Benzene Exposure Analysis via the Biomarker S-Phenylmercapturic Acid and Hemoglobin Levels of Shoemakers in Sukajaya Village, West Java Province, Indonesia

Ranti Ekasari[1]*, Ririn Arminsih[2]

1. Faculty of Medicine and Health Science, Alauddin Islamic State University of Makassar, Gowa, Indonesia.
2. Faculty of Public Health, Universitas Indonesia, Depok, Indonesia

Abstract

In Indonesia, shoe manufacturing is a growing informal industry, making the country the world's fourth largest shoe and sandal producer. In the sizing process, shoe making uses the chemical benzene, exposure to which causes problems in the human hematopoietic system, and, in turn, decreased hemoglobin levels. Therefore, this study aimed to identify benzene in the body via measurement of the s-phenylmercapturic acid (S-PMA) biomarker of shoemakers' hemoglobin levels in Sukajaya Village, Indonesia.

Conducted from March to May 2018, this cross-sectional study used a total sampling method with 73 shoemakers. The inclusion criteria of this study such as the workers must be a man with at least one year of task length and had an active status of worker in workplace. Analytical results showed that workers with high S-PMA concentrations (>0.67 µg/g creatinine) were 1.25 times more likely to have hemoglobin <14 g/dL than those who had low S-PMA concentrations (<0.67µg/g creatinine).

In addition, workers' risk rose to 1.36 after spending a year in the gluing section. Workplace risk control should include constant open ventilation in the gluing section and rotation of workers to other tasks. The worker also should use mask as personal protective equipment.

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Introduction

After China, India, and Vietnam, Indonesia has become the world's fourth largest shoe producer.[1] In West Java, the shoe industry's center was located in Bandung, Tasikmalaya, and Bogor Regencies, especially in the latter's sub-districts of Ciomas, Tamansari, and Dramaga.[2] Specifically, the Tamansari District has 250 units with 1295 workers, and Pasireurih Village workshop had the highest number of workers, 363, compared to Sukajaya with 103.[3]

Shoe making requires the use of strong glues, in which benzene is a solvent. Because of the volatility, the main routers of benzene exposure were through human skin, respiratory, and digestive systems absorb benzene from the air.[4] The chemical spreads throughout the body via absorption from the blood to fat tissue, bone marrow, and urine.[5] The liver then metabolizes benzene by producing several metabolites, among which s-phenylmercapturic acid (S-PMA) in the urine is sensitive for measurement of benzene exposure in the air without being affected by different exposures than for other metabolites.[6]

Given its noninvasive nature, benzene in urine is recommended as a biomarker at air concentrations below 1 ppm.[7] Benzene entering the human body through the gastrointestinal system will result in acute effects, for example, disorders of the blood system (hematology).[8] One of the blood cells is an erythrocyte consisting of hemoglobin, a conjugated protein which functions to breathe by transporting oxygen and carbon dioxide.[9] Thus, exposure to benzene will lead to problems in the hematopoietic system. In fact, benzene can cause disorders in normal blood production, for instance, in the bone marrow, causing decreased blood components—both red and white blood

Corresponding author:
Ranti Ekasari
Faculty of Medicine and Health Science, Alauddin Islamic State University of Makassar
Gowa, Indonesia.
E-mail: ekasariranti@gmail.com

cells and platelets. Then, a reduction of red blood cells can cause anemia.

Study held by Vermeulen *et al.* (2006) on shoe factory in Tianjin, China showed that the average concentration of benzene in the air (1,5 ppm) exceeded the indicator (0,5 ppm) from ACGIH. Besides, there was a significant correlation of benzene concentration in the air with benzene in worker's urine. [10] Another study among Chinese workers by Qu *et al* (2002) also showed that there was a significant correlation between S-PMA with the decrease of blood profile. [11]

Based on data collected from March to May 2018, therefore, this study researched the association between S-PMA urine concentrations and hemoglobin levels of 73 shoemakers in Sukajaya Village, Tamansari Sub-district, Bogor Regency, West Java.

Materials and methods

This observational, cross-sectional study used primary data, measuring the independent variable of S-PMA concentration in workers' urine, using *Liquid Chromatography-Tandem Mass Spectrometry* (LC-MS/MS). The dependent variable of workers' hemoglobin levels was measured via spectrophotometry. Industry task type and length were covariate variables.

The population in this study was all the shoemakers that worked in shoe workplace in Sukajaya Village, Tamansari Sub-district, Bogor Regency, West Java. While the sample in this study must be fulfilled the inclusion and exclusion criteria. The inclusion criteria of subject such as (1) worker was men with at least 17 years old of age; (2) the task length of worker at least one year; (3) worker has an active status in shoe workplace; (4) worker was willing to be a sample by signing the informed consent. Besides, the inclusion criteria of the sample such as (1) not at the location of the study during it is conducted; (2) in illness condition; (3) urinary creatinine level was less than 0,3 g/L or more than 3,0 g/L.

The method of data collection was total sampling with 73 shoemakers as sample in this study. Data analysis used a chi-square test for bivariate analysis, while multivariate analysis used multivariable logistic regression. This study also has passed the ethical review process from the Research and Community Engagement Ethical Committee Faculty of Public Health University of Indonesia. The number of ethical approval was 222/H2.F10/PPM.00.02/2018.

The data in this study was numeric but after analyzing the normality, it was found that the data was not normal. Therefore, the researcher decided to group the data become categorical data by median value for bivariate and multivariate analysis.

Results

Based on numeric data, it showed that shoemakers' length of gluing task ranged from 1 to 25 years, with a median of 5 years. Shoemakers' S-PMA urine concentrations also varied, with the lowest at 0.16 µg/g and the highest at 10.25 µg/g of creatinine. Their median concentration was 0.67 µg/g creatinine. Workers' median hemoglobin (Hb) level was 14.5 g /dL, the lowest Hb level was 11.5 g/dL, and the highest was 17.9 g/dL (Table 1).

Variables	Mean	Median	Deviation Standard	Min-Max
Task Length (year)	7.04	5.00	5.75	1.00–25.00
Concentration of S-PMA (µg/g creatinin)	1.53	0.67	2.17	0.16–10.25
Hemoglobin Level (g/dL)	14.45	14.50	1.16	11.50–17.90

Table 1. Descriptive Distribution of Task Length, S-PMA Concentration, and Hemoglobin Level.

Based on median values, task length, task type and S-PMA concentrations were classified into two categories. Hemoglobin levels also divided into two categories, but the cutoff point based on the standard by Kiswari (2014). According to Kiswari (2014), the normal level of hemoglobin on men was 14-18 g/dL. [9]

According to the categorical data, employees with 1 to 5 years of experience (54.8%) dominated the shoe making workshop, and based on industry task type, the gluing section dominated (69.9%). For S-PMA concentrations, high and low groups' percentages were nearly the same, with workers having hemoglobin levels of 14–18 g/dL (69.9%) (Table 2).

Variables	Total	Percentage (%)
Task Length		
>5 years	33	45.2
1–5 years	40	54.8
Task Type		
Gluing Section	51	69.9
Non-Gluing Section	22	30.1
Concentration of S-PMA		
High (> 0.67 µg/g creatinin)	37	50.6
Low (≤ 0.67µg/g creatinin)	36	49.4
Hemoglobin Level		
<14 g/dL	22	30.1
14–18 g/dL	51	69.9

Table 2. Frequency Distribution of Task Length, Task Type, Concentrations of S-PMA, and Hemoglobin Levels.

Analysis by chi-square test revealed that the total of sample who had high S-PMA concentrations and hemoglobin levels <14 g/dL were 12 workers. Whereas sample who had but low S-PMA concentrations and hemoglobin levels 14–18 g/dL were 26 workers. Odds ratio (OR) values indicated that workers with high S-PMA urine concentrations would be at 1.25 times the risk of hemoglobin levels <14 g/dL compared with workers with low S-PMA concentrations (Table 3).

Variables	Hemoglobin Levels				Total	OR Crude (95% CI)
	<14 g/dL		14–18 g/dL			
	n	%	N	%		
S-PMA concentrations						
High (>0.67)	12	32.4	25	67.6	37	1.25 (0.46–3.40)
Low (≤ 0.67)	10	27.8	26	72.2	36	
Total	22		51		73	

Table 3. Relationship Between S-PMA Concentrations and Hemoglobin Levels.

Multivariable logistic regression analysis additionally revealed that workers with high S-PMA concentrations (>0.67 µg/g creatinine) were at 1.36 times higher risk of having hemoglobin <14 g/dL compared with those with low S-PMA concentrations (<0.67 µg/g creatinine) after controlling by task length and task type variables (Table 4).

Independent Variables	Coefficient B	$OR_{adjusted}$	95% CI	
			Lower	Upper
S-PMA Concentration	0.306	**1.36**	0.46	4.03
Task Length	0.039	1.04	0.38	2.85
Task Type	-0.240	0.78	0.24	2.55
Constant	0.746	2.11		

Table 4. Final Model from Logistic Multivariable Regression.

Discussion

S-phenylmercapturic acid (S-PMA) is one metabolite that can mark benzene's presence in the body—in this study, measured via shoemakers' urine samples. Because benzene is sensitive to measurement of exposure entering the body through inhalation at both high and low concentrations, the American Conference of Governmental Industrial Hygienists (ACGIH) recommends using S-PMA to measure benzene exposure. Besides that, S-PMA metabolites are also not affected by benzene derived from sorbet acid in food. [6]

According to the direction of this study's researchers and under the assumption that shoemakers were exposed to benzene in the morning and a few days earlier, urine sampling was undertaken in the afternoon. Laboratory analysis showed that the average S-PMA value was 1.53 µg/g creatinine, still far below ACGIH's value of Biological Exposure Indices (BEI) of 25 µg/g. The result indicated that the S-PMA concentration was still on safe level in human body.

These results aligned with those of Hoet *et al.*'s (2008) research on 110 petrochemical workers, showing that the average S-PMA value was 1.40 µg /L (µg/g creatinine). [12] However, another study conducted by Wulandari (2016) on 64 workers in a sandal workshop in Cibaduyut showed an average S-PMA concentration of 24.62 µg/g creatinine. [13] Based on the previous research, the S-PMA concentration showed the trend with this study where S-PMA concentration was still within safe concentration.

The existence of benzene in the body is problematic because it is carcinogenic. [8] Therefore, some studies may serve as a reference for BEI determination of lower S-PMA, especially in Indonesia. But still, even on a small concentration, S-PMA as a biomarker of the existence of benzene in human body still be a serious concern.

A study by Kurniawidjaja (2012) found that some brands that was used by workers contained benzene. Those brands are EHA-Bond and Gold Bond glues with 1.34 to 1.52% benzene.[14] Both brands among the other brands were also used on shoe production in Sukajaya Village, indicating that glue used by shoemakers contains benzene in low concentrations.

In the human circulatory system, hemoglobin is a red blood cell component in charge of carrying oxygen and carbon dioxide. It consists of four polypeptide globin chains, each binding an iron-containing heme molecule. Results of Sukajaya Village workers' laboratory analyses showed that most of the workers has a normal level of hemoglobin (69.9%) according to the standard value.

In the Cibaduyut Area, a study by Sanjaya (2016) with 71 shoemakers showed their mean hemoglobin level at 15.34 g/dL $\pm$ 1.14 g/dL.[15] In Pakistan, another study by Khan (2013) with 30 workers showed an average hemoglobin level of 14 g/dL $\pm$ 1.5 g/dL.[16] Significantly, workers' hemoglobin level from previous research and also this study still in the 14–18 g/dL range can be caused by the Health Worker Effect issue, in which research samples include workers only in relatively healthy condition. Workers who may have become ill are not included in samples, likely because they no longer work in the shoe making industry.[17]

The task length and type variables were confounding because the risk of S-PMA concentration on hemoglobin level was 1.25 whereas after controlling for these variables, risk increased to 1.36. Hosseinzadeh and Moosavi-Movahedi's (2016) study using the UV-vis spectroscopic method shows that benzene can alter hemoglobin's heme and prosthetic chains. The body's increased exposure to benzene has the potential to cause a hemolytic condition in which red blood cells die faster than bone marrow can produce them. Results of Constant Wavelength Synchronous Fluorescence Spectroscopy (CWSFS) indicate that heme degradation due to benzene exposure has a poor effect on hemoglobin's structure and function.[18]

Khuder *et al.* (1999) conducted a cohort study on assessment of variation in total blood cell counts in benzene-exposed workers from 1967 to 1994. Including 105 benzene-exposed workers, the study's results showed that the number of red blood cells, hemoglobin level, corpuscular volume (MCV), and platelet count decreased significantly during the observation period.[19] Wiraagni *et al.* (2012) obtained another result in which employees exposed to benzene were at 1.71 times on risk of decreased hemoglobin compared to those not exposed. S-PMA concentrations of employees in 2007 ranged from 0.8 to 47 µg/g of creatinine. Although the average value of normal employee S-PMA concentrations is 11.54 ± 5.28 µg/g creatinine (<25 µg/g creatinine), there were 4.5% of employees with S-PMA concentrations exceeded ACGIH's BEI.[20]

Based on previous research and also this study showed that S-PMA had a role to decrease hemoglobin level in human body. Benzene concentration can also affect S-PMA urine concentration, and, in turn, workshop airspace and ventilation markedly affect benzene concentration. For instance, some workshops have good ventilation, and their doors are always open. Following rules for constant ventilation can maximize air circulation to evaporate benzene and minimize exposure to harmful substances in the air space, including benzene-thus ensuring that benzene concentration does not exceed the standard value. In this study, S-PMA urine concentration did not reach BEI's standard value, so it is unlikely to be causing problems in workers' hematopoietic systems and thus decreased hemoglobin levels.

As indicated by the S-PMA biomarker, urine concentrations in the sample remain small. Even so, benzene in the body is dangerous, especially if it accumulates over lengthy periods, because it is one of 120 chemical compounds categorized as group 1 human carcinogens.[21] Therefore, even small amounts of benzene are likely to cause health hazards, and shoe manufacturing workshops should compensate for the possibility of its presence in the air workers breathe.

Conclusions

As noted, high S-PMA concentration contributed 1.25 time risk to workers had <14 g/dL hemoglobin level compared to workers who had low concentration in their body. Besides task length and types had role to be confounding variables because the risk of S-PMA concentration on hemoglobin level increased to 1.36. Therefore, shoe workshops should ensure good air circulation by extending or adding ventilation and keeping it constantly open during working hours. Another strategy includes rotating workers in and out of a workshop's gluing section and also using mask as a personal protective equipment to minimize the exposure of benzene.

Declaration of Interest

No conflict of interest in this research.

References

1. Permana SH. Increasing the National Footwear/Footwear Industry. Bul APBN [Internet]. 2017; II. Available from:http://berkas.dpr.go.id/ puskajianggaran/ buletin-apbn/ public-file/ buletin-apbn-public-32.pdf
2. Ministry of Industry. Regulation of the Minister of Industry of Indonesia number 152/M-IND/Per/12/2012 about Guide Map for Bogor Core District Industrial Competency Development [Internet]. Indonesia; 2012. Available from: http://regulasi.kemenperin.go.id/site/download_peraturan/1601
3. Department of Trade and Industry Bogor Regency. Recapitulation of Data Collection on Small and Medium Footwear Industries in 2016. Bogor; 2016.
4. Azari MR. Evaluation of Occupational Exposure of Shoe Makers to Benzene and Toluene Compounds in Shoe Manufacturing Workshops in East Tehran. NRITLD 2012;11(4):43–9.
5. Pudyoko S. Relationship between Benzene Exposure and Phenol Levels in Urine and Postgraduate Programs [Internet] [Thesis]. Diponegoro University Semarang; 2010. Available from: http://gizi.depkes.go.id/wp-content/uploads/2011/10/ped-praktis-stat-gizi-dewasa
6. Arnold SM, Angerer J, Boogaard PJ, Hughes MF, O'Lone RB, Robison SH, et al. The Use of Biomonitoring Data in Exposure and Human Health Risk Assessment: Benzene Case Study. Crit Rev Toxicol [Internet]. 2013;43(2):119–53. Available from: http://www.tandfonline.com/doi/full/10.3109/10408444.2012.756455
7. Gun R, Pratt N, Griffith E, Adams G, Bisby J, Robinson K. Update of A Prospective Study of Mortality and Cancer Incidence in the Australian Petroleum Industry. Occup Environ Med [Internet]. 2004;2. Available from: http://oem.bmj.com/content/oemed/52/9/611.full.pdf
8. ATSDR. ToxGuide for Benzene. 2007;2. Available from: https://www.atsdr.cdc.gov/toxguides/toxguide-3.pdf
9. Kiswari R. Hematology and Transfusion. Carolina S, Astikawati R, editors. Jakarta: Erlangga; 2014.
10. Vermeulen R, Lan Q, Li G, Rappaport SM, Joode VW De, Shen M, et al. Assessment of Dermal Exposure to Benzene and Toluene in Shoe Manufacturing by Activated Carbon Cloth Patches. J Environ Monit. 2006;8:1143–8.
11. Qu Q, Shore R, Li G, Jin X, Chen LC, Cohen B, et al. Hematological Changes among Chinese Workers with A Broad Range of Benzene Exposures. Am J Ind Med [Internet]. 2002;42(4):275–85.
12. Hoet P, Smedt E De, Ferrari M, Imbriani M, Maestri L, Negri S, et al. Evaluation of Urinary Biomarkers of Exposure to Benzene : Correlation with Blood Benzene and Influence of Confounding Factors. Int Arch Occup Env Heal. 2008;82(8):985–95.
13. Wulandari P. S-Phenylmercapturic Acid (S-PMA) Level in Urinary as Biomarkers of Exposure to Benzene and Leukocytes of Informal Shoes Industrial Workers in Cibaduyut Bandung [Thesis]. Universitas Indonesia; 2016.
14. Kurniawidjaja LM, Sofia NA, Pudjadi E, Lestari F, Tejamaya M. Respiratory Symptoms and BTX Exposure Health Risk Analysis among the Footware Workers in Ciomas Bogor. J Respirologi Indones. 2012;32(1):36–43.
15. Sanjaya BR. Association of Benzene Exposures and Hemoglobin Study among the Footware male Workers in Cibaduyut West Java. Universitas Indonesia; 2016.
16. Khan AA, Sultan R, Rahman SU. Biochemical and Hematological Analysis after Exposure to Hazardous Materials during Shoe Making. J Biol Life Sci. 2013;4(2):116–38.
17. May W, Asthma C. Pulmonary Perspective Work May Cause Asthma , but Asthma May Also Influence Work. Am J Respir Crit Care Med. 2008;177:4–10.
18. Hosseinzadeh R, Moosavi-Movahedi AAk. Human Hemoglobin Structural and Functional Alterations and Heme Degradation Upon Interaction with Benzene: A Spectroscopic Study. Spectrochim Acta Part A Mol Biomol Spectrosc. 2016;
19. Khuder S, Youngdale M, Bisesi M, Schaub E. Assessment of Complete Blood Count Variations among Workers Exposed to Low Levels of Benzene. J Occup Enviromental Med. 1999;41(9):821–6.
20. Wiraagni IA, Dwiprahasto I, Ngatidjan. The Correlation Between The Intensity Of Benzene Exposure And Complete Blood Count In The Oil And Natural Gas Company Workers In East Kalimantan. J Med Sci. 2012;44(1):99–110.
21. IARC. Benzene. Vol. 1987, IARC Monographs-100F. 2008.