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Brain-derived neurotrophic factor levels and anemia in elementary school children

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ABSTRACT

Iron deficiency can cause BDNF deficits in some areas of the brain. BDNF has an essential role in brain function especially memory and learning and is reported to be low in Iron Deficiency Anemia (ADB) in animal studies. ADB is vulnerable in the age group of children. The purpose of this study was to analyze the relationship between levels of Brain-Derived Neurotrophic Factor (BDNF) with the incidence of anemia in elementary school children in Seluma District. This research is an analytical observational study with a cross-sectional study design conducted in April 2019 of 50 respondents of elementary school children aged 9-12 years in Seluma Regency. Venous blood sampling was performed to measure serum BDNF levels using the Enzyme-Linked Immunosorbent Assay (ELISA) method. Hb levels are measured using the Easy Touch tool. Statistical analysis using the Chi-square test. Based on the measurement results of serum BDNF levels obtained 46% of children have BDNF levels below the average (<3258,6084 ng / mL). Based on the results of Hb measurements, there are 30% of children with anemia. Bivariate analysis showed no significant relationship between BDNF levels with anemia (p> 0.05), the Prevalence Odds Ratio (POR) was 2,250. The staff of community health center can collaborate with schools to provide counseling about anemia and its effects on school children.

Kadar *brain-derived neurotrophic factor* dan anemia pada anak sekolah dasar

Kata kunci:
Anemia
Defisiensi Zat Besi
Brain-Derived Neurotrophic Factor
Anak Sekolah Dasar

ABSTRAK

Defisiensi zat besi dapat menyebabkan defisit BDNF di daerah tertentu dari otak. BDNF memiliki peran penting dalam fungsi otak khususnya memori dan pembelajaran dan dilaporkan rendah pada Anemia Defisiensi Zat Besi (ADB) dalam penelitian pada hewan. ADB rentan terjadi pada kelompok umur anak-anak. Tujuan penelitian ini adalah untuk menganalisis hubungan antara kadar Brain Derived Neurotrophic Factor (BDNF) dengan kejadian anemia pada anak Sekolah Dasar di Kabupaten Seluma. Penelitian ini merupakan penelitian obsevasional analitik dengan rancangan studi cross-sectional dilaksanakan pada bulan April 2019 terhadap 50 responden anak Sekolah Dasar yang berusia 9-12 tahun di Kabupaten Seluma. Dilakukan pengambilan darah vena untuk mengukur kadar BDNF serum dengan menggunakan metode Enzyme-Linked Immunosorbent Assay (ELISA). Kadar Hb diukur dengan menggunakan alat Easy Touch. Analisis

statistik menggunakan uji Chi square. Berdasarkan hasil pengukuran kadar BDNF serum diperoleh 46% anak mempunyai kadar BDNF di bawah rata-rata (< 3258,6084 ng/mL). Berdasarkan hasil pengukuran Hb terdapat 30% anak anemia. Analisis bivariat menunjukkan tidak ada hubungan yang bermakna antara kadar BDNF dengan anemia (p>0,05), Prevalence Odds Ratio (POR) adalah 2,250. Petugas Puskesmas dapat melakukan kolaborasi dengan pihak sekolah untuk memberikan penyuluhan tentang anemia dan dampaknya bagi anak sekolah.

Introduction

Anemia is defined as a body condition where the levels of hemoglobin (Hb) in the blood are lower than normal (WHO, 2011). Hemoglobin is one component in red blood cells/erythrocytes which has the function to bind oxygen and deliver it to all body tissue cells. Body tissue to perform its function requires Oxygen. Lack of oxygen in the brain and muscle tissue will cause symptoms, namely a lack of concentration and being less fit to do activities. Hemoglobin forms red blood cells/erythrocytes which are a combination of protein and iron (Kemenkes RI, 2016).

The most significant contributor to anemia is iron deficiency. About 50% of cases of anemia are caused by iron deficiency, but the proportion may vary between population groups and in different regions, this depends on local conditions (WHO, 2001). According to WHO anemia affects around 800 million children and women. Iron deficiency is the most widespread micronutrient deficiency in the world that often results in chronic iron deficiency or iron deficiency anemia (defined by WHO as a hemoglobin level <11g / dl) (WHO, 2015).

Globally low hemoglobin concentrations (anemia) affect 43% of children aged 5 years and 38% of pregnant women (Stevens et al., 2013). The prevalence of anemia in school-age children shows a fairly high rate globally at 37%, whereas in Thailand it is 13.4% and in India 85.5% (Khomsan, 2012). The results of the 2013 Basic Health Research (Riskesdas) in Indonesia, the proportion of anemia in school-age children (5-14 years) was 26.4% (Kemenkes, 2013). Iron deficiency anemia can affect cognitive and motor development, causing fatigue and low productivity (Balarajan *et al*., 2011).

Iron deficiency can cause BDNF deficits in some areas of the brain (Estrada, J.A., et al, 2014). BDNF has an important role in brain function especially memory and learning and is reported to be low in iron deficiency anemia in animal studies (Nassar, 2014).

The development of nerve cells or neurons occurs through neurogenesis, which is a process of producing functional neurons through precursors, which have traditionally been seen to occur only during the embryonic and perinatal stages in mammals (Ming & Song, 2011). The process of neurogenesis is very dependent on the group of proteins that spur growth, development, plasticity and endurance of neurons, this group of proteins is called neurotrophin. One such neurotrophin is Brain-Derived Neurotrophic Factor (BDNF) (Binder, D.K., Scharfman, H.E., 2008). BDNF is the most common growth factor in the Central Nervous System (CNS), which is important for CNS development and neuronal plasticity (Autry & Monteggia, 2012).

Anemia can also be caused by infectious diseases such as malaria. On the other hand iron deficiency seems to offer some protection against malaria, iron supplementation can increase the susceptibility of populations vulnerable to infection. As a result, the use of population scale iron supplementation in malaria endemic areas is currently very controversial. Iron deficiency anemia and malaria coexist in most tropical regions of the world. Malaria contributes to iron deficiency anemia by causing intravascular hemolysis with subsequent loss of iron hemoglobin in the urine (Miller, 2013).

Seluma Regency is one of the regencies in Bengkulu Province which ranks fourth in malaria endemic cases and has not yet received the title of malaria elimination (Dinas Kesehatan Provinsi Bengkulu, 2018). In addition to being still endemic in malaria, Seluma Regency is also included as the only lagging regency in Bengkulu Province based on Presidential Regulation No.131 of 2015 (Perpres, 2015). Oladeinde, et al (2012) stated that 81.9% of children infected with malaria parasites with a prevalence of anemia in children by 47.3% (Oladeinde BH et al., 2012). Malaria is a risk factor for developing anemia in children. Molecular epidemiological research on the relationship between BDNF levels and anemia in school children is still very limited. Therefore, further research is needed to analyze the relationship between BDNF levels and anemia in elementary school children in Seluma Regency.

The purpose of this study was to analyze the relationship between levels of *Brain-Derived Neurotrophic Factor (*BDNF) with anemia in elementary school children in Seluma Regency in 2019.

Method

This study is an analytic observational study using a *cross-sectional* study design. The population in this study were elementary school children recorded in Seluma District. The sample in this study were elementary school children in Seluma District who met the inclusion criteria and passed the exclusion criteria. The inclusion criteria in this study are: Elementary School children in grades 4-5 aged 9-12 years old

who have attended school at least one year and are willing to take part in the research. While the exclusion criteria in this study are suffering from chronic diseases (HIV, Hemophilia, Thalassemia); had menstruated and was not present at the time of the study.

The sampling technique in this study was by means of *Multi Stage Random Sampling*, beginning with the selection of districts based on the highest malaria incidence data in Seluma district, from 14 selected 5 sub-districts, namely Lubuk Sandi District, West Seluma District, East Seluma District, North Seluma District and Talo District. Furthermore, by using the simple random sampling method, 10 students from elementary schools in each subdistrict were selected who met the inclusion criteria so that finally obtained 50 samples of grades 4 and 5 aged 9-12 years.

This research was conducted after obtaining approval from the Health Research Ethics Committee of the Faculty of Public Health, Sriwijaya University No: 78 / UN9.1.10 / KKE / 2019. All study subjects were asked for *informed consent* before a blood draw was made to the respondent (students). Approval of the participation of respondents in this study was also requested from parents, because respondents were underage and were still under the supervision of parents.

Taking 2 mL venous blood sampling was performed by health analysts from the local health center who were competent to check BDNF and Hb levels. Measuring serum BDNF levels using the *Enzyme-Linked Immunosorbent Assay* (ELISA) method with Human BDNF ELISA KIT (Cat. No. E-EL H0010, Elabsience). After the measurement results are obtained the determination of the cut off point for BDNF levels is based on the average value. Furthermore BDNF levels are categorized into 2, which is below the average (<3258.6084 ng/mL) and above the average (>3258.6084 ng /mL). Measurement of hemoglobin levels with *Easy Touch*. Data analysis was performed using the SPSS version 19.0 program. The statistical analysis used was the *Chi Square test*.

Results and Discussion

Table 1
Frequency Distribution of Respondent Characteristics

Characteristics	Total	
	n = 50	%
Gender		
Male	21	42,0
Female	29	58,0
Age		
9 -10 year	34	68,0
>10-12 year	16	32,0
Father's Education		
Low (<SMA)	30	60,0
High (≥SMA)	20	40,0
Mother's Education		
Low (<SMA)	36	72,0
High (≥SMA)	14	28,0
Father's job		
Farmer/laborer	36	72,0
PNS/TNI/Police	3	6,0
Entrepreneur	11	22,0
Mother's job		
House wife	29	58,0
Farmer/laborer	15	30,0
Farmer/laborer	3	6,0
Entrepreneur	3	6,0

Table 1 shows the total research subjects were 50 respondents who met the inclusion criteria namely elementary school students grade 4 and 5 aged 9-12 years consisting of 21 men (42.0%) and 29 women (58.0%) with the most number is 9-10 years of age (68.0%). The majority of fathers' education is low (60.0%) with work generally as a farmer / laborer (72.0%). Mother's education is still largely low (72.0%) and the majority of occupational mothers are housewives (58.0%).

Table 2
Relationship of Serum BDNF levels with Anemic

BDNF Levels	Anemia Status				Total	*p-value*	*Odds Ratio*
	Anemia		Not Anemia				
	n	%	n	%	N		
Under Average	9	39,1	14	60,9	23	0,322	2,250 (CI= 0,655-7,734)
Above Average	6	22,2	21	77,8	27		

To find out whether there is a relationship between the independent variable and the dependent variable, a bivariate analysis is performed. In this study the bivariate analysis uses the *chi square test* because both the dependent and independent variables are categorical data.

Based on the results of measurements of serum BDNF levels found that 58% of children have BDNF levels above the average (> 3258.6084 ng/mL). However, the results of measurement of hemoglobin levels obtained 30% of children experience anemia. This result is higher when compared with the results of riskesdas in 2013 that the proportion of anemia in school-age children was 26.4% (Ministry of Health, 2013). However, the results of this study are similar to those of Prihatin and Irawati (2011) which state that anemic child is found at age 9 years (39.3%) and children aged 10 years (60.7%) (Concerned, A ., Irawati, A., 2011). This shows that anemia is not only influenced by BDNF levels. Mother's education can also affect the incidence of child anemia. In this study the majority of mothers had low education. According to Permaesih D. and Herman S. (2005) that there is a significant relationship between education level and anemia. A high level of education is expected to affect knowledge and information about better nutrition. Knowledge about nutrition will affect one's food consumption choices (Permaesih, D., Herman, S., 2005).

In this study it was found that there were 39.1% of anemic children with below-average BDNF levels and 22.2% of anemic children with above-average BDNF levels. From the results of statistical analysis, it was found that there was no significant relationship between BDNF levels and anemia with *p value* = 0.322 (p> 0.05). The *Prevalence Odds Ratio* (POR) is 2,250 (CI = 0,655-7,734) meaning that children with BDNF levels below the average will be at risk of anemia by 2,250 times compared with children who are above average (table 2).

The results of this study indicate that children who are anemia and not anemia do not have differences in BDNF levels. This study has the same results as a study conducted by Nassar, et al (2014) in Cairo Egypt of 27 children with anemia status which showed that BDNF levels were not significantly lower in children with iron deficiency anemia (Nassar, 2014). ADB has been found to affect brain metabolism, neurotrasmitter function and myelination (Madan, N., et al., 2011).

A recent study by Munoz and Humeras in humans and mice found that iron plays an important synaptic plasticity (SP), which can produce long lasting neurological consequences even after correction of Iron Deficiency. They show changes in the hippocampus, striatum, amygdale or prefrontal cortex, in addition to interactions between these systems. They found that cognitive changes correlate with changes in neural plasticity which are cellular substrates of memory and learning (Munoz, P., Humeras, A., 2012). In another study it was reported that iron deficiency can cause cognitive impairment by reducing the expression and function of IGF-I / II and BDNF in specific areas of the brain (Estrada, J.A., et al, 2014).

Anemia has proven to be a public health problem that affects low, middle and high income countries and has significant adverse health consequences, as well as negative impacts on social and economic development (Stevens et al., 2013). Iron deficiency anemia can affect cognitive and motor development, causing fatigue and low productivity (Balarajan et al., 2011).

Iron dependence can also have an effect on parasitic growth through a mechanism that is different from direct utilization by the parasite. Iron has many effects on the immune system (McDermid & Prentice, 2006). Some Plasmodium species, especially P. vivax, live special lives in young reticulocytes. Reticulocyte production can be limited to anemic hosts, and this has been proposed as a mechanistic explanation for a study showing an inverse relationship between severe anemia and P. vivax infection (Manning et al., 2012).

Conclusions and Recommendations

The proportion of anemia in elementary school students in Seluma Regency is 30%. Serum BDNF levels are not significantly associated with anemia in elementary school children. Children who have serum BDNF levels below average will be at risk of anemia by 2,250 times compared with children who have serum BDNF levels above average.

Staff of community health center can collaborate with the school to remember that the high prevalence of anemia among elementary school children in Seluma Regency is expected to the policy makers in Seluma District to develop an anemia prevention and prevention program by providing nutritional supplements along with iron prophylaxis, folic acid tablets for anemia prevention to school children, especially women who are preparing for menstruation. The school is expected to be able to work closely with related parties in schools such as UKS, BP teachers and related cross sectors such as Community Health Center and PKK (Dharma Wanita) to provide counseling about anemia and its effects on school children, nutritional counseling, reproductive health services in preventing anemia. Conducting a balanced nutrition program campaign for children in school so that a healthy eating pattern is achieved. The need for a healthy school canteen.

This study was limited to a *cross-sectional* study design with a relatively small number of samples. It is hoped that further research will be done with *case control* or experimental research designs so that BDNF levels can be compared between cases and controls.

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