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The Influence of Lead (Pb), Zinc (Zn), Ratio Lead (Pb) to Zinc (Zn) in Attention Deficit Hyperactivity Disorder (ADHD)

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ABSTRACT

Background: Attention Deficit Hyperactivity Disorder (ADHD) is a common childhood psychiatric disorder often encountered in clinical practice with major symptoms of inattention, hyperactivity, and impulsivity. Pollution of lead (Pb) is thought to be cause of ADHD that affects the cognitive deficit of the brain. Zinc supplementation (Zn) can improve the symptoms of ADHD by increasing dopamine transporters binding. The aims of this study is to compare the level of Pb and Pb to Zn ratio on the subject of ADHD and normal children.

Method: This is an observational analytic study with case control design on 44 respondents. Statistical analysis using non-parametric test Man Witney.

Result: There is no significant difference of Pb level in children with ADHD and normal children with p = 0,431 and there is a significant difference of Zn level in ADHD and normal children with p = 0,011 and significant difference in Pb to Zn ratio with p = 0,015.

Keyword: *Lead (Pb), Zinc (Zn), Ratio Pb to Zinc (Zn) , ADHD*

BACKGROUND

Exposure to lead (Pb) in the environment has a neurotoxic effect resulting in behavioral disorders and cognitive deficits[1]. For decades there has been considerable effort to reduce lead levels in the environment[2]. Lead may adversely affect cognitive disorders, decreased IQ scores, learning disabilities in mathematics, reading and verbal memory [3].

Metaanalysis study by Goodlad et al concluded that the diagnosis of ADHD is increasing, thus attracting researchers to analyze the factors of heavy metals as factors causing ADHD[4]. Lead is the most responsible for mental disorders and thus requires clinical attention[5]. In humans, small amounts of metal can adversely affect health and psychological disorders such as ADHD[6].. Pb adversely affects the child in the form of mental retardation disorder and impulsivity[5,7-9]. Pb exposure is more common in hair than blood. Pb levels in hair tend to be more sedentary and reflect Pb levels in the subjects compared with temporary blood[10-15]. While the trace elements Zinc (Zn), is an essential nutrient in animals and humans[16,17]. In ADHD children it is suspected that there is a decrease in Zinc levels that cause concentration and attention disorder [11,18]. The impact of high lead levels and low levels of Zinc can lead to impaired cognitive function and learning disabilities in children[19]. Measurement of Pb and Zinc levels in hair and Zinc to Pb ratio is expected to help reduce the risk of ADHD severity[11]. Zinc plays an important role in the metabolism of neurotransmitters and prostaglandins, by maintaining the function and structure of the brain. Dopamine plays an important role in the pathophysiology of ADHD and the melatonin hormone plays an important role in the regulation of

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dopamine, as of the administration of Zinc is expected to improve ADHD symptoms. Zinc levels of children with ADHD are thought to be lower than normal children. With the administration of Zinc supplementation, it will be able to correct the existing disorder[17,20,21].

METHOD

This is a a case control study in grade 1 to grade 6 students of Bina Karya Elementary School Surabaya. With the use of random sampling formula, we get the number of samples of 23 ADHD subjects and 21 non ADHD subjects who meet the inclusion criteria. The inclusion criteria of the study were ADHD patients aged 6-12 years old, mothers of ADHD patients with minimum junior high school education, able to communicate using Indonesian, cooperative, and did not experience severe psychosocial stressors.

Examination of lead and zinc levels were used hair samples by Atomic Absorption Spectrophotometry (AAS) method. Abbreviated Conners Teacher Rating Scale is used to assess ADHD scores. This scale was developed by C. Keith Conners, Ph.D. While the validity and reliability in the Indonesian has been done by Sasanti Juniar in 1999.

To assess the psychosocial stressors, it used Social Readjustment Rating Scale by Holmes and Rahe (1967).

RESULTS

Table 1 Mother and respondent demographic data

		ADHD Category			
	Normal		ADHD		
	Frequency	%	Frequency	%	
Gender	Girl	6	28,57%	7	30,43%
	Boy	15	71,43%	16	69,57%
Occupation	Not occupied	16	76,19%	15	65,22%
	Occupied	5	23,81%	8	34,78%
Income	<1.000.000 / month	11	52,38%	19	82,61%
	1.000.000-3.000.000 / month	6	28,57%	3	13,04%
	>3.000.000 / month	4	19,05%	1	4,35%
Husband and wife relationship	Poor	0	0,00%	3	13,04%
	Good	21	100,00%	20	86,96%
Relationship among family member	Poor	0	0,00%	5	21,74%
	Good	21	100,00%	18	78,26%
Maternal age	25-31 y.o	1	4,76%	2	8,70%
	32-38 y.o	9	42,86%	5	21,74%
	39-45 y.o	8	38,10%	11	47,83%
	46-52 y.o	2	9,52%	4	17,39%
	53-59 y.o	1	4,76%	1	4,35%
Children age	≤12 tahun	19	90,48%	22	95,65%
	> 12 tahun	2	9,52%	1	4,35%

The results in table 1 show 44 respondents consisting of 23 respondents ADHD and 21 respondents non ADHD. From the age of children found the most age is less than 12 years with a percentage of 46.3% in non-ADHD respondents and 53.7% of ADHD respondents. The order of the most children is the first child of 56.52%.The highest maternal education in ADHD and non ADHD respondents was others each was 11 (50%). Maternal age in respondents ADHD mostly in the range 39-45 years of 11 people (57.9%), while the mother of respondents non ADHD as many as 9 people (64.3%). Most mothers of ADHD and non-ADHD children do not work and with the most income is less than Rp 1000,000 per month. Husband and wife relationship is poor on the mother of ADHD respondents of 3 people (100%) and the relationship between family members is poor as many as 5 people.

Table 2. Statistical Analysis Results of Pb level, Zn level, and Pb to Zn ratio

	Median (Minimum – *maximum*)	**p value**
Pb on ADHD (n = 23)	10,74 (4,76-18,05)	0,431
Pb on non ADHD (n=21)	11,39 (4,78-24,08)	
Zn on ADHD (n = 23)	307,84 (82,75-511,96)	*0,011*
Zn on non ADHD (n=21)	177,55 (17,56-448,39)	
Pb/Zn on ADHD (n = 23)	0,03 (0,02-0,15)	*0,015*
Pb/Zn on non ADHD (n=21)	0,06 (0,02-0,22)	

significant p< 0,05

DISCUSSION

From the demographic data of the respondents, the result of the sample of ADHD, boys patients were 16 children and girls were 7 children. This result is consistent with previous findings that the prevalence of ADHD is greater in males in comparison between 3-4 boys versus 1 girl[22-24]. From the demographic characteristics of mothers that consist of age, education, occupation, and income, it is found that the age of mothers in ADHD children is majority older than mothers of non-ADHD children. This result is inconsistent with previous studies which concluded that the maternal age of ADHD children was younger than that of non-ADHD children[25]. This result can be obtained because the parents' knowledge of the problems is still low so they do not understand how to handle their children disorder.

The results of the research was the majority of mothers are other education, namely elementary and junior high school, this result obtained based on interviews that many mothers was married at a young age and can not continue to higher education because there is no cost and some others mothers experience pregnancy.

From the data about the occupation of the mother found that most mothers was unoccupied. In parent interviews it is found that most mothers should take care of their children at home because many father work outside as a driver, private employee and work as a handyman. This result is also in accordance with previous research that the mother of many ADHD children who have lost their job or can not work because they have to take care of their own ADHD child[25]. The results of maternal earnings working on mothers of ADHD and non-ADHD children were the largest in less than a million rupiah but the majority stated the results were sufficient. This result is because most of the respondents are Javanese who put togetherness, *gotong royong* and *nrimo* culture and emphasize the existence of life as flowing water surrender to God and shame to express the shortcomings[26,27].

Statistical analysis used Mann Whitney non parametric comparative test. The data were not normally distributed and there was no significant difference between Pb levels in ADHD and non ADHD children. This result is consistent with the theory that causes of ADHD this day is unclear. High levels of Pb may cause cognitive, emotional and behavioral disorders but Pb is not the determining factor that causes ADHD. This theory also corresponds to results in the field showing high Pb levels in non-ADHD subjects[28]. The results showed that Pb levels in ADHD respondents were lower than those for non-ADHD respondents but this condition still requires clinical attention because Pb is toxic and a global health problem in the environment and may

interfere with biochemical processes in the brain[29]. Lead exposure still requires more research because it is an important issue in the global health of the world, especially in developing countries[3,30].

There was a significant difference in Zinc levels in ADHD children and non ADHD. From the above results it can be considered to administer zinc on ADHD subjects. This result is consistent with the literature which states that in ADHD subjects there is deficiency or excess of Zn level[31]. Zinc plays an important role in protein and DNA synthesis, wound healing, bone structure and improvement of the immune system. Zinc deficiency may involve impaired growth, loss of hair, diarrhea, immune system decline and dermatitis[11]. Zinc deficiency also causes late growth process, late puberty, erectile dysfunction and hypogonadism in men. It is said that 5% of the world's population suffers from zinc deficiency[31]. Zinc is a trace element because the concentration in plasma is only about 12-16μM, in the body there are 2-4 grams of zinc with a majority in skeletal bone and muscle. The body does not store zinc and zinc intake is obtained from food. The recommended dosage for girls and boys ages 4 to 8 months is 5mg, 14 to 18 years of age in women by 9 mg and men by 11 mg[31]. The concentration of zinc persists constantly in hair, skin, heart, muscle, as in plasma, liver, bone and testes. Chronic zinc deficiency is more sedentary in hair than in plasma[31]. Zinc is an essential micronutrient of physiological metabolism. Zinc plays an important role in catalyzing enzyme activity, contributing to protein structure and gene expression regulation[20]. Other studies suggest excess zinc levels may also cause ADHD.

There was a significant difference between the ratio of Pb to Zn in ADHD and non ADHD children. From the examination there are differences in the ratio of Pb and Zn where the high Pb level come with lower Zn level. Chronic lead exposure adversely affects physical growth, development of the nervous system, memory impairment, learning disorders, cognitive deficits, psychological and behavioral disorders[5]. Infants and children are at high risk of lead pollution, with levels below 10 μg/100 ml may cause growth disturbance[29]. Much effort has been made to reduce lead exposure in infants and children. The chelation program is used as the ultimate management but the therapeutic process is risky, with 50% suffering the side effects of losing the minerals needs[13]. The chelation is also not useful in improving cognitive, behavioral and neurocognitive disorders[32]. Therapy on lead can increase the cytotoxicity and astrocyte activity. Lead exposure causes astrocyte damage. Lead can increase lysosomal density and nucleus inclusions, increase the area of reticulum of endoplasma, increase lactic dehydrogenase (LDH) damage, and decrease the levels of the sufydryl group that can be overcome by antioxidant administration. The lead deposit in astrocyte leads to the accumulation of protein in the endoplasmic reticulum, increased protein response, and breakage of cel cycles[29].

CONCLUSION

There was a significant difference between Zinc levels in ADHD and non ADHD subjects and Pb/Zn ratios in ADHD and non ADHD subjects.

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