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Relationship between Anemia Status, Sleep Quality, and Cognitive Ability among Young Women Aged 15-24 Years in Indonesia (Analysis of Indonesian Family Life Survey (IFLS) 5)

Hubungan Status Anemia, Kualitas Tidur, dan Kemampuan Kognitif pada Wanita Muda Usia 15-24 Tahun di Indonesia (Analisis Data Indonesian Family Life Survey *(IFLS) 5)*

Siti Helmyati[1,2], Lutfi Afida Fauziah[2*], Pinaes Kadibyan[2], Nova Lidia Sitorus[3], Charisma Dilantika[3]

[1]Department of Health Nutrition, Faculty of Medicine, Public Health and Nursing, Gadjah Mada University, Indonesia
[2]Center for Health and Human Nutrition, Faculty of Medicine, Public Health and Nursing, Gadjah Mada University, Indonesia
[3]Danone Specialized Nutrition, Indonesia

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Correspondent:
Lutfi Afida Fauziah
lutfiafida01@mail.ugm.ac.id

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ABSTRACT

Background: *Anemia is still one of the nutrition problems in Indonesia. Women of reproductive age, including the age group 15-24 years, is a group with higher risk of anemia. Iron deficiency anemia is a common cause of anemia. Iron is one of the micronutrients that important for the body, including brain. Some studies suggest that iron deficiency is associated with sleep quality and cognitive ability. Iron has a complex effect on the dopaminergic system by being a cofactor of tyrosine hydroxylase which is part of dopamine D2 receptor function. Neuromodulation by the dopaminergic system plays an important role in sleep regulation. It can also interfere with the brain's ability to spread nerve impulses that have potential to cause several disorders, one of which is motor and cognitive disorders.*
Objective: *This study aims to determine the relationship of anemia status with sleep quality and cognitive abilities in young women aged 15-24 years in Indonesia based on IFLS 5.*
Methods: *This study used cross sectional design and secondary data from IFLS 5 with subjects totaling 2016 young women aged 15-24 years. This study used chi-square as statistical test with significance level p<0.05.*
Results: *The prevalence of anemia in young women aged 15-24 years was 39.93%. It was found that there was no relationship between anemia status and sleep quality consisting of sleep disturbance (p=0.624) and sleep quality (p=0.693) and there was no relationship between anemia and cognitive ability (p=0.702).*
Conclusions: *Anemia status has no significant relationship with sleep quality and cognitive ability.*

INTRODUCTION

Anemia is a nutritional issue that is included in Indonesia's three nutritional problems, often known as triple burden of malnutrition. Anemia is defined as a condition in which there is decrease in hemoglobin levels in the blood so that levels are below normal values[1]. People who are at higher risk of getting anemia based on gender, particularly women between the ages of 14 and 50 years or women of reproductive age. They require more iron than males of similar age. According to Primary Health Research (Riskesdas) in 2018, the prevalence of anemia in children aged 5-14 years was 26.8%, while it was 32% in women aged 15-24 years in Indonesia[2].

Anemia can be diagnosed by testing hemoglobin levels. Hemoglobin is a compound found in erythrocyte cells that delivers oxygen from the lungs to all parts of the body, therefore an anemic person does not receive enough oxygen-rich blood. This might lead to fatigue or weakness, dizziness, shortness of breath, migraines, or

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irregular heartbeat[3]. Hemoglobin levels are influenced by some factors, including age, gender, genetics, ethnicity, altitude, menstrual cycles, nutrional intake, past medical history, and sleep quality[4].

Iron deficiency anemia is a prevalent source of anemia. This condition can be caused by several factors, including an insufficient amount of iron in the food consumed, decreased iron absorption and availability as a result of infectious diseases and other chronic inflammation[5]. Iron is known to be one of the crucial micronutrients for the body, one of which is the brain. This is because iron is essential for maintaining neural tissue's metabolic and energy needs, as well as the processes of neurogenesis, axon myelination, and neurotransmitter synthesis[6]. It has been noted that iron deficiency, particularly in the brain, is reported to trigger changes in the metabolism of neurotransmitters like dopamine, serotonin, and noradrenaline.[7].

Several studies have suggested that iron deficiency is related to sleep quality and sleep disorders[7–9]. The effects of iron on the dopaminergic system are complex. It serves as a cofactor for tyrosine hydroxylase, which is necessary for dopamine D2 receptor function. Neuromodulation by the dopaminergic system plays an important role in sleep regulation, which includes modulating the quality, quantity and duration of REM (Rapid Eye Movement) sleep[7]. The process by which iron deficiency impairs sleep quality may also be linked to the development of RLS (Restless Leg Syndrome). RLS is a sensory neurology problem distinguished by a strong desire to move while resting and the presence of leg discomfort such as throbbing, burning, or tingling[10]. Iron deficiency can affect brain dopamine levels and D3 receptor activation, contributing to RLS[11]. Moderate to severe RLS can cause restlessness during sleep and frequently shortens sleep duration, resulting in poor and disturbed sleep quality[12].

Apart from affecting sleep quality, Iron-deficiency anemia has been shown to affect brain function, such as cognitive function and learning achievement[7]. Aside from sleep regulation, iron deficiency-induced metabolic changes in neurotransmitters and a decrease in dopamine D2 receptors can disrupt the brain's ability to transmit nerve impulses, potentially resulting in motor and cognitive disorders, changes in social behavior, and/or pathological development[6]. The Indonesian Family Life Survey, or IFLS, is a long-term nationwide survey. It contains an assortment of socioeconomic and health data, such as Hb levels, sleep quality, and cognitive test results. There has been extensive research into the relationship between anemia status, sleep quality, and cognitive ability However, IFLS data is still infrequently used in studies on this particular topic. Therefore, using IFLS 5 data, this study was to determine the relationship between young Indonesian women aged 15-24 years' anemia status and their sleep quality and cognitive ability.

METHODS

This research employs quantitative methods and a cross-sectional design. Secondary data from the Indonesian Family Life Survey, or IFLS, was used in this research. IFLS is a longitudinal survey conducted by the RAND Corporation in collaboration with SurveyMeter, a local survey company. IFLS data is divided into five batches; this study includes IFLS data from batch five, which occurred between 2014 and 2015. Data Batch 5 IFLS data was collected between September 2014 and September 2015, and it represents 83% of the Indonesian population from 13 provinces. These provinces include four on the island of Sumatra, which are Lampung, North Sumatra, West Sumatra, and South Sumatra; five on the island of Java, which are DI Yogyakarta, DKI Jakarta, Central Java, East Java, and West Java; and four other provinces, which are West Nusa Tenggara, Bali, South Kalimantan, and South Sulawesi[13]. This research's target population includes all young Indonesian women aged 15 to 24, as well as those who participated in the IFLS 5 survey (2014-2015). The classification of young women in this study corresponds with the WHO definition, which includes the age group 15-24 years as young man and/or young woman[14]. The study's inclusion criteria were as follows: 1) the research subject was female; 2) she was between the ages of 15 and 24; 3) she had hemoglobin (Hb) examination results; 4) she had sleep quality data; and 5) she had cognitive test results. Meanwhile, the study's exclusion criteria were that the research subjects' data were incomplete. In this study, the inclusion and exclusion criteria were met by 2016 young women. Figure 1 illustrates the data cleaning process as follows:

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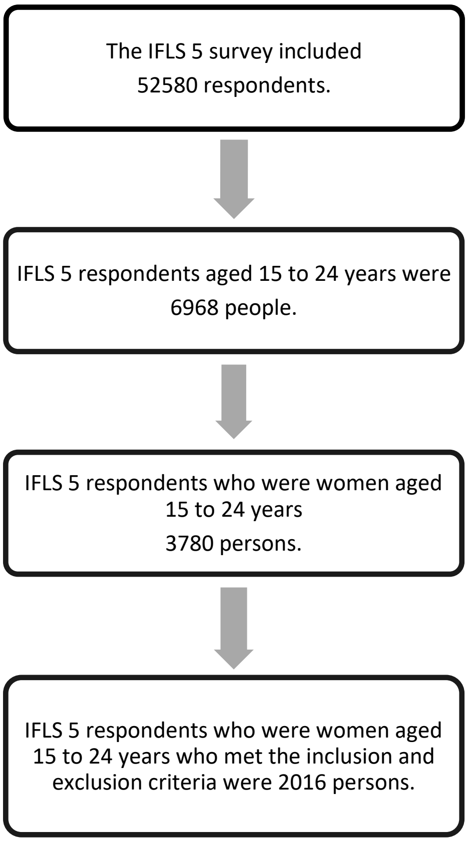

Figure 1. The data cleaning process

This research uses several data including the respondent's age, gender, Hb or hemoglobin test results, the respondent's sleep quality, cognitive test results, area of residence, and the economic status of the respondent's family. Data on respondent age and gender were taken from the IFLS 5 US Book questionnaire, at question points us03 and us01. The IFLS 5 Book K questionnaire's question point SC05 was then used to acquire data on the area of residence. Residential areas are divided into urban and rural locations. Data on respondents' economic situation were gathered from the IFLS 5 Book 1 Section KS and Book 2 Section KR surveys, which provide information about household expenses.

Data on respondents' sleep quality were collected using the new IFLS 5 Book 3B Section TDR questionnaire, which included questions about sleep quality and sleep disorders. The questionnaire includes questions about sleep disorders and sleep-related disorders, which are based on questions from PROMIS, or the Patient-Reported Outcomes Measurement Information System. PROMIS is an individual-centered measurement instrument that assesses and monitors physical, mental, and social health in children and adults[15]. The sleep-related PROMIS was created to help adults self-report their sleep-wake functioning. The PROMIS questionnaire includes questions that assess respondents' self-reported perceptions of the quality, depth, and disturbance of their sleep in the previous week or seven days[16]. The questionnaire categorizes sleep disorders into five categories: "Never", "Rarely", "Sometimes", "Often", and "Always". Meanwhile, sleep quality is classified into five categories: "Very Bad," "Bad," "Fair," "Good," And "Very Good."

Meanwhile, respondents' hemoglobin levels were determined using the IFLS Questionnaire 5 US Section US Book (Health Measurement). In IFLS batch 5, hemoglobin levels were measured with the HemoCue hand-held meter model Hb201+ and HB201 micro cuvettes. According to WHO, anemia is defined as having a hemoglobin level of <12 g/dL in women and <13 g/dL in men.

Data on cognitive ability was obtained from the IFLS 5 Book EK15+ questionnaire, which consists of a short version of the Raven's Colored Progressive Matrices cognitive test and several simple arithmetic questions that have previously undergone a pretesting process[13]. Raven's Colored Progressive Matrices, or RCPM, is a nonverbal cognitive test designed to evaluate fluid intelligence and gfactor[17]. Fluid intelligence is a reasoning capacity that may be tested by assigning activities that require addressing new problems; it is also associated with the ability to process information and learn something[18,19]. Meanwhile, Spearman's theory refers to the g factor as the cognitive ability component, which includes both eductive capacity (the ability to comprehend information) and reproductive ability. Eductive ability is the ability to process information, whereas reproductive ability is the ability to comprehend, recall, repeat, and transmit information from one person to anothe[20]. In RCPM, respondents are required to select the missing element from six options presented in an image[17]. Each correct and proper answer

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will receive one point. Aside from RCPM questions, the IFLS 5 questionnaire includes 5 math questions, with correct and incorrect responses worth one point each. The assessment is conducted using a percentile ranking of the total points from the exam results, which are then classified into five categories: excellent, good, average, below average, and poor.

Before the survey was conducted, the RAND IRB (Institutional Review Board) and the SurveyMeter Institute reviewed and approved the IFLS 5, or Indonesian Family Life Survey 5, data utilized in this study. In IFLS 5, RAND's Human Subjects Protection Committee assigned the ethical clearance number s0064-06-01-CR01[21].

The STATA computer program version 13.1 for Windows is used to process data, which includes merging, cleaning, and analyzing. The current research employs descriptive and bivariate analysis. Descriptive analysis seeks to identify the frequency distribution and sociodemographic features of respondents. The descriptive analysis findings are given in tabular format, including frequencies and percentages. In bivariate analysis, the statistical test utilized is chi-square. The chi-square test was utilized for categorical data to examine the relationship between anemia status, sleep quality, and cognitive ability at a significant level of p-value < 0.05. A significant relationship between variables is defined by obtaining a p-value <0.05.

RESULTS AND DISCUSSION

Results

The sociodemographic characteristics of the respondents can be seen on Table 1. A total of 2016 young women aged 15 to 24 had been chosen based on inclusion and exclusion criteria. Table 1 shows that the majority of respondents, 1690 (83.83%), were between 15 and 19 years old, with an average age of 17.44 ± 1.74. Aside from age, additional factors of respondents evaluated included place of residence and family financial status. Based on the respondents' place of residence, 1252 persons, or 67.76% of the total, reside in urban areas. Meanwhile, based on the financial status of the respondents' families, it is known that respondents with a lower financial status had the highest number, 894 people (44.35%).

According to this research, the prevalence of anemia is 33.93% of total research respondents, or 684 persons, with the majority of respondents' not experiencing anemia (66.07%, or 1332 people). Anemia is diagnosed using a hemoglobin (Hb) examination. In this research, anemia is defined as Hb levels less than 12 g/dL. An individual is not considered anemic if their Hb test result is 12 g/dL or more (≥12 g/dL).

Meanwhile, sleep quality is measured using a questionnaire from the new IFLS 5 questionnaire, which includes questions about sleep quality and sleep disorders. The questionnaire includes questions about sleep disorders and sleep-related disorders, as well as questions from PROMIS (Patient-Reported Outcomes Measurement Information System)[13]. In this research, sleep disorders and sleep quality were included as sleep quality variables, with the majority of respondents never experiencing sleep disorders (49.85%) and having enough sleep quality (56.70%).

The cognitive ability variable is assessed using a questionnaire that includes a simplified version of the Raven's Colored Progressive Matrices cognition test plus some simple arithmetic questions[13]. The assessment is based on the percentile ranking of test results[13]. The assessment is based on the percentile ranking of the test results, which are then classified into five categories: excellent, good, average, below average, and poor. In terms of cognitive ability, the majority of research respondents (54.17% or 1092 participants) fell into the average category.

The bivariate analysis results can be seen in Tables 2 and 3. Table 2 shows the findings of the analysis of the relationship between anemia status and sleep quality, which includes both sleep disorders and sleep quality. The findings of this research show that there is no significant relationship between anemia status and sleep quality or sleep disorders (p-values = 0.624 and 0.693, respectively). Meanwhile, Table 3 shows the findings from the analysis of the relationship between anemia status and cognitive ability. Based on the findings of this analysis, it indicate that there is not a significant relationship between anemia status and cognitive ability (p-value = 0.702).

Table 1. Respondent Demographics

Variable	n	%
Anemia Status		
Anemia	684	33,93
Not Anemic	1332	66,07
Sleep Quality		
Sleep Disorder		
Never	1005	49,85
Seldom	331	16,42
Sometimes	499	24,75
Often	148	7,34
Always	33	1,64
Sleep Quality		
Awful	24	1,19
Bad	135	6,70
Sufficient	1143	56,70

Good	551	27,33
Very Good	163	8,09
Cognitive Ability		
Intellectually superior	58	2,88
Excellent	318	15,77
Average	1092	54,17
Below average	424	21,03
Intellectually deficit	124	6,15
Age		
15-19 year old	1690	83,83
20-24 year old	326	16,17
Mean age ($\underline{x}$= 17,44 ± 1,74)		
Area of Residence		
Urban	1252	62,10
Rural	764	37,9
Family Economic Status		
Lower	894	44,35
Intermediate	421	20,88
High	701	34,77

Table 2. Relationship between Anemia Status and Sleep Quality

Dependent Variable (Sleep Quality)	**Independent Variable (Anemia status)**				***p-value***
	Anemia		**Not anemic**		
	n	**%**	**n**	**%**	
Sleep Disorder					0,624
Never	333	48,68	672	50,45	
Seldom	123	17,98	208	15,62	
Sometimes	163	23,83	336	25,23	
Often	54	7,89	94	7,06	
Always	11	1,61	22	1,65	
Sleep Quality					0,693
Awful	6	0,88	18	1,35	
Bad	49	7,16	86	6,46	
Sufficient	378	55,26	765	57,43	
Good	196	28,65	355	26,65	
Very Good	55	8,04	108	8,11	

Table 3. Relationship between Anemia Status and Cognitive Ability

Dependent Variable (Cognitive ability)	**Independent Variable (Anemia status)**				***p-value***
	Anemia		**Not anemic**		
	n	**%**	**n**	**%**	
Excellent	23	3,36	35	2,63	0,702
Good	101	14,77	217	16,29	
Average	366	53,51	726	54,50	
Below Average	149	21,78	275	20,65	
Poor	45	6,58	79	5,93	

Discussion

The results of this research show that, out of the 2016 respondents, 33.93% of the total respondents—young women between the ages of 15 and 24—had anemia. These findings suggest that anemia has a significant prevalence and remains a serious or moderate concern since the prevalence rate exceeds the stated limit of 20%[22]. According to WHO, anemia prevalence values of <5% indicate there is no public health problem, 5-19% indicate a mild problem, 20-39% indicate a moderate level public health issue, and ≥ 40% indicate severe issues[23]. This finding differs from the national prevalence of anemia in young women aged 15 to 24 years, which was 18.4% in 2013 and 32% in 2018[2,24]. This shows that the prevalence of anemia increases from year to year. These differences could occur due to inconsistent observations or data gathering among provinces and regions in Indonesia.

According to bivariate analysis, there is no significant relationship between anemia status and sleep

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quality variables, both sleep disorders and sleep quality have p-values of 0.624 and 0.693, respectively. This conclusion contrasts with several earlier research. Sincan et al. reported in their study that there is a significant relationship between anemia, particularly iron deficiency anemia, and sleep quality, with iron deficiency anemia having a detrimental effect on sleep quality and quality of life[8]. Similar findings were reported by Murat et al, who found that iron deficiency anemia influenced sleep quality and that sleep quality was lower in patients with iron deficiency anemia than in healthy people[7]. A Chinese study investigated the relationship between anemia and difficulties sleeping or insomnia. This study discovered that persons with anemia had a 1.32 times greater likelihood of having insomnia than those who were not anemic[25].

Anemia, particularly iron deficiency anemia, can impair sleep quality by affecting the dopaminergic system. Iron serves as a cofactor for tyrosine hydroxylase, which is necessary for dopamine D2 receptor activity. The dopaminergic system's neuromodulation is critical in sleep regulation, since it modulates the quality, quantity, and duration of REM (Rapid Eye Movement) sleep[7]. Holst, et al. in his research studying sleep-wake regulation in humans. His study discovered that the dopamine transporter helps to regulate sleep-wake balance in humans[26].

The mechanism by which iron deficiency affects sleep quality is also related to the occurrence of RLS (Restless Leg Syndrome). RLS is a sensory neurology problem distinguished by a strong desire to move while resting and the presence of leg discomfort such as throbbing, burning, or tingling1[10]. Iron deficiency can affect brain dopamine levels and D3 receptor activation, contributing to RLS[11]. According to Peirano et al., alterations in neurotransmitters, particularly in the dopaminergic system as a result of iron deficiency, are one of the primary causes of RLS[27]. Moderate to severe RLS can cause restlessness during sleep and often shorten sleep time, resulting in poor and disturbed sleep quality[12].

The differences in the study's results could be explained as differences in questionnaires for assessing sleep quality, as this study used questions from PROMIS, or Patient-Reported Outcomes Measurement Information System, where the answers were more subjective and did not indicate specific things, particularly regarding sleep disorders. Furthermore, the questions in this study's questionnaire are just a part of the questions in PROMIS, which may contribute to the lack of specificity in the data collected[13]. Meanwhile, in other studies, sleep quality was measured using more accurate instruments such as the PSQI questionnaire or the Pittsburgh Sleep Quality Index. PSQI is used to assess sleep quality during the past month. This instrument has been widely used and tested for reliability and validity[28]. Meanwhile, PROMIS measures respondents' sleep quality during the last week or seven days. This may be one of the explanations for why the research failed to find a significant relationship.

Numerous research findings have demonstrated a reciprocal trigger relationship between anemia and sleep quality. According to Murat et al., having poor quality sleep while suffering from anemia may worsen the condition. This is supported by Fitriani, et al., who report that anemic patients typically experience poor-quality sleep, which might worsen their anemia[29]. This happens because when sleeping, the body undergoes a process of repairing damaged cells, and if the duration of sleep is insufficient or less than the ideal time, the process of renewing and repairing these cells will not run optimally, and will interfere with the process of forming Hb or hemoglobin, so that the levels of hemoglobin produced will not meet the body's needs. [30]. According to Garno et al. and Carley and Farabi, deep sleep occurs in the Non-Rapid Eye Movement (NREM) stage, during which hormones, specifically growth hormone (GH) or growth hormone, are produced to encourage the process of repair and renewal of body cells, including blood cells. Thus, if a person does not reach the depth of sleep then the person may suffer from anemia[31,32]. Meanwhile, during REM (Rapid Eye Movement) sleep, certain brain areas, specifically the frontotemporal area, have increased metabolism and blood flow. A neuroimaging study discovered that cerebral blood flow in the frontotemporal region was connected with hemoglobin levels and anemia status, while another indicated that cortical thinning in the frontotemporal region was associated with shorter sleep duration[25,33].

Aside from reducing sleep quality, anemia caused by iron deficiency has been shown to influence brain function, such as cognitive ability and learning achievement[7]. Cognitive ability is closely related to IQ. However, this study found that there was not a significant relationship between anemia status and cognitive ability in young women aged 15-24 years (p-value> 0.05). These findings are consistent with research by Latifah et al., who found that anemia is not related to cognitive abilities, particularly intelligence and learning achievement[34]. In addition, Halliday et al.'s research found that anemia had no bearing on differences in cognitive abilities such as comprehension, nonverbal reasoning, literacy performance, or numeracy skills[35]. Samson et al. found no indication that iron status, anemia, or iron intake affect intelligence. Furthermore, there is no evidence that iron supplementation during adolescence, with or without additional micronutrients, or food-based therapies, improves intelligence[36].

However, the findings of this research contradict a number of previous studies, including those conducted by Widjayanti et al., Nassar et al., and Chamberlain et al., which demonstrated that there was a relationship between anemia and cognitive function[37–39]. Dumilah and Sumarmi in their study, stated that iron deficiency anemia in adolescents not only causes mental retardation, but also affects concentration, excitement for learning, and ability to understand, indicating a reduction in cognitive function[40]. There are several different mechanisms by which anemia can affect cognitive abilities. Iron is essential for the maintenance of the high metabolic and energy requirements of nervous tissue, neurogenesis, axon myelination, synaptic development, neurotransmitter synthesis, and

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metabolism[6]. The synthesis of neurotransmitters including dopamine and norepinephrine in the hippocampus, striatum, and cortex is iron-dependent. Metabolic changes in these neurotransmitters, as well as a reduction in dopamine D2 receptors, may impair the brain's ability to send nerve impulses, potentially leading to motor and cognitive impairments, changes in social behavior, and/or pathological development[6,41].

The differences in these results may be caused by other factors that can influence cognitive abilities. These include both internal and external factors. Internal factors, or those that originate within the body, can include genetics, nutritional needs, health, eating habits, children's intelligence, and focus, interests, attitudes, talents, and motivation. External factors or variables that originate from outside the body might be in the form of experience and information received from interactions in the surrounding environment, including family and school, as well as food intake and parenting patterns offered by parents to their children[42,43]. Alswat et al discovered that children with highly educated parents, who get sufficient sleep each night, exercise regularly, and keep a healthy diet, have better cognitive ability and achievement[44]. Aside from that, the types of cognitive tests utilized in each study varies, with this study using a questionnaire that included a short version of the Raven's Colored Progressive Matrices cognitive test as well as some simple arithmetic questions.

This research has various advantages, including the use of national scale data with a huge sample size that covers 13 out of 34 provinces, or 83% of Indonesia's total population. Data collection is also carried out by trained enumerators. However, this study has a weakness, especially sleep quality data, which is still subjective and does not demonstrate specific things, particularly in terms of sleep disorders, therefore it should be explored further using instruments that more objectively define sleep quality.

CONCLUSION

According to this research, the prevalence of anemia among young women aged 15 to 24 in Indonesia remains high, at 33.93%. According to the findings of this research, there is not a significant relationship between anemia status and sleep quality and cognitive abilities in young female subjects aged 15-24 years in Indonesia, as determined by an analysis of IFLS wave 5 data. Future study can utilize more specific and objective tools to measure sleep quality, or other sleep-related factors, such as sleep duration.

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CONFLICTS OF INTEREST AND SOURCE OF FUNDING

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