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Relationship Of Concentration And Risk Quotient (RQ) Of Benzene, Toluene And Xylene (BTX) With Malondialdehyde (MDA) Levels And Neurotoxic Risk In Workers Exposed To BTX In Surabaya

Abdul Rohim Tualeka[1], Juliana Jalaludin[2], Retno Adriyani [3] , Syamsiar S Russeng[4], Pudji Rahmawati[5], Ahsan Ahsan[6], Indri H Susilowati[7], , Rasmaliah[8], Suwardi[9], Laela Agrista Devilia[10]

[1]Department of Occupational Health and Safety, Faculty of Public Health, Airlangga University, 60115, Surabaya, East Java, Indonesia; abdul-r-t@fkm.unair.ac.id
[2]Department of Environmental and Occupational Health, Faculty of Medicine and Health Sciences, Putra Malaysia University, Malaysia; [1]Department of Occupational Health and Safety, Faculty of Public Health, Airlangga University, 60115, Surabaya, East Java, Indonesia,juliana@upm.edu.my,
[3]Department of Environmental Health, Faculty of Public Health, Airlangga University, 60115, Surabaya, East Java, Indonesia; retnoadriyani@fkm.unair.ac.id
[4]Department of Occupational Health and Safety, Faculty of Public Health, Hasanuddin University, Makassar, Indonesia; syamsiarsr@yahoo.co.id
[5]Department of Development of Islamic Society, State Islamic University Sunan Ampel, Surabaya, Indonesia; rahmawatipudji@yahoo.co.id
[6]Faculty of Nurse, Brawijaya University, Malang, Indonesia; ahsanfkub@yahoo.com
[7]Faculty of Public Health, University of Indonesia, Depok, Indonesia; indri@ui.ac.id
[8]Department Epidemiology, Faculty of Public Health, University Sumatera Utara,Email: rasmaliah59@gmail.com
[9]Politeknik Kesehatan, Kemenkes Maluku, Indonesia,Email: suwardi@poltekkes.ambon.kemenkes.go.id
[10]Department of Occupational Health and Safety, Faculty of Public Health, Airlangga University, 60115, Surabaya, East Java, Indonesia; laela.agrista.devilia-2020@fkm.unair.ac.id
Corresponding author:
Abdul Rohim Tualeka, Department of Occupational Health and Safety, Public Health Faculty, Airlangga University, 60115, Surabaya, East Java, Indonesia; abdul-r-t@fkm.unair.ac.id

ABSTRACT

Benzene, toluene and xylene (BTX) are organic solvents that can cause neurotoxic effects on The body of workers exposed to these materials. Therefore, this study aims to determine the relationship between BTX concentration and RQ with MDA levels and neurotoxic risk in workers exposed to BTX in five industries in Surabaya. This research was conducted in five industries in Surabaya that use BTX as a solvent in the production process. This industry is located in Osowilangun, Ketintang, Jemursari, Kalijudan and AUP. The research design used was Cross Sectional with a total sample of 69 people. The variables studied included BTX concentration, RQ benzene, MDA levels, and neurotoxic risk. Data were analyzed using the Spearman correlation test. There was no significant relationship between benzene and xylene concentration and RQ with MDA levels and neurotoxic risk in the sample ($p > 0.05$). There was no significant relationship between BTQ RQ and MDA levels in the sample ($p > 0.05$). There was no significant relationship between BTX concentration and neurotoxic risk in the sample ($p > 0.05$). There was a significant relationship between Toluene concentration and MDA levels in the sample ($p < 0.05$). There was a significant relationship between Toluene RQ and MDA with neurotoxic risk in the

sample (p <0.05). There was no significant relationship between RQ BTX with MDA, BTX concentration and neurotoxic risk, and RQ benzene and xylene with neurotoxic risk in workers in five industries in Surabaya. Nevertheless, there was a significant relationship between RQ Toluene with neurotoxic risks and between MDA and neurotoxic risk in workers in five industries in Surabaya.

Keywords: Concentration, RQ, BTX, MDA, Neurotoxic

INTRODUCTION

Damage to the central nervous system can occur due to exposure to chemicals that are neurotoxic, use of drugs are neurotoxic, and have metabolic disorders such as diabetes or uremia. The main focus in public health is the relationship between neurological damage and toxic substances found in the workplace. In the United States, neurotoxic disorders are among the 10 biggest diseases, the largest contribution is caused by toxic substances resulting in neurobehavioral disorders(Health and Safety Executive (HSE) 2014; Lodovici and Bigagli 2011).

Neurotoxic is defined as adverse changes or functional disorders of the nerves, both the central nervous system and peripheral nervous system caused by exposure to chemicals, physical and biological agents better known as neurotoxic or neurotoxic substances. This disorder results in changes in memory, attention, mood, disorientation, deviations in thinking, as well as somatic, sensory, and cognitive functions as neurotoxic effects due to the use of neurotoxics(Faradisha 2018).

Lee et al., found that painting workers in shipyards were exposed to organic solvents mixing with paint and affecting neurobehavioral changes(Lee et al. 2005). Research conducted by Dick found that the use of organic solvents in painting can cause nervous system effects and including headaches that will eventually result in death(Dick 2006). Long-term, health effects include leukemia, kidney cancer, scleroderma and central nerve damage. Thetkathuek et al., in their study suggested that the neuropsychomatic symptoms of workers who use organic solvents for paint (Toluene and Xylene) are headache, lethargy, fatigue, loss of libido, nausea, vomiting and loss of appetite (70%)(Thetkathuek et al. 2015).

BTX is a chemical that is toxic to health, both carcinogenic or triggers cancer(Gammon and Santella 2008; Reid et al. 2012; White et al. 2014), increases oxidative stress(Bae et al. 2010) and non-carcinogenic such as affecting the hematopoietic system, central nervous system and reproductive system(Han et al. 2011; Raslan, Elbadry, and Darwish 2018). This is a Volatile Organic Compound (VOC), a compound containing carbon which evaporates at a certain pressure and temperature or has high vapor pressure at room temperature. The most commonly known VOCs are solvents and other types that are widely used are monomers and deodorizers(Tunsaringkarn et al. 2012).

Toxic properties of BTX in high levels of exposure cause neurotoxic symptoms. Continuous exposure to high levels of BTX can cause damage to the human bone marrow, DNA damage to mammalian cells and damage to the immune system. Mild exposure causes irregular heartbeat, headaches, dizziness, nausea and even fainting if exposure is continued for a long time. Early manifestations of toxicity are anemia, leukocytopenia, and thrombocytopenia(Singh A.K., Tomer Neetu 2012).

Organic solvents such as BTX that enter the body oxidize to proteins, lipids and will produce Malondialdehyde (MDA). An increase in MDA levels is a sign of an increase in free radicals in the blood, this even becomes a benchmark to determine the risk of cancer that will occur in workers exposed to benzene. Evidence shows that organic solvents can express their toxicity by producing ROS that can cause cell damage(Ulakoğlu et al. 1998; Valcke, Nong, and Krishnan 2012). Therefore, the aim of this study is to determine the relationship between BTX concentration and RQ with MDA levels and neurotoxic risk in

workers exposed to BTX in five industries in Surabaya.

METHODS

This is an observational, cross-sectional study conducted in five industries in Surabaya that uses BTX as a solvent in its production process. They are located in Osowilangun, Ketintang, Jemursari, Kalijudan and AUP. The population in this study was 90 workers exposed to BTX in five industries in Surabaya. The research sample was taken using the accidental sampling method with the number of study samples was 69 respondents. The variables to be examined in this study are BTX concentration, RQ benzene, MDA levels and neurotoxic risk. Analysis of the data used is descriptive and bivariate analysis using the Spearman correlation test.

RESULT

Frequency Distribution of Characteristics of Respondents exposed to BTX in Five Industries in Surabaya. Respondent characteristics include age, sex, level of education, and work area. The following table distributes the characteristics of respondents who work in the Surabaya shoe industry.

Table 1. Frequency Distribution of Characteristics of Workers Exposed to BTX in Five Surabaya Industries

Characteristics of Respondents	Frequency	Percentage
Age		
16-25	12	17.4%
26-35	13	18.8%
36-45	24	34.9%
46-55	13	18.8%
56-65	7	10.1%
Sex		
Male	58	84%
Female	11	16%
Level of Education		
Primary	9	13%
JHS	20	29%
SHS	37	53.7%
Undergraduate	3	4.3%
Working Area		
Osowilangun	12	17.4%
Ketintang	19	27.5%
Jemursari	10	14.5%
Kalijudan	17	24.6%
AUP	11	16%

Source: primary data

Based on table 1, most industrial workers aged 36-45 years (34.9%), male sex (84%) and high school/vocational education level (53.7%). Most workers work in the Ketintang region (27.5%).

BTX Concentration Measurement Results

Table 2. Results of BTX Concentration Measurement in five industries in Surabaya

Concentration	Frequency	Percentage	Average
Benzene			
>0,05 ppm	51	74%	4,6 ppm
≤0,05 ppm	18	26%	
Toluene			
>20 ppm	24	34.8%	28,5 ppm
≤20 ppm	45	65.2%	
Xylene			
>100 ppm	1	1.4%	26,5 ppm
≤100 ppm	68	98.6%	

Source: primary data

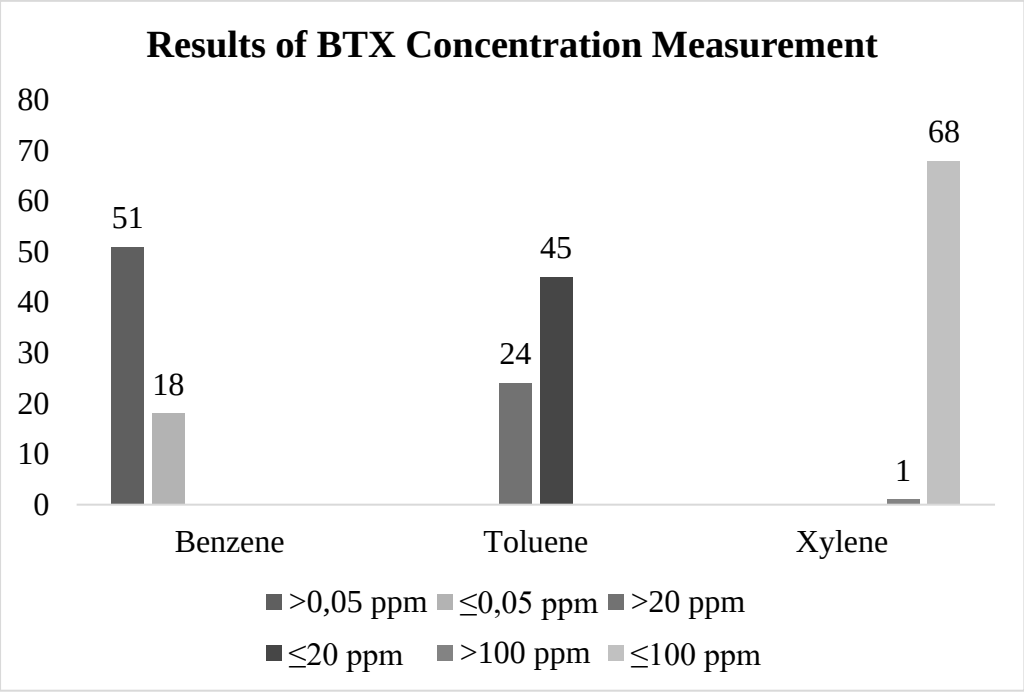

Figure 1. Results of BTX Concentration Measurement

Based on the BTX concentration measurements in table 2, the average benzene concentration value at the site is 4.6 ppm. This is above the stipulated TLV (Minister of Manpower, 1997) for 8 hours of work (0.05 ppm) for benzene. The average values of toluene concentration and xylene concentration were 28.5 ppm and 26.5 ppm, respectively. This exceeds the determined TLV (20 ppm for toluene) and does not exceed the TLV for xylene of 100 ppm (Ministry of Manpower of the Republic of Indonesia, 1997). Based on table 2, the majority of workers (74%) are in the Benzene concentration above the TLV. The majority of workers (65.2%) were in toluene concentrations below the TLV. The majority of workers (98.6%) were at xylene concentrations below the TLV.

BTX Risk Character (RQ)

Table 3. Distribution of BTX RQ Frequency in Workers Exposed to BTX in five industries in Surabaya

Risk Characteristics	Total	
	N	%
Benzene		
Unsafe (≥1)	47	68.1%
Safe (<1)	22	31.9%
Toluene		
Unsafe (≥1)	50	72.5%
Safe (<1)	19	27.5%
Xylene		
Unsafe (≥1)	60	87%
Safe (<1)	9	13%

Source: primary data

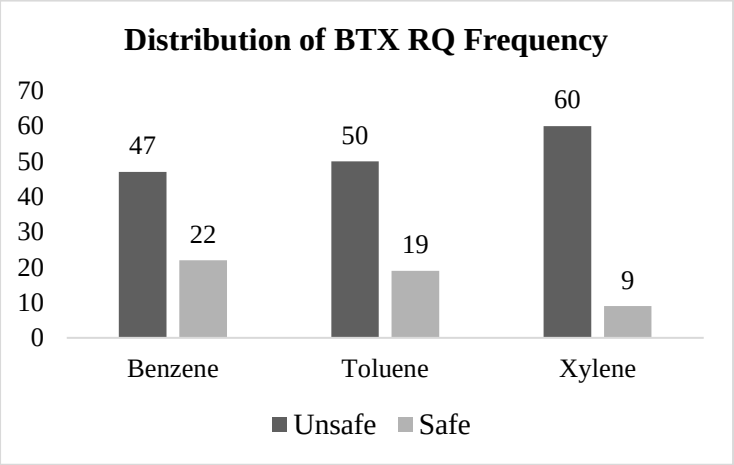

Figure 2. Distribution of BTX RQ Frequency

Health risk characteristics are stated as Risk Quotient (RQ, Risk Level) calculated by dividing the intake or intake (Ink) by reference (RfC). The calculation results of Risk Quotients (RQ) can indicate the level of health risks of workers due to exposure to BTX in the work environment. If the RQ value is more than or equal to 1 (RQ> 1) then workers who are exposed to BTX have health risks due to BTX exposure. RQ value less than 1 (RQ <1) indicates that workers exposed to BTX are still safe from health risks due to BTX exposure (Kolluru, 1996). Based on the RQ calculation in table 3, the majority of workers (68.1%) have RQ≥1 value for benzene exposure, which means they have a health risk impact due to benzene exposure. The majority of workers (72.5%) have an RQ≥1 value for toluene exposure which means the majority of workers have a health risk impact due to toluene exposure. The majority of workers (87%) have an RQ≥1 value for xylene exposure which means it has an impact on health risks due to xylene exposure. In conclusion, the majority of workers have a health risk impact due to BTX exposure in the workplace.

Neurotoxic Risk

Table 4. Frequency Distribution of Neurotoxic Risk

Variable	Category	Total	Percentage
Neurotoxic Risk	Risky	40	58%
	Not risky	29	42%

Source: primary data

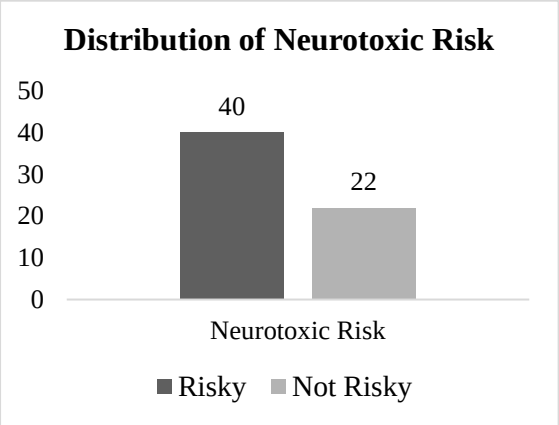

Figure 3. Distribution of Neurotoxic Risk

Table 4 shows that as many as 40 (61.4%) respondents had neurotoxic risks due to exposure from BTX compounds in the work environment, while 22 (42%) respondents did not have neurotoxic risks due to exposure from BTX compounds in the work environment.

Relationship between Benzene, Toluene, Xylene and MDA Concentrations

Table 5. Statistical Test Results between BTX Concentrations and MDA levels

MDA Levels	P-Value	Correlation coefficient	N
Benzene	0.826	-0.027	69
Toluene	0.030	0.262*	69
Xylene	0.184	-0.162	69

Source: primary data

Based on the results of the statistical tests in table 4, there was no significant relationship between the concentrations of benzene, xylene and MDA levels in workers in five industries in Surabaya (p> 0.05). There was a significant relationship between Toluene concentration and MDA levels in workers in five industries in Surabaya (p <0.05).

Relationship between RQ Benzena, Toluena, Xylene and MDA

Table 6. Statistical Test Results between BTX Concentrations and MDA levels

MDA Levels	P-Value	Correlation coefficient	N
Benzene RQ	0.375	-0,109	69
Toluene RQ	0.173	0.166	69
Xylene RQ	0.620	-0.061	69

Source: primary data

Based on the results of the statistical tests in table 6, there is no significant relationship between RQ benzene, toluene and xylene with MDA levels in workers in five industries in Surabaya (p> 0.05).

Relationship between Benzene, Toluene, Xylene Concentration and Neurotoxic Risk

Table 7. Statistical Test Results of BTX Concentration and Neurotoxic Risk

Neurotoxic Risk	P-Value	Correlation coefficient	N
Benzene	0.215	-0.151	69
Toluene	0.856	-0.022	69
Xylene	0.703	-0.047	69

Source: primary data

Based on the results of the statistical tests in table 7, there was no significant relationship between the concentrations of benzene, toluene, xylene and neurotoxic risk in workers in five industries in Surabaya (p> 0.05).

Relationship between RQ Benzene, Toluene, Xylene and Neurotoxic Risk

Table 8. Statistical Test Results Between BTX Concentration and Neurotoxic Risk

Neurotoxic Risk	P-Value	Correlation coefficient	N
RQ Benzene	0.103	-0.198	69
RQ Toluene	0.036	-0,253*	69
RQ Xylene	0.359	-0.112	69

Source: primary data

Based on the results of the statistical tests in table 8, there is no significant relationship between RQ benzene, xylene and neurotoxic risk in workers in five industries in Surabaya (p> 0.05). There was a significant relationship between Toluene RQ and neurotoxic risk in the workers studied (p <0.05).

Relationship between MDA levels and Neurotoxic Risk

Table 8. Relationship between MDA levels and Neurotoxic Risk

Neurotoxic Risk	P-Value	Correlation coefficient	N
MDA Levels	0.050	-0.237	69

Source: primary data

Based on the results of the statistical tests in table 9, there is a significant relationship between MDA and neurotoxic risk in the workers studied (p <0.05).

DISCUSSION

The results showed that there was a significant relationship between Toluene RQ and neurotoxic risk in workers in the five industries studied (p <0.05). This study is in line with research conducted by Faradisha on the relationship of risk characteristics and neurotoxic risks in printing workers in the plastic sack industry(Faradisha 2018). Tunsaringkarn et al., examined SPBU workers in Thailand with the result that workers who had a risk of exposure to toluene RQ ≥ 1 at work experienced headaches (61%), fatigue (29%) and throat irritation (11%)(Tunsaringkarn et al. 2012). Maryiantari showed that respondents with RQ ≥ 1 experienced headaches (20%), fatigue (18.2%) and cough (18.8%)(Maryiantari 2016).

Toluene is a non-carcinogenic toxin so the risk characteristics are stated as Risk Qoutient (RQ) which can be calculated by dividing the intake value by reference (RfC). Many factors influence the value of RQ which has the most contribution, namely the length of service of the respondent. In this study the majority of workers had> 8 years of service. Hormes, Filley and Rosenberg show that workers exposed to chronically toluene vapor for 2 years or more show abnormalities in neurology(Hormes, Filley, and Rosenberg 1986). This is supported by the research of Aydin et al., that chronic toluent exposure through inhalation can cause lesions in white matter in the brain by using cranial MR (Magnetic Resonance)(Aydin et al. 2002). Hee concluded that workers exposed to organic solvents had twice the risk of diagnosing neurological and/or psychiatric defects when

compared to workers unexposed workers(Hee 1993).

Several factors such as age, sex, body composition and health status can affect toluent metabolism when entering the body ATSDR(ASTDR 2017). In this study the majority of respondents were in the age range 36-45 years. According to Suma'mur P.K., at the age of 40 years physical capacity such as vision, hearing and reaction speed decreased which could also affect the results of the questionnaire filled out by respondents because some of the questions contained in the Q18 questionnaire were related to respondent's memory(Suma'mur 2009). Physiologically with increasing age the ability of body organs will naturally decrease. This condition worsens with unhealthy environmental conditions and other factors such as smoking habits, non-compliance with PPE, length of exposure and a history of diseases related to the nervous system. They likely to cause complaints associated with neurotoxic symptoms(Gamble 2000).

There was a significant relationship between MDA and neurotoxic risk in the workers studied ($p < 0.05$). Increased levels of MDA in the blood are neurotoxic and cause apoptosis. MDA has been widely studied as a biomarker of cognitive impairment markers especially in patients with mild cognitive impairment (MCI) and Alzheimer's disease. In one study about the relationship of MDA levels and cognitive function MMSE scores were negatively correlated with MDA levels ($r = -0.3$, $p = 0.028$)(Torres et al. 2011).

MDA can inhibit brain mitochondrial complexes I, II, and V. This will cause destabilization of the mitochondrial potential membrane that plays a role in the occurrence of cellular energy reserve deficiencies. MDA is also known to inhibit brain mitochondrial pyrupate dehydrogenase (PDH) and -ketoglutarate dehydrogenase (KGDH) by the formation of adducts with sulfhydryl groups on lipoic acid in the enzyme complex. This enzyme is vital in the Kreb cycle and the phosphorylation oxidation reaction by regulating the decrease in NAD + to NADH. A research on the hippocampus of mice shows that MDA is toxic to cells. MDA reacts with Na +/ K + -ATPase of the plasma membrane causing membrane depolarization, opening of the voltage gate channel, Ca2 + will enter the cytosol and activate the apoptotic cascade. At the level of cortical neurons MDA can activate phospo-p53 and cyclins D1 and D3 which the end result will also activate protease caspase 3 effectors. The more apoptosis of neuron cells in the brain by MDA, the higher the risk of cognitive impairment(Long et al. 2009).

CONCLUSION

There was no significant relationship between RQ BTX with MDA, between BTX concentration and neurotoxic risk also between RQ benzene and xylene with neurotoxic risk in workers in five industries in Surabaya. But, there was a significant relationship between RQ Toluene with neurotoxic risks and between MDA and neurotoxic risk in workers in five industries in Surabaya.

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Ethical Clearance: The study was approved by the institutional Ethical Board of the Public Health, Airlangga University

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