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Correlation between Lead Serum Level and Total Immunoglobulin E(Ige) Level in School-Aged Children

Yuni Handayani Gusmira [a, b, *], Lily Irsa [a], Bidasari Lubis [a], Rita Evalina [a], Mahrani Lubis [a]

[a] Department of Child Health, Medical School, University of Sumatera Utara, Indonesia
[b] H. Adam Malik General Hospital, Medan, Indonesia

Abstract

Correlation between lead serum level and total Immunoglobulin E (IgE) level in school-aged children. Gusmira Y.H., Irsa, L., Lubis, B., Evalina, R., Lubis, M. Lead poisoning may cause various health problems including immune system. Research objective is to determine the correlation between serum lead levels with total IgE level in school-aged children. A cross sectional study had been conducted in Juli 2015 to children aged 9-12 years old in an elementary school industrial area with lead exposure, Medan, Sumatera Utara. Children with atopy and worm infection were excluded. Lead serum level and total immunoglobulin E level were obtained. Data analysis to see correlation between blood lead level and total IgE level was used Pearson correlation test (r) if normal data distribution and Spearman test if abnormal data distribution with significance level P <0.05. From 42 subjects, 27 were boys and 15 girls, the mean age was 10.3 year (SD 1.09), 18 subjects with medium risk of allergic. The mean serum lead level was 2.57 µg/dL (SD 0.58, 95 %CI 2.42-2.74), the mean IgE total level was 1155 IU/L (SD 3340, 95%CI114.43-2196.22). From the Spearman test we obtained r= 0.023, p=0.887. It can be concluded that here was an increase in total IgE levels and blood lead levels but statistically no correlation between lead serum level and total IgE level among school aged children.

Keywords: lead serum level, total immunoglobulin E, children.

1. Introduction

Plumbum or better known as lead is one of heavy metals that can cause health problems including disturbances of hematology, nervous system, cardiovascular, kidney, endocrine, and immunology (Lubis et al., 2003; Farias et al., 2014). The toxic effects in children can arise from the lowest level of lead concentration at 5 µg/dL to the lethal concentration at about 150 µg/dL. According to the Center for Disease Control and Prevention (CDC) the toxic effect of lead can be observed at the serum level of 5 µg/dL (Farias et al., 2014; Mener et al., 2014).

One of the effects of lead exposure is impairment of immune system. The immune system is particularly sensitive to lead poisoning. Lead is immunotoxic even at a very low level (Mener et al., 2014). Lead will shift T-helper 1 (Th1) dependent immunity toward T-helper 2 (Th2) dependent immunity resulting in increasing allergic sensitization through increasing production of interleukins, cytokines, and immunoglobulin E (IgE) (Mener et al., 2014). An increase in IgE level will stimulate allergic reactions. This may be related to increased prevalence of allergies in recent

* Corresponding author
E-mail addresses: yunihandayanigusmira@gmail.com (Y.H. Gusmira)

years. Data from the World Allergy Organization (WAO) 2013 stated that the prevalence of allergy is increasing worldwide by the rate of 10-40 %. Epidemiological studies show that indoor and outdoor pollution affect respiratory health, including an increased prevalence of asthma and allergic diseases (Pawankar et al., 2013). The impact of allergies is the decreased quality of life, increased medical costs, impaired concentration, growth and development (Sudewi et al., 2009). Previous research conducted in Medan, North Sumatera, reported that air lead levels in industrial areas in Medan had exceeded the threshold value from the government which was 2µg/m (Mener et al., 2014; Pawankar et al., 2013; Sudewi et al., 2009; Girsang, 2008). The objective of this study is to determine the correlation between blood lead levels and total immunoglobulin E level in primary school children.

2. Materials and methods

This study was a cross sectional study determining the correlation between blood lead level and total IgE level in elementary school age children in Medan. The research was conducted at Al Washliyah Elementary School Timbang Deli Village, Medan Amplas district, North Sumatra in June 2015. Sample size was calculated using sample size formula for correlation study. Sample were obtained consecutive sampling method and consisted of 4th to 6th grader elementary school students. The inclusion criteria were children aged 9-12 years old and exclusion criteria are children with atopy or allergies and infected with a worm. The samples were given questionnaires for baseline characteristic and risk of atopy and examination of lead level, total IgE level, skin prick test (SPT) and stool examination. Risk of atopy was determined using Indonesian Pediatric Allergy Immunology Working Grup trace card scoring system. Blood is taken using a vacutainer as much as ± 6cc in venous area of cubiti. Then divided into 3cc inserted into tubes that already contain EDTA (preservative Ethylene Diamine Tetraacetic Acid) for examination of lead and 3cc are inserted into empty tubes for examination of total IgE. The study profile can be seen in Fig. 1.

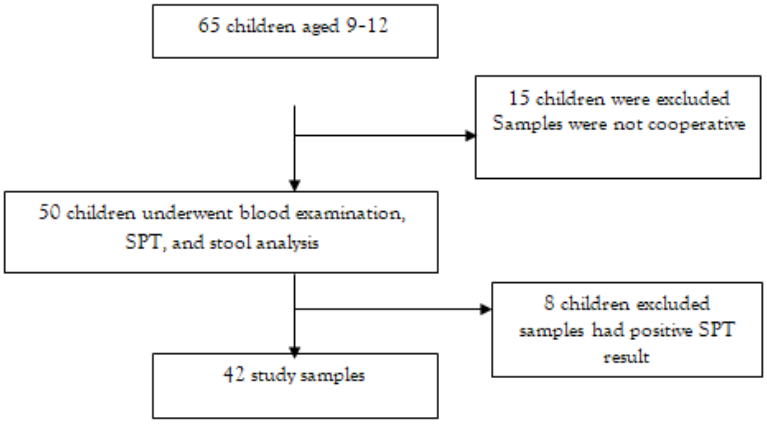

Fig. 1. Study Profile

The serum lead concentration was evaluated with Atomic Absorption Spectrophotometer (AAS) in µg/dL units, with equation (1).

$$\frac{1000}{\text{sample weight}} \text{x} \frac{50}{1000} \text{x AAS concentration (mg/L)} \quad (1)$$

Total IgE level was examined using Mini Vidas tool with ELFA (Enzyme Linked Fluorescence Immuno Assay) method. The normal value of total IgE level is <150 IU/ml.

Data was analyzed using Statistical Package for the Social Sciences software (SPSS). Bivariate analysis was performed using chi-square. Data analysis to see correlation between blood lead level and total IgE level was used Pearson correlation test (r) if normal data distribution and Spearman test if abnormal data distribution with significance level P <0.05.

3. Results

We obtained of 42 elementary school children aged 9-12 years who met the criteria of inclusion and exclusion. The baseline characteristics are shown in Table 1.

Table 1. Baseline characteristics

Characteristics	N
Sex, n(%)	
Female	15 (36)
Male	27 (64)
Nutritional status, n(%) Good nutritional status Malnourished	 29 (69) 13 (31)
Atopy risk, n (%)	
Low risk	24 (57)
Medium risk	18 (43)
IgE Level, n (%) High (≥150 IU/ml) Normal (<150 IU/ml)	26 (62) 16 (38)
Lead level, mean (SD), µg/dl ≥2,57 µg/dl < 2.57 µg/dl	2,57 (0,58) 23 (55) 19 (45)
Age, year, mean (SD)	10.3 (1.09)
Body weight, kg, mean (SD)	27.79 (7.57)
Body height, cm, mean (SD)	132.33 (8.89)
BW/BH, %, mean (SD)	95.91 (15.04)

Of 42 samples obtained, 64 % were male with an average age of 10.3 years. The mean height and weight were 27.79 kg and 132.33 cm, respectively. Most samples had good nutritional status with average of weight for height of 95.91 %. More than half of the samples (57 %) had a low atopy risk and 62 % of the samples had total immunoglobulin E levels of >150 IU/ml. Fifty five percent of samples in this study had serum lead level of 2.58 µg/dl. Table 2 showed the factors affecting lead exposure in this study where painted house had a significant relationship with lead exposure in this study (p <0.01).

Table 2. Factors affecting lead esposure

	Lead level		P
	<2.57 µg/dl (n=19)	≥2.57 µg/dl (n=23)	
Sex Male Female	 14 5	 13 10	 0.25[a]
Age 9 years 10 years 11 years 12 years	 7 7 4 1	 7 6 7 3	 0.34[b]
Nutritional Status Malnutrition Good nutritional status	 7 12	 6 17	 0.45[a]
Total IgE level >150 IU/ml <150 IU/ml	 12 7	 14 9	 0.88[a]

House location			
Near main road / very crowded	6	3	0.06[b]
Big crowded road	6	5	
Less crowded road	7	15	
Painted house			
Yes	17	19	0.43[a]
No	2	4	
Painted part of the house			
Only the insides	7	1	0.01[a]
Both inside and outside	10	19	
Chipped paint			
Yes	11	9	0.23[a]
No	6	11	

[a] Chi square
[b] Mann witney

Table 3 showed that 33 % of children used tap water for drinking, but there was no significant relationship between drinking water sources and lead (p = 0.95). In terms of subject habits, we also did not find significant relationship with lead level. Table 4 showed that there was no correlation between lead level and total immunoglobulin E level with r = 0.023 (p = 0.087).

Table 3. The sources of lead exposure in terms of subject habits

	Lead levels		**p**
	≥2.57 µg/dl (n=23)	<2.57 µg/dl (n=19)	
Daily water source			
Tap water	14	12	0.95[a]
Well water	7	4	
Bottled water	2	3	
Canned food / drink consumption by family members			
Yes	4	1	0.24[b]
No	19	18	
Street foods consumption			
Yes	5	3	0.47[b]
No	18	16	
Nail biting, sucking fingers, biting pencil / pen habit			
Yes	7	6	0.94[c]
No	16	13	
Handwashing habit before/after meal			
Yes	14	9	0.26[a]
No	3	1	
Sometimes	6	9	

[a] Mann-Whitney
[b] Fisher Exact
[c] Chi Square

Table 4. The correlation of lead levels with total immunoglobulin E levels

Parameter	Mean	SD	r*	95%CI	P
Pb, µg/dl	2.57	0.58	0.023	2.42-2.74	0.887
IgE, IU/ml	1155.33	3340.27		114.43-2196.23	

*Spearman test

4. Discussion

We found no correlation between serum lead level and total IgE level in elementary school children in this study (p = 0.887, r = 0.023). This result is different from previous studies. Earlier experimental and epidemiological studies have shown that lead exposure is involved in the changing of humoral and cellular mediated immunity and developing allergies by increasing IgE, eosinophils and bronchial responses (Mishara, 2009; Sun et al., 2003; Wells et al., 2014; Min et al., 2008). A study in Cairo in 2011-2012 enrolling 200 children to determine the association between lead exposure and bronchial asthma, there was an association between lead level with total IgE in children aged 5-14 years, and the relationship between lead level and asthma severity was found (Mohammed et al., 2015).

A study conducted in the USA on 1430 children aged 2-12 years showed an association between blood lead level and total IgE level and reported that elevation of lead level at 1 µg/dl will increase IgE level by 11.1 % (Wells et al., 2014). A study on 279 children in Missouri found that blood lead levels was ranging from 1-45 µg/dL, and found an association between elevated blood lead level and elevated total IgE level (Lutz et al., 1999). Study in Kairo found a positive association between the serum lead and total IgE levels was statistically significant in subjects with *D. farinae* sensitization, which indicated that the immunologic effects of lead exposure may be greater in people with allergic sensitization (Kim et al., 2016). The difference from the results of this study may be due different geographic areas, lifestyles, dietary habits, genetic variation, exposure rates, duration, concentrations, and laboratory methods.

The mechanism of the relationship between lead exposure and total IgE elevation remains unclear. However, lead exposure will cause in IgE-mediated type1 hypersensitivity. Lead will increase Th2 immune response and inhibit Th1 response and also increase Th2 / Th1 cytokine ratio. The effect is dependent on the enhanced production of cytokines and interleukins (IL), thereby promoting isotype switching to IgE. Exposure to lead seems to be associated with atopic sensitization and modulation of several cytokines (e.g. IL-12, IL-10, interferon (IFN)-ɣ, and IL-4 production) and with T-cell dysregulation (Wells et al., 2014; Yang et al., 2014; Wang et al., 2017). Lead exposure during allergic sensitization may induced increased tracheal responsiveness, eosinophil count, and IL-4 concentration. Lead exposure has also result in a decrease in lymphocyte count, IFN-ɣ concentration and IFN-ɣ/IL-4 ratio (Wang et al., 2017).

Sixty two percent of samples in this study had total IgE levels above 150 IU/ml. Study in Taiwan found lead level were positively linked with serum IgE (β=0.26 kU/l per In-unit increase lead concentration (Wang et al., 2017). In accordance with the results of this study can be concluded that any increase in lead levels have positive correlation with increased levels of IgE. But in our study did not examine other factors that might cause elevated IgE levels.

In this study we found that school-aged children in Medan Amplas area had an average lead level of 2.57 µg/dl, with the lowest value of 1.48 µg/dl and the highest value was 3.99 µg/dl. There was no safe lead level observed in these children (*Centers for Disease Control and Prevention*, 2014). The lead level in children in elementary school was still within the threshold limit, which according to the Center for Disease Control and Prevention (CDC) is of 5 µg/dL (*Centers for Disease Control and Prevention*, 2014). We must to prevent further elevation of lead level in the serum of children in elementary school, where normally no lead levels are detected in the serum more attention is needed to reduce the effects of lead poisoning.

The location of this study was an industrial area where it had bus terminals and some large factories producing molding and building material components, liquor, fodder, snacks, and others. According to a 2008 study, Medan Amplas had the highest airborne lead content with the concentration of 32.67 µg/m^3 (Pawankar et al., 2013). This becomes one of the factors of lead exposure in children living in the area. Potential sources of lead includes vehicle exhaust fumes with leaded gasoline, industrial pollution, lead dust that attached to roadside foods or beverages, as well as exposure from the workplaces of parents which are brought home such as smelting or metal recycling, welding, and printing. This is the same with the study in Cairo study, where the average children who have lead levels >10µg/dl are living in industrial environments, urban areas, and slums (Moawad et al., 2016).

Other lead sources from environment are from city plumbing pipes, lead dust on floors, cosmetics, and food or beverages in canned package (Suherni, 2010). WHO establishes a lead limit

in water of 0.1 mg/L. In contaminated the water source, almost all lead is present in the sediment, and partly dissolved in water. Indonesia also has a lead threshold limit for clean and drinking water based on Permenkes RI number 416 dated 1990 that is equal to 0.05 mg/L (Naria, 2005).

A research in Canada in 2012, involving 306 children aged 1 to 5 years, indicated that there was an association between increased blood lead level of 1.78 mg/dL and lead contaminated water, which reached 3.3 ug/L (Levallois et al., 2014). This study found that twenty-seven children used tap water as the source of water for daily necessities and found no association between lead level and drinking water sources, but they did not examine the concentration of lead in the water source for daily needs in the location.

Most children in our study always washed their hands before meal, did not eat street foods, were not non-food eater, had no nail or pencil biting habit. This reduced the lead exposure. The main route of lead exposure in children is through the digestive tract. The curiosity and hand-to-mouth habit of children give easier access for lead to enter the digestive tract thus increasing the lead exposure risk. In addition, the absorption of lead in the gastrointestinal tract of children is three times greater than adults (Levallois et al., 2014).

In the study, the numbers of male samples were more than female and there was no relationship between lead and gender. In the study of NHANES III (National Health and Nutrition Examination Surveys) between 1999-2004 in the United States, males had a slightly higher incidence of lead poisoning than females. This may be related to outdoor activities, where males play more frequently in the outside than females (Jones et al., 2009). A meta-analysis study in China on children aged 0-18 years also found that males had slightly higher risk than females in the lead poisoning (Li et al., 2015).

The limitations of this study are environmental risk factors, the study relied on reporting by parents; the specific products and environments were not directly tested for presence of lead and we did not examine other factors affecting the increase in IgE. For the future, further research or cohort is needed to determine whether there is an increase in lead levels in school-aged children and possible risk factors that lead to elevated levels.

5. Conclusion

There is no correlation between serum lead level and total IgE level in elementary school-aged children. But it should be of concern to us that all children in this study has been exposed to lead, where there should be no lead in the blood and most of the children has high total IgE level. This may be due to several factors which are not investigated in this study. Attention is needed to present further increase in the serum lead level and to minimize the effects caused by lead poisoning.

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