Correlation of zinc level and cognitive in obese children

I Made Yullyantara Saputra\textsuperscript{a},* , I Gusti Lanang Sidiartha\textsuperscript{b} , I Putu Gede Karyana\textsuperscript{c}

\textbf{ABSTRACT}

\textbf{INTRODUCTION}

Obesity is a global health problem. Based on the WHO (World Health Organization), the obesity rate reaches 300 million people. Obesity in children reaches 17.6 million in children under 5 years old. The prevalence of obesity in children increases from year to year in developed and developing countries. In the United States, a survey of the NCHS (National Center for Health Statistics) obesity prevalence in children increased significantly from 5.2\% to 16.9\% in the period 1974-2012, the prevalence of obesity was higher in women 17.2\% compared to men 14.5.\textsuperscript{1} In Southeast Asia the prevalence of obesity ranges from 4\% -5.3\%, with the highest prevalence in the country of Malaysia, which is 8.8\% (7.1\% -10.7\%), while in Indonesia it ranges from 6\% (5.3\% -8.2\%).\textsuperscript{2}

One of the comorbidities that occurs is obesity can reduce cognitive. A research conducted in Brazil showed cognitive in obese patients examined by IGT (Ioa Gambling Task) tests to measure memory and concentration obtained values $F = 1.79$ when compared with not obese.\textsuperscript{3} Obese patients showed structural changes in the brain, namely a decrease in hippocampal volume which is the center for learning and memory, compared to healthy children. Obese children are often found with low zinc levels. This study aimed to prove there is positive correlation between zinc levels and cognitive in obese children.

\textbf{Methods:} This was a cross sectional study with consecutive sampling to 88 obese children aged 6-12 years old in primary school. Data collected include age, sex, weight, height, physical activities, zinc, and cognitive score. Data analysis performed with multivariate test which is linear regression analysis, and correlation test.

\textbf{Results:} We analyzed 88 subjects with obesity in this study. The result showed positive correlation between zinc levels and cognitive, in which $r = 0.6$ and $p < 0.01$. Multivariate analysis used linear regression to assess the pure correlation between zinc and cognitive, the analysis showed that the correlation between zinc and cognitive is $\hat{a} = 0.836$ points.

\textbf{Conclusion:} This research proved that there is a strong positive correlation between zinc levels and cognitive in obese children.

\textbf{Keywords:} Children, zinc, cognitive, obesity.


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\textbf{ABSTRACT}

\textbf{Introduction:} Obesity is a global health problem. The World Health Organization (WHO) stated that obesity reached 300 million people. Obesity can cause numerous comorbidities; one of them is decrease in cognitive ability. Patients with obesity show a structural change in the brain, which is the decrease in hippocampus volume, which is the center for learning and memory, compared to healthy children. Obese children are often found with low zinc levels. This study aimed to prove there is positive correlation between zinc levels and cognitive in obese children.

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and low birth weight, problem in hearing and traumatic brain injury.

Subjects who fulfill the inclusion and exclusion criteria, checked for zinc serum levels and cognitive using raven test. This study was approved by the Research Ethics Committee of Udayana Medical School, Sanglah Hospital, Denpasar.

Subjects were consecutively enrolled until completing the required sample size. Sample size calculation using the formula based on consideration of analytic, numeric correlation, with alpha 0.05, power 80, and r = 0.3. According to this, the minimum sample size was 88.

Obesity was classified if BMI ≥ percentile 95 according to age and sex of the child. Zinc levels are zinc levels in serum subject as measured by quantitative particle enhanced immunoturbidimetric assay. We determined the cut off point of zinc level is 70 mmol/L from the previous study.

Data obtained were analyzed by computer program. Data analysis was done with subject characteristics that were presented descriptively in the form of tables and narratives. Bivariate analysis performed using Pearson correlation to assess the correlation between zinc levels and cognitive in obesity. Multivariate analysis done with logistic regression (ENTER method) between various confounding variables. The entire statistical test was performed by using SPSS ver.21 where p values < 0.005 were considered as significant.

RESULT

This research was conducted for 6 months, from July to December 2018 at nine elementary schools in Denpasar and Badung. During the study period there were 102 obese children, 7 children refused to take blood, four blood samples underwent lysis, and 3 children were not present at the IQ test because of illness, so that 88 obese children met the inclusion criteria.

From the characteristics of the study, we obtained male subjects of 52.3%. The mean age was 9.9 years. The average calorie, protein, and fat intake were 2359 kcal/day, 91 gr/day and 61.8 gr/day, respectively. The average physical activity of children is based on the Baecke questionnaire was 6.01, which is mild physical activity (Table 1).

The mean zinc level was 58.1 mmol/L and as many as 73 (83%) children had zinc deficiency (Figure 1). The IQ scores of children is normal 90.7 points, as many as 45 (51.2%) children have IQs below normal.

Pearson correlation test was used because the data distribution was normal. Data analysis showed a strong positive correlation between zinc levels and cognitive values with r = 0.605 and p < 0.01. Furthermore, a linear regression test was conducted to determine the effect of zinc on cognitive values, with R² = 0.367 and coefficient beta of 0.864 (CI 95% 0.62-1.10) (Table 2).

DISCUSSION

Concentration of zinc in the brain increases with the process of growth from birth and the concentration of zinc is kept constant in the brain. About 90% of the total zinc in the brain is zinc metalloprotein. While the rest is in presynaptic vesicles and is histochemically reactive. Zinc levels in this study ranged from 43 to 74 mmol/L with a mean of 58.1 mmol/L. Zinc levels in obese children lower than normal children (43 mmol/L versus 85 mmol/L).

The mechanism of low zinc levels in obesity is still unclear, some theories said due to the low activity of the superoxide dismutase enzyme, this enzyme plays a role in the uptake of zinc from extracellular to intracellular, besides it is believed the hypothalamus gets a signal that in obesity, the body is in good nutrition so that absorption of zinc in the intestine will be reduced. In obesity, the leptin was found in high levels. High leptin levels are believed to inhibit zinc absorption but the mechanism is still unclear. This is evidenced by the high level of zinc which is

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<td>Age, years, mean (SD)</td>
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<td>Physical activity, mean (SD)</td>
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<th>Table 2. The effect of zinc on cognitive values</th>
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discretion in the urine of obese children.\textsuperscript{13}

The cognitive value of this study was obtained from IQ scores, the average IQ score in this study was 90.7 (normal). IQ values are grouped into 6, which are intelligent, normal, normal, normal, below and below normal. In this study no children with superior IQ were found (121-131 points), 45 children with abnormal IQ scores (51.2%) with details of IQ below normal (66-79 points) as many as 21 children (23.9%), lower normal (80-90 points) as many as 24 children (27.3%). The other research found cognitive scores were within the normal range (± 1 z-score), but the obese group had lower attention (ES: 0.41, CI: 0.17-0.64; p < 0.001) and impulsivity higher (ES: 0.39, CI: 0.15-0.62; p = 0.03).\textsuperscript{14} Research found that obese children have a negative correlation with IQ (total IQ / T-IQ, verbal IQ / V-IQ, and IQ / P-IQ performance), in obese children, V-IQ is significantly correlated with onset of obesity (r = 0.335, p = 0.05), while P-IQ and T-IQ correlated with BMI (r = −0.341, p = 0.03). Research conducted in Denmark found that the risk of atrophy in the brain increases with the increase of BMI, with the risk of atrophy of 13 to 16% per 1.0-kg/m² increase in BMI.\textsuperscript{15}

This study showed a strong positive correlation between zinc levels and cognitive values with r = 0.605 and p < 0.01. The results of linear regression show the magnitude of the effect of zinc on cognitive (IQ) was 0.367 (37%) with p < 0.01. These results are reinforced by multivariate analysis with the aim of assessing the relationship of pure zinc levels with cognitive values, after taking into account all those suspected of being confounding variables. Some research showed that zinc increased VIQ only in the information subtest (p = 0.009). The effect of zinc supplementation was more significant in relation to PIQ, because this score increased in terms of image completion, image arrangement, block design, and object assembly (p = 0.0001, for all subtests).\textsuperscript{16} The meta-analysis study found no significant overall effect of zinc intake on cognitive function index, in which intelligence, mean difference < 0.001 (95% CI -0.12-0.13) p = 0.95; executive function 0.08 (95% IK, -0.06-0.022) p = 0.26; and the average difference in motor skills was 0.11 (95% CI -0.17-0.39) p = 0.43.\textsuperscript{17} There are several small indicators of improvement in aspects of executive function and motor development after zinc supplementation but further research is needed to investigate this. Zinc supplementation over a period of time can improve cognitive verbal memory scores increased by 3.4 ± 2.5 after zinc supplementation was given for 3 months.\textsuperscript{8}

Zinc can improve cognitive ability because zinc is needed to arrange neurons. Zinc plays a role in synaptic neurotransmission in the mammalian brain, zinc acts as an endogenous neuromodulator of several important receptors including Gamma-Amino-Butiric-Acid (GABA) and N-methyl-D-Aspartate (NMDA) receptors. Apart from being a neurotransmitter, zinc also plays a role in brain maturation. Lots of zinc is needed for cerebellar development compared to other areas in the brain, because growth and differentiation of the cerebellum takes place quickly after birth.\textsuperscript{18}

By increasing zinc levels, some research showed we are able to restore communication significantly in the hippocampus region to improve learning and memory skills. The results of this study conducted in mice can be extrapolated to humans because zinc is known to play the same role in the brains of both species. Other research found that zinc supplementation in obesity can increase zinc serum, and reduce insulin resistance. Long-term insulin resistance can damage the blood brain barrier function and insulin activity. Insulin resistance causes exposure to long-term neurons to high levels of insulin which causes neuronal degeneration and causes irreversible memory damage, zinc intake as soon as possible can prevent further degradation of neurons.\textsuperscript{19}

CONCLUSION

The result of this study proved that zinc levels below <70 mmol/L strongly correlate with low cognitive level in obese children.

CONFLICT OF INTEREST

The author reports no conflicts of interest in this work.

ETHICAL CLEARANCE

This study have been approved by Ethical Committee of Faculty of Medicine, Udayana University/Sanglah Hospital Denpasar No. 424/UN.14.2/KEP/2018 and has obtained permission from Research and Development Unit of Faculty of Medicine, Udayana University/Sanglah Hospital Denpasar No. 2018.02.1.0029.

AUTHOR CONTRIBUTION

All authors fully contributed to the research and publication.

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