde and diabetes

Malondialdehyde	Diabetes				Total		P-Value
	Abnormal		Normal				
>2.6 µmol	11	14%	66	86%	77	100%	0.75
< 2.6 µmol	0	0%	0	0%	0	0%	
Total	11	14%	66	86%	77	100%	

Based on table 12, it shows that 11 of the employees which is 14% is having a high glucose level whereas 66 (86%) of the workers showing a glucose level within normal range although being exposed to high level of toluene. Statistical analysis of Pearson correlation test shows a P-value of 0.75 (>0.05), indicating there is no correlation exist between MDA and diabetes.

Discussion

Based on the result obtained on toluene concentrations in five locations of industry that uses toluene as organic solvents in Surabaya, it is known that the highest toluene concen-trations observed at Osowilangun area which is 289.3 ppm and the lowest concentration observed at AUP area which is 0.0036 ppm with an average of 32.98 ppm concentration of toluene. From the results there are 8 measurement points that have toluene concentration level above the NAB as indicated by ACGIH in 2011 which is above 20 ppm. Meanwhile, there are 11 measurement points that have toluene low toluene concentration (<20ppm).The obtained average results of air toluene concentration levels are also above the NAB levels set by ACGIH in the year 2011. The obtained results are classified as in high level when compared with the results of Agustina's research (Agustina. 2016) which shows the concentration of toluene in car painting industry which ranges from 0.0019 ppm to 18.5726 ppm.

This results also shows a very high intensity of toluene concentration on the air compared to the results of Badjagbo et. al., (2010) obtained who showed toluene concentration of 0.2927 ppm in the air (Badjabo et. al., 2010).

Based on the results, it shows that there is risk of increase of cholesterol due to exposure of toluene concentration in industry as the prevalence ratio shows 1.03 (> 1.0). This statement supported by Kaukiainen et. al., in 2004, states that cholesterol level in body greatly influenced by exposure to hazardous chemicals such as toluene. This statement further supported by Savolainen et. al., in 1990 who confirmed that exposure to toluene activates cytochrome P-450 isoenzymes 2B1/2 and 2E1/2 which influences the cholesterol metabolism (Savolainen et. al., 1990).

On top of that, results obtained shows that there is a high risk of getting diabetes due to toluene exposure. This results supported by Crossin et. al., in 2019 who noticed an alteration in glycemic control due to toluene induced metabolic dysfunction. According to the researchers, employees that is being exposed to toluene tend to have high glucose level compared to controlled group (Crossin et. al., 2019). Airaksinen et. al., in 2011 proved that long term exposure to toluene increases the risk of getting diabetes which correlates with the results obtained in this study.

Furthermore, the results obtained in this shows that there is a significant correlation exist between toluene concentration and the level of malondialdehyde which shows a prevalence ratio of 1.01. This statement supported by Halifeoglu et. al., in 2000, who observed high amount of malondialdehyde among 18 employees of paint thinner industry compared to the control groups (Halifeoglu et. al., 2000). This results further supported by Stajkovic et. al., (2009) who stated that a small concentration of toluene can greatly increase malondialdehyde level in RBC based on the results obtained on toluene treated on ROS rats (Stajkovic et. al., 2009). Coskun et al., in 2006 study results correlates with this statement as well as he observed significant increase of malondi-aldehyde on toluene exposed rats sciatic nerve (Coskun et. al., 2006).

Conclusion

There are 8 measurement points at work sites with toluene concentration above the NAB and 11 measurement points with toluene concentration below the NAB indicated by ACGIH (2011) (NAB = 20ppm). Majority of the workers are in the zone of low toluene concentration (<20ppm) which is 52% of the total workers. Majority of the employee which is 65% is being exposed to unsafe Risk Qoutient (RQ). Majority of the employee having cholesterol level within range which is 31 employee out of total workers. Majority of the working having glucose level within range which is 40 workers out of total employee. Those workers that has been exposed to high level of toluene have significant increase in malondialdehyde in their erythrocytes. There is correlation exist between toluene concentration and cholesterol (p>1.0). There is no correlation between toluene concentration and diabetes (p>0.25). Significant relation was observed between toluene exposed industry workers with increased level of malondialdehyde in erythrocytes.

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