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Zinc deficiency and school-age children's memories

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ABSTRACT

Zinc deficiency is associated with cognitive and motor delay in children. Moreover, it is associated with deficits in activity and attention in nutritional deficiency children. This study was conducted to evaluate the correlation between zinc deficiency with memory of children. A cross sectional study design was employed from June 1st to 30th, 2013 among school-age children in Klaten District, Central Java who met inclusion and exclusion criteria. Sixty five eligible children were assessed their health, socio-economic and nutritional status. Hemoglobin levels were measured by the standart cyanoblue method. Plasma zinc levels were analyzed with flame atomic absorption spectrophotometry (AAS). Short-term memory (STM) was measured using the instrument Wechsler Intellegence Scale for Children (WISC0 subtest Digit Span Memory Test and long term memory (LTM) was assessed using the recall of narrative. Independent t-test was used to compare the STM or LTM between groups of each independent factors. Linear regression analysis was used to determine the independent factors associated with the STM or LTM. The STM scores of the children with zinc deficiency (6.1 ± 1.3) was significantly higher than those with normal zinc level (10.7 ± 3.1) [p = 0.0004; 95%CI = -6.98 – (-2.14)]. However, the LTM for both group of the children were not significantly different (p = 0.658; 95%CI = -3.16 – 2.01). A significant correlations between zinc levels, hemoglobin level and socio-economic status with the STM scores were observed (p < 0.05), whereas nutritional status was not (p > 0.05). In contrast, no significant correlations between zinc levels, hemoglobin levels, socio-economic status, nutritional status and the LTM scores was observed in the school age children (p > 0.05). In conclusion, zinc deficiency is associated with STM loss in the school age children, however it is not associated with LTM loss. Moreover, hemoglobin level and socio-economic status are found to be independent factors for STM loss, however they are not independent factors for LTM loss.

ABSTRAK

Defisiensi zink dikaitkan dengan keterlambatan perkembangan motorik dan kognitif pada anak. Defisiensi zink juga dikaitkan dengan penurunan aktivitas dan perhatian pada anak-anak yang kekurangan gizi. Penelitian ini dilakukan untuk mengkaji hubungan antara defisiensi zink dengan memori anak usia sekolah. Penelitian *cross sectional* dilakukan mulai 1 sampai 30 Juni 2013 pada anak usia sekolah di Kabupaten Klaten, Jawa Tengah. Sebanyak 65 anak yang memenuhi kriteria inklusi dan eksklusi diukur status kesehatan, sosial ekonomi dan nutrisinya. Kadar hemoglobin diukur dengan metode *cyanoblue*. Kadar zink plasma ditetapkan dengan *flame atomic absorption spectrophotometry* (AAS). Memori jangka pendek (STM) diukur dengan alat *WISC subtest Digit Span Memory Test* dan memori jangka panjang (LTM) diukur dengan mengingat cerita. Uji-t independen dilakukan untuk membandingkan STM dan LTM berdasarkan kadar zink, kadar hemoglobin, status sosial ekonomi dan nutrisi anak antar kelompok masing-masing faktor independen. Uji regresi linear dilakukan untuk mengevaluasi hubungan faktor independen dengan STM dan LTM. Nilai STM anak dengan defisiensi zink (6,1 ± 1,3) lebih tinggi bermakna dibandingkan anak dengan kadar zink normal (10,7 ± 3,1) [p = 0,0004; 95%CI = -6,98 – (-2,14)]. Namun demikian, nilai LTM pada kedua kelompok anak tidak menunjukkan perbedaan bermakna (p = 0,658; 95%CI =

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-3,16 – 2,01). Terdapat hubungan bermakna antara kadar zink, kadar hemoglobin dan status ekonomi dengan nilai STM ($p < 0.05$), namun demikian status nutrisi tidak menunjukkan hubungan bermakna ($p > 0.05$). Sebaliknya tidak terdapat hubungan bermakna antara kadar zink, kadar hemoglobin, status ekonomi dan gizi dengan nilai LTM ($p > 0.05$). Dapat disimpulkan, defisiensi zink berhubungan dengan kehilangan STM pada anak sekolah, namun demikian tidak berhubungan dengan kehilangan LTM. Selanjutnya, kadar hemoglobin dan status ekonomi terbukti sebagai faktor independen terhadap kehilangan STM, namun bukan terhadap kehilangan LTM.

Keywords: zinc deficiency - short-term memory - long term memory - school-age children - anemia

INTRODUCTION

Zinc deficiency is a major public health problem in many developing countries including Indonesia. Although severe zinc deficiency is considered rare, mild-to-moderate zinc deficiency is likely prevalent throughout the world today. In India, the prevalence of zinc deficiency in children was 43.8-73.3%.[1,2] In China, the high prevalence of zinc deficiency (38.2%) in preschools children was reported by Liu.[3] In Southeast Asia the prevalence of zinc deficiency in population was estimated to be 71.2%.[4] In West Java, Indonesia the prevalence of zinc deficiency in children of breastfeeding mothers was 17%.[5] However, in Nusa Tenggara Miller *et al*.[6] reported that 50% of children were zinc deficient.

Zinc is a trace mineral to all organims due to its important role in gene expression, cell development and replication.[7,8] Zinc is known to serve as the active center of about 300 enzymes, and is an essential trace element in humans.[9] Symptoms and diseases caused by Zn deficiency has been defined, as condition characterized by anorexia, growth retardation, skin disorders, alopecia, gonadal hypofunction, delay wound healing, impaired immune function, hypogeusia, pica, depression, ataxia, reduced glucose tolerance, increase incidence of ischemic heart disease, increase carcinogenesis and abnormal pregnancy.[9,10]

Zinc deficiency can influence multiple organ systems especially when it occurs during a time of rapid growth and development, such as infancy, when nutritional demands are high.[8] Zinc deficiency has been directly associated with cognitive and motor delay in children. Moreover, zinc deficiency may be associated with deficits in activity, attention, and motor development that commonly occur in nutritional deficient children.[10]

The purpose of this study was to evaluate the correlation between zinc deficiency with memory of school-age children. Furthermore, factors that influence the zinc deficiency in the school-age children were also reported.

MATERIALS AND METHODS

Subjects

A cross sectional study design was employed from June 1 to 30, 2013 to evaluate the correlation between zinc deficiency and memory among school-age children in Klaten District, Central Java, Indonesia who met inclusion and exclusion criteria. The inclusion criteria for this study were a) the primary school children aged 9-12 years and b) children who had breakfast. The exclusion criteria were a) the child was sick such as diarrhea, ARI in the last 3 days; b) has a history of head injury, and c) in the course of treatment/drug consumption.

Procedures

Eligible school-age children were recruited and parents were invited to participate in the study. An explanation concerning the procedure and prupose of the study was informed to the parents. After

written informed consent was obtained from the parents, children were assessed their health, socio-economic and nutritional status. Socio-economic status was assessed based on income obtained by their parents. The results of the assessment were classified based on poverty threshold in Central Java proposed by Indonesian Central Agency of Statistics in September 2012. Nutritional status assessment was based on Body Mass Index (BMI) according to the age. Cut off value for the classification of nutritional status was measured according to Ministry of Health, Republic of Indonesia.[11]

Five mL venous blood sample was taken from the children using a closed tube heparinized and centrifused to obtain the plasma. Plasma samples were immediately stored at -20 ^{o}C until analysis. Plasma hemoglobin levels were measured by the standard cyanoblue method. Plasma zinc concentrations were analyzed with flame atomic absorption spectrophotometry (AAS) using trace-element free procedures.

Short-term memory was measured using the instrument WISC subtest Digit Span Memory Test, namely Digital-Span Forward and Backward Digital-Span. Assessment of LTM was performed using the recall of narrative/ story. In this assessment, children were asked to respond in writing after listening to a story. Recall of the memory was conducted twice, first one was 15 minutes after listening to the story and the second one was after two weeks later. The protocol of the study was approved by the Medical and Health Research Ethics Committee, Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta.

Statistical analysis

Data were presented as the mean ± standard deviation (SD) or the frequency distribution. The independent t-test was used to comparison the STM or LTM between groups of the each independent factors for the STM or LTM i.e plasma zinc level, hemoglobin level, socio-economic status and nutritional status of the children. Multivariate linear regression analysis was used to determine the independent factors associated with the STM or LTM. A p-value less than 0.05 was considered to be statistically significant. All analyses were performed using the SPSS computer software.

RESULTS

Sixty five eligible school-age children were involved in this study. The characteristics of the school-age children are presented in TABLE 1. Most school-age children had normal serum zinc level (89%), normal blood hemoglobin level (97%), high socio-economic status (80%) and normal nutritional status (63.1%).

TABLE1. The characteristics of the school-age children

Variables	n	Mean ± SD or %
Age (years)	65	10.65 ± 0.73
Body weight (kg)	65	32.10 ± 10.23
Body height (cm)	65	138.29 ± 7.97
Body mass index (kg/m2)	65	16.52 ± 3.92
Zinc level		
• Deficiency	7	10.8
• Normal	58	89.2
Hemoglobin level		
• Anemia	2	3.1
• Normal	63	96.9
Socioeconomic status		
• Low	13	20
• High	52	80
Nutritional tatus		
• Not Normal	24	36.9
• Normal	41	63.1

The STM and LTM scores of the school age children with zinc deficiency and those with normal zinc level are presented in TABLE 2.

The STM scores of the children with zinc deficiency (6.1 ± 1.3) was significantly higher compared to those with normal zinc level (10.7 ± 3.1) [p=0.0004; 95%CI= -6.98 – (-2.14)]. However, the LTM of the both group of the children were not significantly different (p=0.658; 95%CI= -3.16 – 2.01).

TABLE 2. The STM and LTM scores of school-age children with zinc deficient and those with normal zinc level

Variable	STM Mean ± SD	Δ mean	t	p (95% CI)	LTM Mean ± SD	Δ mean	t	p* (95% CI)
Zn level								
• Deficiency	6.1 ± 1.3	-4.6	-3.8	0.0004 -6.98 – (-2.14)	7.8 ± 3.0	-0.57	-0.01	0.658 -3.16 – (2.01)
• Normal	10.7 ± 3.1				8.4 ± 3.2			

** t-test with a significance level p<0.05*

The STM and LTM scores of the school age children based on the hemoglobin level, socio-economic status and nutritional status are presented in TABLE 3. The STM scores of the children with anemia (15.0 ± 3.6) was significantly higher compared to those with normal hemoglobin levels (10.0 ± 3.2) (p=0.010; 95%CI= 17.27 – 8.77). Moreover, the STM scores of the children with low socio-economic status (8.3 ± 3.2) was significantly lower compared to those with high socio-economic status (10.7 ± 3.2) [p=0.019; 95%CI= -4.37 – (-0.39)]. However, the STM of school-age children with not normal nutritional status (10.2 ± 3.0) was not significantly different compared to those with normal nutritional status (10.2 ± 3.5) [p=0.99; 95%CI= (-1.73)- 1.71]. In contrast, the LTM of the children was not influenced by hemoglobin level, socio-economic status and nutritional status (p>0.05).

TABLE 3. The STM and LTM scores based on the hemoglobin level, socio-economic and nutritional status

Variable	STM Mean ± SD	Δ mean	t	p (95% CI)	LTM Mean ± SD	Δ mean	t	p* (95% CI)
Hemoglobin								
• Anemia	15.0 ± 3.6	5	2.67	0.0096 (1.27-8.77)	10 ± 2	1.71	0.90	0.372 [-2.09 – (5.51)]
• Normal	10.0 ±3.2				8.3 ± 3.2			
Socio-economic status								
• Low	8.3 ± 3.0	-2.4	-2.39	0.019 [-4.37-(-0.39)]	6.9 ± 2.9	-1.81	-1.85	0.068 [-3.76 – (0.14)]
• High	10.7 ± 3.2				8.7 ± 3.2			
Nutritional status								
• Not normal	10.2 ± 3.0	-0.01	-0.01	0.99 [-1.73-(1.71)]	8.4 ± 3.2	0.01	0.01	0.991 [-1.65-(1.67)]
• Normal	10.2 ± 3.5				8.4 ± 3.2			

The association between independent and external variables the STM and LTM scores in the school age children are presented in TABLE 4 and 5. Although plasma zinc level, hemoglobin level, socio-economic status, nutritional status were chosen to be analyzed in multivariate stepwise liniear regression, only zinc levels, hemoglobin levels and socio-economis status were found to be independent factors for STM deficits. A significant correlation between zinc level, hemoglobin level and socio-economic status with the STM scores were observed in the school age children ($p<0.05$), whereas nutritional status was not ($p>0.05$).

In contrast, plasma zinc levels, hemoglobin levels, socio-economic status, and nutritional status were found not to be independent factors for LTM deficits. No significant correlation between zinc levels, hemoglobin levels, socio-economic status, and nutritional status with the LTM scores was observed in the school age children ($p>0.05$).

TABLE 4. The association between plasma zinc level, hemoglobin level, socio-economic status, nutritional status and the STM score of school age children

Variable	Model 1 Coefisien /95% CI	Model 2 Coefisien /95% CI	Model 3 Coefisien /95% CI	Model 4 Coefisien /95% CI	Model 5 Coefisien /95% CI
Zinc level	-4.6* [-6.98 – (-2.14)]	-4.4* [-6.70 – (-2.01)]	-4.2* [-6.37 – (-1.97)]	-4.4* [-6.64 – (-2.08)]	-5.94* [-8.91 –(-2.97)]
Hemoglobin level			6.1* 2.19 – 10.1	4.4* 1.0 – 7.74	6.56* 0.90 – 12.20
Socio-economic status		-2.1* [-3.95 – (-0.32)]	-1.9* [-3.62 – (-0.20)]	-1.9* [-3.69 – (-0.18)]	-3.16* [-5.51 – (-0.80)]
Nutritional status				-0.83 -2.30 – 0.64	-1.38 -3.10 – 0.33
Zn-socio-economic status interaction					3.66 -1.69 – 9.00
Zn-nutritional status interaction					4.88 -1.55 – 11.32
Hemoglobin-nutritional status interaction					-3.11 -10.12 – 3.89
Socio-economic-nutritional status interaction					2.60 -1.28 – 6.48
Constanta	10.7	11.1	10.9	11.2	4.52
R^2	0.18	0.25	0.35	0.33	0.39
n	65	65	65	65	65

**significant with p value <0.05*

TABLE 5. The association between plasma zink level, hemoglobin level, socio-economic status, nutritional status and the LTM score of school-age children

Variable	Model 1 Coefisien /95% CI	Model 2 Coefisien /95% CI	Model 3 Coefisien /95% CI	Model 4 Coefisien /95% CI	Model 5 Coefisien /95% CI
Zinc level	-0.6 -3.16 – 2.00	-0.5 -3.06 – 2.10	-0.3 -2.88 – 2.22	0.58 -0.36 – 0.48	-1.29 -4.77 – 2.20
Hemoglobin level		2.7 -1.97 – 7.29	2.3 -2.25 – 6.91	0.32 -0.30 – 0.94	0.96 -5.66 – 7.59
Socio-economic status			-1.7 -3.68 – 0.28	-0.25 -0.58 – 0.68	-3.18* [-5.94 – (-0.42)]
Nutritional status				-0.0002 -0.27 – 2.20	-0.68 -2.70 – 1.33
Zn-socio-economic status interaction					3.93 -2.35 – 10.20
Zn-nutritional status interaction					-0.07 -7.62 – 7.48
Hemoglobin-nutritional status interaction					0.68 -7.54 – 8.90
Socio-economic-nutritional status interaction					2.83 -1.72 – 7.38
Constanta	8.4	8.3	8.7	8.77	9.0
R^2	0.003	0.02	0.07	0.06	0.103
n	65	65	65	65	65

**significant with p value <0.05*

DISCUSSION

This study showed that zinc deficiency was associated with STM deficits in the school-age children. The STM score of the children with zinc deficient was significantly higher compared to the children with normal zinc levels. Moreover, hemoglobin levels and socio-economic status were found to be external variables that affected the STM score of the children. Further analysis using linear regression test showed a significant correlation between zinc deficiency and the STM score of the children.

This result is in accordance to previous studies. A study in India conducted by Umamaheswari *et al*.[12] showed that zinc deficiency is associated with STM of children in the age group of 6-11 years. Furthermore, supplementation with zinc was able to improve only non-verbal form of memory. However, it was not able to improve IQ scores of the children. It was also reported that zinc deficiency interfered with academic performance among elementary school-age children.[13] Zinc deficiency has been directly associated with impairment of cognitive and motor function in children. Moreover, zinc deficiency may be associated with deficits in activity, attention, and motor development that commonly occur in nutritional deficient children.[8,10]

Several investigators have contributed to understanding the mechanisms responsible for the

role of zinc in impairment of cognitive development. However, the mechanisms linking zinc deficiency with cognitive development remains unclear. Zinc is an essential trace element in humans due to its function as essential catalytic component of about 300 enzymes.[9] Many of these enzymes are clearly needed for normal DNA replication and cellular proliferation. Other zinc dependent enzymes also play important role in normal central nervous system function. In addition, zinc plays an essential structural role in nuclear receptors that involved in cellular proliferation, brain development, and neurogenesis.[13] Therefore, zinc deficiency might have implications for brain development, cognition and the mood regulation. It appears that zinc deficiency may lead to deficits in children's neuropsychologic functioning, activity, or motor development, and thus interfere with cognitive performance.

This study showed that the hemoglobin levels contributed to STM deficits in the school-age children. The STM score of the children with anemia was significantly higher compared to the children with normal hemoglobin levels. Moreover, a significant negative correlation was also observed between hemoglobin levels and the STM score. The interaction of iron and zinc has been suggested by several authors in experimental animals and observations in human.[14] Competition in the iron and zinc absorption has been reported. High iron levels might decrease the ability of zinc absorption. Furthermore, it might cause impairment of STM memory of the children with high hemoglobin levels. This study is also in aline with the study conducted by Black[15] which reported that zinc deficiency can increase tissue iron levels lead to the oxygen release and caused the tissue damage.

This study also showed that the socio-economic status contributed to STM deficits in the school-age children. The STM scores of the children with low socio-economic status was significantly lower compared to that of the children with high socio-economic status. Moreover, a significant positive correlation was also observed between hemoglobin level and the STM score. Rosmalina,[16] reported that zinc deficiency are common in lower socio-economic communities in rural areas. This condition occured due to the limitations of the public to access and meet the food which containing high levels of zinc in their daily foods.[17]

In contrast, this study showed that zinc deficiency was not associated with the LTM deficits in the school-age children. Moreover, the LTM of the children was not also affected by hemoglobin levels, socio-economic status and nutritional status. Further analysis using linear regression test showed no correlation between zinc deficiency, hemoglobin levels, socio-economis status and nutritional status with the STM score of the children. Nilawati *et al.*[18] reported that nutritional status did not affect cognitive development in children under two years old. Furthermore, Kretsch *et al*.[19] showed that long-term diet significantly slowed simple reaction time, but did not reduce the ability of attention, motor performance or memory obese adult women. It was also reported that calorie restriction or dieting was not associated with a consistent pattern of cognitive impairment.[20] The LTM loss is more affected by irreversible structural and functional damage of brain rather than the nutritional status. The possible causes of the LTM loss include traumatic brain injury and neurodegenerative diseases such as Alzheimer's disesase, dementia, Huntington's disease, multiple sclerosis, Parkinson's disease and schizophrenia.[21]

CONCLUSION

In conclusion, zinc deficiency is associated with STM loss in the school age children in Klaten, however it is not associated with LTM loss. Moreover, hemoglobin level and socio-economic status are found to be independent factors for STM loss, however they are not independent factors for LTM loss.

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