Literature Review: Association of Iron Deficiency Anemia with Cognitive Function in Adolescents

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Abstract: The prevalence of anemia in adolescents in Indonesia shows a high number with a percentage that is close to the category of severe public health problems. Anemia has an impact on the decline in cognitive function which in turn will affect intelligence, mental health, psychosocial, and the maturation process. A literature review study design by searching for research articles on the parameters of the relationship between iron deficiency anemia and cognitive function of adolescents aged 10-19 years using Google Scholar and ScienceDirect databases in the range of publication years between 2017-2022. 10 selected articles with 8 articles being conclusive and 2 articles being inconclusive, within parameters of learning achievement, school performance, concentration, cognitive response, cognitive behavior, irritability, expressed emotion, EEG, and mediation models In general, there is a significant relationship between anemia and cognitive function. However, this function itself has various aspects and measurement parameters so that further systematic studies are needed to find deeper patterns of relationships in a wider range of age groups.

1   INTRODUCTION

Anemia is a type of Non-communicable Disease (NCD) which is still a serious health problem. Low levels of hemoglobin in the blood (anemia) are the most common nutritional problems. In a study it is said that by 2020 anemia affects at least 2 billion people worldwide, of which about 89% of them are in developing countries (Youssef, Hassan & Yasien, 2020). Another study in 204 countries also stated that the prevalence of anemia globally in 1990-2019 experienced an increase in cases from 1.42 billion (1990) to 1.74 billion (2019). This study shows that there are 3 regions that contribute the highest anemia in the world, namely South Asia, West Africa, and Central Africa (Gardner & Kassebaum, 2020).

In Indonesia, the prevalence of anemia, especially in children and adolescents, is quite high. The results of the 2013 Indonesia Basic Health Research show that the prevalence of anemia is close to a Severe Public Health Problem with an anemia prevalence limit of 40%. It was recorded that 26.4% of cases of anemia occurred at the age of 5-14 years and 18.4% of cases at the age of 15-24 years, where

the proportion of cases in women was higher than men (Kemenkes RI, 2013). Meanwhile, according to the results of the 2018 Indonesia Basic Health Research, the prevalence of anemia in adolescent girls has increased from 37.1% (2013 survey) to 48.9% (2018 survey), with the highest proportion being in the 15-24 year old and 25-34 year age group (Ministry of Health RI, 2014). 2019).

Anemia is a condition in which hemoglobin (Hb) levels are less than 13.5 g/dL (men) and less than 12.0 g/dL (women) or hematocrit (Htc) levels are less than 41.0% (men) and less than 36.0% (women). the difference between the normal limits of Hb and Htc is determined based on gender, age, and ethnicity (Badireddy & Baradhi, 2022). Based on the factors causing the condition of low hemoglobin levels or anemia, it is divided into several types, but the most common is Iron Deficiency Anemia (IDA). Anemia is a serious problem because it has an impact on decreased immunity, impaired growth and development, decreased fitness and productivity, decreased cognitive function, and the risk of premature and low birth weight in pregnant women (Apriyanti, 2019).

The incidence of anemia in adolescents (10-19 years) requires special attention, low hemoglobin levels in this age range have a direct or indirect health impact on sufferers. In addition, anemia in adolescents also affects psychological, social, and economic aspects related to decreased productivity and decreased cognitive function. The extent of the impact of anemia (Fe) makes it one of the four highest adolescent health problems that are a priority for national handling along with the problems of stunting, chronic lack of energy, and obesity (Indonesiabaik.id, 2018).

Cognitive function is a complex function of the brain that involves aspects of perception, attention, memory and learning, as well as executive functions which include planning, reasoning, decision making, inhibitory control, and attentional set-shifting (O'Regan, Cronin & Kenny). There are 3 main areas of cognitive function development during adolescence, namely the development of logical reasoning skills, the development of abstract thinking skills, and the development of the capacity to understand how they feel and how others perceive them (Sanders, 2013). Impaired cognitive development in adolescents due to iron deficiency anemia will of course have an impact on cognitive function decline, which in turn will affect mental health, psychosocial, and adolescent maturation processes both as individuals and as future parents.

2   METHODS

The writing method is a literature review with article sources from national and international journals in the range of publication years between 2017-2022 using Google Scholar and ScienceDirect databases. The Boolean Operators based search technique with the keywords "association" AND "iron deficiency anemia" AND "cognitive function" AND "adolescent" for international articles and the keywords "hubungan" AND "anemia" AND "fungsi kognitif" AND "remaja" for national articles.

The initial keyword search results obtained a total of 1,760 articles (2017-2022 publications) of this number, then screening was carried out on the titles and types of articles (non-reviewed articles) including duplication, so that 77 articles were obtained. Next, screening was carried out in the abstract section covering samples, methods, and research outcomes so that 34 articles were obtained. After that, the final stage of screening was carried out in the content section with the parameters of the suitability of the article with the purpose of writing through an assessment, until a total of 10

publication articles were determined with 4 articles (international indexed journals) and 6 articles (national indexed journals) selected as literature review materials.
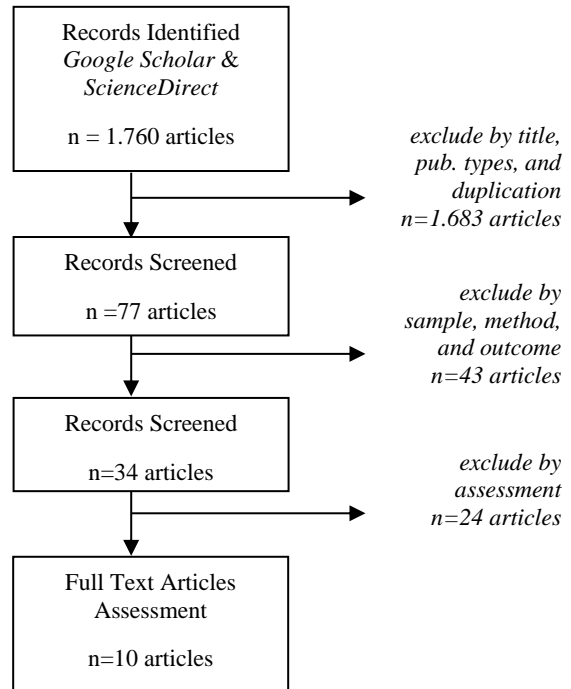

Figure 1. Articles Selection Flow Chart

The reasons for selecting these 10 articles were based on the suitability of the variables, the suitability of the subject, and the suitability of the results of the discussion with the purpose of writing a literature review. A brief assessment of the articles was also carried out including the population and sample, confounding factors, inclusion-exclusion criteria, and statistical analysis used. Selected articles are then compiled using a review table to facilitate writing the results and discussion.

3   RESULTS

Through a review of 10 articles, 8 research articles were found which stated that there was a significant relationship between low hemoglobin levels (anemia) and adolescent cognitive function (conclusive). But on the other hand, there are also 2 articles which state otherwise that there is no significant relationship between anemia and adolescent cognitive function (inconclusive).

Table 1 Matrix of Review Articles

Main Author	Method	Participants	Main Results
Dumilah PRA 2017	*cross sectional*	56 High School students of Bina Insani age 12 years old	there is a relationship ($p=0.042$) between anemia and student achievement
Puspitasari HKE 2018	*cross sectional*	29 female students aged 15-18 years at SMA Negeri 9 Semarang	tthere is no relationship between hemoglobin levels on learning achievement
Siauta JA 2018	*cross sectional*	52 students at Kelila State Junior High School, Central Mamberamo Regency	there is a significant relationship between anemia and learning achievement of adolescent girls ($p=0.000$)
Rotua M 2018	*cross sectional*	67 students of SMAN 14 Palembang	adolescents level of hemoglobin associated with student achievement ($p=0.046$)
Ucar HN 2019	*cross sectional*	89 Turkish teenagers aged 17-19 years	there is a significant relationship between adolescents with *Iron Deficiency* (ID) and *Iron Deficiency Anemia* (IDA) on cognitive function related to irritability ($p = 0.001$)
Prasetya KAH 2019	*cross sectional*	213 class XI students at SMAN 1 Abiansemal Badung	there is no relationship between academic achievement and students who are anemic and not anemic ($p=0.091$)
Sharma S 2019	*case control*	180 girls aged 10-19 years in Jaipur, India	there was a significant difference ($p=0.001$) between the anemia group and the control group with regard to cognitive responses *Auditory Reaction Time* (ART) and *Visual Reaction Time* (VRT)
Mosino A 2020	*case control*	10 . 835 teens ages 12-19 in Mexico	a significant relationship between anemia and the performance of completing school education in adolescents.
Pandiangan RR 2022	*cross sectional*	40 students of SMPN 5 Satu Atap Panguruan	there is a significant relationship ($p = 0.000$) between anemia and learning achievement.
Wender MJ 2022	*randomized controlled trial* (*post-hoc analysis*)	246 teens in MaharashtraIndia12-16 years old	there is a significant relationship between serum ferritin status (*predictor*) and Hb level (*moderator*) on cognitive function of adolescent brain.

4 DISCUSSIONS

Anemia is a condition in which hemoglobin levels are below normal limits, the causative factor is due to low levels of iron in the body for an abnormally long period of time. Dumilah and Sumarmi (2017) in their journal explain that iron deficiency anemia that occurs in adolescence not only has an impact on mental retardation, but also reduces concentration, enthusiasm for learning, and understanding abilities, which is a decline in cognitive function. In line with this, Rotua M (2018) explained that hemoglobin (Hb) levels can affect success in learning. Children with anemia tend to have poor concentration, weak memory, low problem-solving skills, less than optimal intelligence, and behavioral problems. In his research through the Chi-Square Test, it was said that there was a relationship between hemoglobin values and learning achievement (p=0.046), where

at least 68.4% of subjects with normal hemoglobin values had good learning achievements.

Siauta, Indrayani & Bombing's research (2018) stated that there was a strong relationship between the incidence of iron-nutrient anemia and student achievement. Furthermore, the low concentration of the brain causes decreased learning ability which will linearly affect adolescent learning achievement. This is supported by the findings of Devi & Rahayu (2018) where the results of measuring learning concentration using the Bourdon Wiersma Test on adolescent girls, stated that there is a relationship between hemoglobin levels and learning concentration which includes aspects of speed, accuracy, and constancy. The functions of the human brain are subclassified into distributed functions and localized functions. Concentration is a part of brain function that is distributed along with attention, memory, higher executive functions, as well as social conduction and personality. This cognitive function of the brain has a relationship with hemoglobin leves, including the process of

maturation of cognitive function during the adolescent phase (Ginsberg, 2005).

A similar study by Pandiangan et al (2022) showed the results that anemia had a relationship with learning achievement, where low Hb levels in adolescents were able to reduce learning concentration, whereas high Hb levels were associated with high intellectual intelligence scores (Chi-Square p=0.000). This study also shows that calorie intake through breakfast habits is also associated with learning concentration. The absence of breakfast causes the body to lack glucose so that the condition becomes weak, which will cause impaired learning concentration.

Research by Ucar, Koker & Tekin (2019) states that adolescents with a diagnosis of Iron Deficiency Anemia (IDA) and Iron Deficiency (ID) tend to experience disturbances in the aspect of irritability compared to adolescents without IDA and ID (Kruskal-Wallis p=0.001). Through the SLEES instrument, this study also shows a significant relationship between adolescents with IDA and ID on perceived expressed emotion, which refers to the high emotional sensitivity felt by adolescents regarding the attitudes of family members around them (one-way Anova p=0.007). Irritability is a state that involves feelings of anger or frustration, impatience and irritability over small things. People with irritability have a tendency to react with anger to the slightest provocation, they have a short temper and low emotional control. This condition is associated with functional changes in the part of the brain that regulates emotional mediation and aspects of cognitive control (Cerqueira et al, 2010).

In a study that examined the mediation model between dietary variables of biofortified grains and Fe, blood iron content, cognitive behavior, and brain Concurrent Electroencephalography (EEG) test showed there was a significant relationship. This experimental design study in India, which initially involved 246 adolescents aged 12-16 years, performed a nutritional intervention using iron-fortified pearl millet in the treatment group and conventional pearl millet in the control group for 6 months with periodic evaluation, of which the remaining 74 adolescents (excluded n=172) in the final analysis. The model obtained through post-hoc analysis shows a mechanism whereby serum ferritin (body iron reserves) as a predictor and Hb levels as a moderator have a strong relationship with cognitive function of the adolescent brain (Wenger et al 2022). The relationship between low Hb levels

and adolescent cognitive function It is also proven in the observations of Sarma et al (2019) that this researcher measured the response speed of anemic patients using Auditory Reaction Time (ART) and Visual Reaction Time (VRT). The results of the analysis showed that there was a significant difference between the anemic group and the control group in the speed of response to ART and VRT (one-way Anova p=0.001). In addition, there was also a linear relationship between the severity of anemia and an increase in ART and VRT scores in adolescent girls (p=0.001). The response speed of ART and VRT is significantly correlated with adolescent academic achievement, which means that it also shows a positive correlation with brain cognitive function (Kumar et al., 2020).

Through the Mexican National Health and Nutrition Survey 2012 on 10,835 adolescents aged 12-19 years in Mexico, it was found that there was a significant relationship between the incidence of anemia and the punctuality of graduating at school for both boys (p=0.313) and girls (p=0.464). Adolescents with good iron nutritional status have a higher chance of completing school education without delay. Although most studies analyze the potential consequences of anemia on students instantly using cognitive test measures. However, the results in this study provide additional references that are able to support the evidence of a link between anemia and student performance in school in long-term observations, namely through observations of students' ability to complete school without delay (Mosino, Villagomez & Patron, 2020).

Different results were shown in the Puspitasari & Nissa study (2018), where the Contingency Coefficient Correlation test obtained (p=0.653) which showed there's no relationship between hemoglobin levels and academic achievement of adolescent girls with obesity. Similar to this is shown through the research of Prasetya, Wihandani & Sutadarma (2019) which states that there is no relationship between learning achievement with anemic and non-anemic students (p=0.091). This shows that learning achievement is not only influenced by cognitive function and its relationship with anemia status, but also due to the influence of other factors, such as interests, talents, motivation, learning methods, school environment, the role of parents, including other nutritional status. such as obesity, acute lack of energy, and stunting in adolescents.

5   CONCLUSIONS

The results of the study of 10 published research articles found that 8 articles gave a significant (conclusive) effect of low hemoglobin Hb levels (iron deficiency) on the cognitive function of adolescents aged 10-19 years. Meanwhile, 2 other articles stated that no significant (inconclusive) relationship was found between low hemoglobin Hb levels with adolescent cognitive function. The cognitive aspect has various aspects and measurement parameters, so further studies are needed through a systematic review research design to find a deeper understanding between iron nutritional anemia and cognitive function using a single parameter in a wider range of age groups.

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