IODINE DEFICIENCY ASSOCIATED WITH ADOLESCENT COGNITIVE PERFORMANCE IN ENDEMIC IODINE DEFICIENCY ENDEMIC AREA

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ABSTRACT

Background: Iodine deficiency is one of the most important public health problems today, especially among children and pregnant women who are considered the highest-risk groups. These diseases hinder the socio-economic development of the affected areas. This study aimed to determine iodine deficiency associated with adolescent cognitive performance in endemic iodine deficiency endemic area.
Subjects and Method: This was a cross-sectional study conducted in Bulu district, Temanggung. A sample of 120 adolescents range age 11-14 years old was selected by cluster sampling. The dependent variable was Cognitive performance. The independent variable was Iodine deficiency. The data were collected by questionnaire, measurement and assessment. This study was analyzed by multiple logistic regression.
Results: On cognitive performance. Adolescent IQs are below average (69.2%), mathematics tests (64.2%), and Indonesian language tests are below average (47.5%). A total of (30.8%) adolescents showed insufficient iodine intake, goiter enlargement (30.2%), stunting (35%), and anemia (20.8%). The linear regression model on IQ showed goiter enlargement as a factor associated with decreased IQ, even after accounting for confounding factors ($p = 0.013$; $R2 = 0.07$). Subjects with goiter enlargement had lower mean IQ (Mean = 10.32). IQ was related to Indonesian achievement ($p = 0.031$; $R2 = 0.13$), while UIE ($p = 0.031$), father's education ($p = 0.011$), and IQ ($p < 0.001$) were identified as factors related to math test scores ($R2 = 0.23$). After accounting for confounding factors.
Conclusion: Iodine deficiency is negatively associated with cognitive performance in areas of endemic infested iodine deficiency. Goiter enlargement, which is an indicator of long-term iodine deficiency status, correlates with IQ. UIE, which reflects current indicators of iodine deficiency status, affects academic achievement. The cognitive impact of iodine deficiency lasts into adolescence. Therefore, ensuring adequate iodine intake in adolescents is essential to optimize their cognitive performance.

Keywords: cognitive performance, iodine deficiency, early adolescence, nutrition, nutrition

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BACKGROUND

Dunn (2003) stated that iodine deficiency causes serious health effects throughout the developmental age, known as the spectrum of IDD (Hetzel, 2005). Delange (2001) and Hetzel (2000) stated that iodine deficiency's main impact is brain damage. Therefore the elimination of brain damage due to IDD is the target of a continuous IDD management program. Every year, 39 million newborns worldwide face the risk of decreased intellectual capacity due to iodine deficiency (Melse-boonstra and Jaiswal, 2010).

Iodine's importance as an essential micronutrient is due to its significant role in synthesizing thyroid hormones. Thyroxine (T4) and Triiodothyronine (T3) are very important in determining normal physical and

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mental development in animals and humans, in the formation and development of the brain, and in regulating body temperature. Deficiency in thyroid hormone will cause growth retardation and maturity in almost all organ systems (Kennedy, et al., 2003; Jayakrishnan and Jeeja, 2002; Hetzel, 1993).

The International Child Development Steering Group mentions cognitive stimulation, iodine deficiency, anemia, and stunting as the main risk factors for child failure in developing countries (Walker et al., 2011). Nutritional problems are a problem in the development cycle throughout the ages. Nutrition during growth is one of the determinants of intelligence. The WHO Department of Child and Adolescent Health states that attention to food during adolescence is still limited, except about pregnancy. Therefore, studies on adolescents are still needed, among others, to document nutritional status and micronutrients (Delisle, et al., 1999). The relationship between micronutrients and cognitive development in adolescents also needs clarification (Halterman, et al., 2003). WHO defines adolescence as the second decade of life, or aged between 10-19 years, with ages 10-14 years in their early adolescence (Zlotkin, 2003).

Based on the above background, the question arises, how is the relationship of iodine deficiency to the development of intelligence and learning achievement of adolescents? Does iodine deficiency status increase the likelihood that adolescents in IDD endemic areas will experience impaired cognitive development?

SUBJECTS AND METHOD

1. Study Design

This was a cross-sectional study conducted in Bulu district, Temanggung.

2. Population and Sample

A sample of 120 adolescents range age 11-14 years old was selected by cluster sampling.

3. Study Variables

The dependent variable was Cognitive performance. The independent variable was Iodine deficiency.

4. Study Instruments

Data collection was carried out by questionnaire, measurement and assessment.

5. Data Analysis

This study was analyzed by multiple logistic regression.

RESULTS

The data on the social characteristics of the subjects showed (table 1) that the main occupation of the subject's father was mainly farmers (58.3%), as well as the work of the subject's mothers, who primarily were farmers (51.7%). A relatively large proportion of the father (25%) and mother (17.5%) of the subjects worked as laborers.

Most of the parents of the subjects had a low level of education. A total of 75% of the subject's fathers and 86.8% of the mothers underwent primary school education. Only 11% of the fathers and 4.1% of the subject's mothers attended high school and college education.

Some of the indicators used to determine the nutritional status of the subjects (table 2). In this study, the goiter gland enlargement as measured by the palpation method was used as an indicator of the subject's IDD status, and it was known that 30% had an enlarged goiter gland detected as a sign of disturbance due to iodine deficiency. Anemia was experienced by 20.8% of respondents and stunting in 30.8% of respondents.

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Table 1. Demographic Characteristic

Variable	n	%
Father's Education		
Not in school	1	0.8
Elementary School	90	75
Junior High School	16	13.2
Senior High School	11	9.3
College	2	1.7
Mother Education		
Not in School	1	0.8
Elementary School	104	86.8
Junior High School	10	8.3
Senior High School	4	3.3
College	1	0.8
Occupation of father		
PNS	1	0.8
Private	11	9.2
Laborers	30	25
Owners of farmers	70	58.3
Traders	3	2.5
Others	5	4.2
Employment		
civil servants	1	0.8
Private	5	4.2
Laborers	21	17.5
Owners of farmers	62	51.7
Traders	10	8.3
Not working	15	12.5
Others	6	5
Order in the family		
1st child	58	48.3
children to 2	40	33.3
3child to	13	10.8
child> = 4	9	7.5
Number of children in family		
1	13	10.8
2	55	45.9
3	3	1
>= 4	21	17.5

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Table 2. Nutritional Status

Variable	n	%
Stunting	42	35
Normal	78	65
Anemia		
Anemia	25	20.8
Normal (Hb <12g / dL)	95	79.2
Iodine intake (UIE level)		
(median 144.5± 86.9 μg / L)		
Less (< 100μg / L)	37	30.8
Enough (≥100μg / L)	83	69.2%
Goiter enlargement		
Normal	84	70
Enlargement	36	30

The subject's Iodine intake adequacy status was measured using the urine Iodine excretion indicator (EIU) median 144.5 ± 86.9 μg/L in the current study area, including crowded endemic regions.

Further analysis using multiple linear regression showed that the variables of HB and EYU levels, stunting, gender, and puberty did not affect intelligence. Likewise, the birth order and the number of children in the family, fathers, and mothers' education also do not affect intelligence. This minimizes the possible bias of these factors towards concluding. After controlling for these factors, the results showed that the goiter enlargement status significantly decreased intelligence level ($p < 0.05$).

Subjects suffering from IDD have a mean IQ of 10.32 points lower than subjects without IDD. However, seen from these factors' contribution to intelligence, the result is minimal, namely 7%. There are still 93% other factors that affect adolescents' intelligence that is not included in the study.

Table 3. Factors Affecting Intelligence

Variable	Coefficient B	SE	t	p
(Constant)	82.174	22.194	3.703	<0.001
HB (g / dl)	-1.120	1.48	-0.759	0.450
(μg / L)	-0.012	0,021	-0.567	0.572
Goiter (Normal/goiter)	10.325	4.07	2.54	0.013
Birth order (≤3 /> 4)	2.986	2.33	1.29	0.202
Number of children (≤3 /> 4)	-3.22	2.40	-1.343	0.182
Father's education (high / low)	1.39	4.36	0.32	0.751
Maternal education (high / low)	-3.294	5.592	-0.59	0.557
Stunting (z-score tb/um)	1.972	1.76	1.122	0.264
Gender (male / female)	1.724	3.584	0.481	0.632
Puberty (not yet / pubescent)	-1.507	3.631	-0.415	0.68
Adj R^2		0.070		

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Table 4. Factors Affecting Mathematics Learning Achievement

Variable	**Coefficient**	**SE**	**t**	**p**
(Constant)	5.79	1.63	3.561	0.001
HB (g / dl)	-0.042	0.099	-0.429	0.669
(µg / L)	0. 003	0.001	2.190	0.031
Goiter (normal = 1 / mumps = -0,141 0,271 - 0,522 0,603)	-0.141	0.271	-0.522	0.603
The order of birth (1 = 1 / to ≥4 = -0,032-0,205 0,838)	-0.032	0.16	-0.205	0.838
Number of Children ((1 = 1 / ≥4 = 4))	-0.033	0.16	-0.213	0.832
Father's education (high = 1 / low = 0)	0.708	0.274	2.583	0.011
Maternal education (high = 1 / low = 0)	-0.06	0.110	-0.537	0.592
Stunting (z-score tb / um)	-0.082	0.12	-0.710	0.479
Gender (male = 1 / female = 2)	-0.273	0.25	-1.109	0.270
puberty (not = 1 / pubescent = 2)	-0.33	0.25	-1.317	0.191
Intelligence (IQ points)	0.025	0.006	4.117	<0.001
AdjR2	0.232			

Analysis multiple linear regression is carried out on several factors that are assumed to affect mathematics learning achievement. The results show that the factor that significantly influences learning achievement in this study is the intelligence factor ($p < 0.01$). Father's education also has a significant effect on the subject's intelligence. Meanwhile, the nutritional status factor related to mathematics learning achievement was EYU status ($p < 0.05$). The practical contribution of the factors above to mathematics achievement is 23.2%.

Linear regression analysis was performed on several factors assumed to affect Indonesian learning achievement. The results show that the factor that significantly influences learning achievement in this study is the intelligence factor ($p < 0.05$). The practical contribution of the factors above to Indonesian language achievement is 12.5%.

Table 5. Factors that Affect Indonesian Language Learning Achievement

Variable	Coefficient	SE	t	p
(Constant)	6.745	1.740	3.875	<0.001
HB (g / dl)	-0.141	0.106	-1.33	0.19
(µg / L)	0.001	0.001	0.87	0.39
Goiter (normal = 1 / goiter = 0)	-0.320	0.290	-1.11	0.272
Birth order (1st = 1 / to ≥4 = 4)	-0.16	0.17	-0.94	0.351
Number of children (1 = 1 / ≥4 = 4)	0.206	0.17	1.220	0.23
Father's education (low = 0 / high = 1)	-0.04	0.084	-0.451	0.653
Maternal education (low = 0 / high = 1)	0.05	0.118	0.39	0.70
Stunting (z-score tb / um)	-0.02	0.124	-0.143	0.89
Gender (male = 1 / female = 2)	0.345	0.263	1.31	0.193
Puberty (not yet = 1 / puberty = 2)	-0.192	0.27	-0.720	0.473
Intelligence (IQ points)	0.015	0.007	2.181	0.031
Adj R2	0.125			

DISCUSSION

Children who live in areas that are endemic to IDD have a greater risk of experiencing cognitive impairment. Many studies have compared school children living in IDD endemic and non-endemic areas. The results show that children living in endemic areas have more inadequate cognitive development levels and school achievement (Grantham-McGregor et al., 1999; Tee et al., 1999; Huda et al., 1999; Qian, et al. ., 2005). The meta-analysis results of 18 studies involving 2,214 subjects showed that the mean IQ and psychomotor scores in subjects who experienced IDD were 13.5 points lower than subjects from the non-IDD population (Bleichrodt and Born, 1993).

The trend distribution of children's IQ curves in endemic areas shows a leftward trend, with a mean IQ deficit of 11 points in populations in IDD endemic areas. This result was confirmed by a meta-analysis of 36 recent studies conducted in China (Qian, et al., 2005) and a meta-analysis of previous studies. Therefore, in endemic goiter areas there is a higher prevalence of learning difficulties in school children (Bleichrodt and Born, 1993). This study further elaborates on the results of previous studies. When areas previously declared endemic to be replete of iodine deficiency, it turns out that the risk of iodine deficiency still affects cognitive performance, even in early adolescence.

The role of iodine in cognitive abilities, among others, is a nutrient that is important for neurological growth, affecting neurogenesis, neuronal and glial cell differentiation, myelination, neuronal migration, and synaptogenesis (Georgieff 2007; Choudry and Nashrullah, 2018). The thyroid hormone's physiological role is to ensure the coordination of different developmental events through the regulation of cell differentiation and genetic expression of the brain. The spectrum of impaired cognitive abilities ranging from mental retardation to impaired development of intelligence and less learning is a consequence of the impact of iodine deficiency which affects the synthesis of thyroid hormones in a critical period of brain formation (Sethi and Umesh, 2004; Zimmermann, 2008; Redman, et al., 2016). Unicef (2005) states that the elimination of IDD contributes to eradicating hunger and extreme poverty by increasing learning abilities and intellectual potential, which increases the opportunity to get a better income. The economic and social burden due to pathology and diseases related to IDD can also be prevented.

The factor that is proven to affect mathematics learning achievement in this study is EIU. At the same time, IDD status based on goiter enlargement is related to intelligence and not significantly associated with learning achievement. This seems to be related to the nature of nutritional status and cognitive performance measured in this study. Intelligence is a cognitive performance that is formed in the long term, so it is more related to the enlargement of the thyroid gland, which is an indication of long-term thyroid dysfunction. The status of iodine adequacy with the EIU indicator reflects current health status, which is more related to the actualization of current cognitive abilities, namely learning achievement. Nutritional intake related to learning achievement is also in line with previous research (Bleiwess-Sande, 2019; Burrows, et.al., 2017).

This mechanism is explained by Levinger (1996) with *active learning capacity model,* which explains the mechanism of the relationship between nutritional status and learning achievement. Current nutritional status, or temporary nutritional status, is related to *learning receptiveness* or children's readiness and ability to receive learning. Long-term nutritional status, such as goiter enlargement, is more related to *aptitude*, which often refers to IQ. Piaget (in Groth-Marnat, 1990) states that intelligence is a

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continuous process of reorganization of cognitive structures that develops in line with the growth and development of a person since his birth.

Although some experts claim that iodine deficiency during sensitive periods of brain formation is irreversible and the biological mechanism of the impact of thyroid hormone deficiency in childhood is unclear (Zimmermann, 2016), later studies conducted on children with higher age show that indications that iodine supplementation at a higher age, namely school age, can still improve children's cognitive abilities (Isa, et al., 2000; Zimmermann, et al., 2006; Gordon, et al., 2009). This is possible because the impact of iodine deficiency on cognitive abilities can occur at every stage in the development cycle to varying degrees. (Mustard, 2006). Although not directly related, goiter enlargement indirectly impacts learning achievement through its effect on intelligence. Linear regression analysis on the factors that affect learning mathematics and Indonesian achievement shows that one of the factors that influence achievement is intelligence. At the same time, in this study, IDD is related to a decrease in the level of intelligence in adolescents. This research is in line with research in Egypt which proves that IQ is related to achievement (Engelhardt, et al., 2019), especially arithmetic and language (Monr, et al., 2016).

The results of these previous studies, plus the results of this study, provide optimism that although long-term cognitive performance such as IQ may not be associated with current iodine adequacy, ensuring iodine adequacy in adolescence is associated with cognitive performance related to learning achievement. There are several weaknesses in this study, including the research design *cross-sectional* so that it cannot determine cause and effect, other factors that influence achievement that have not been measured in this study, for example, motivation, social support, and indicators of iodine deficiency that do not include thyroid hormone.

It can be concluded that iodine deficiency is negatively related to cognitive performance in replete endemic areas of endemic iodine deficiency. Goiter enlargement, which is an indicator of long-term iodine deficiency status, correlates with IQ. UIE, which reflects current indicators of iodine deficiency status, affects early adolescent academic achievement. The cognitive impact of iodine deficiency lasts into adolescence. Therefore, ensuring adequate iodine intake in adolescents is essential to optimize their cognitive performance.

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