CORRELATION OF ANEMIA IN PREGNANT WOMEN WITH STUNTING INCIDENCE: A REVIEW

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ARTICLE INFO

Published: June 26th, 2023

The prevalence of stunting is still one of the biggest nutritional problems in the world. Around 150.8 million children under five years old were stunted in 2017, or 22.2% of the population. In 2017, more than half (55%) of children under the age of five who had stunting were from Asia, and more than a third were from Africa (39%). North Asia has the biggest percentage (58.7%) of Asia's 83.6 million children under the age of five. From 2005 to 2017, there was a 36.4% annual increase in the prevalence of stunting in toddlers in Indonesia. One of the factors that cause stunting and low birth weight babies (LBW) is pregnant women who experience anemia. Anemia is a condition of decreasing blood hemoglobin concentration due to micronutrient deficiencies, especially iron, which often occurs in the world affecting more than half of the global population. The most susceptible demographics to anemia are children and women at childbearing age. This research uses the study literature review method. The study was conducted using the results of research from 2016 – 2022 regarding the correlation of anemia in pregnant women and stunting. It is known that macronutrients and micronutrients are correlated with the occurrence of stunting and anemia. It is certainly necessary to make efforts to improve health in both pregnant women and children to prevent the occurrence of anemia.

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INTRODUCTION

Z-score for height according to age that is less than -2 standard deviations (SD) based on growth standards might indicates stunting, a persistent nutritional issue during the time of development and growth. Stunting in toddlers can inhibit development and growth with negative impacts in the form of decreased intellectuality, susceptibility to non-communicable diseases (de Onis & Branca, 2016). Stunting is linked to an increase of child morbidity, and mortality, as well as decreased levels of cognitive and academic success in children (WHO, 2014). In addition, there is strong evidence that stunting risk factors are fetal growth limitations, insufficiently born months (premature), and environmental exposure such as poor sanitation. Stunting occurs within the first 1000 days of life, and its impacts are probably irreversible after this time (Nachvak et al., 2020).

The proportion of short toddlers in Indonesia tends to be static. According to the Baseline Health Research survey from 2007, there were 36.8% children in Indonesia who were stunted. The percentage dropped slightly to 35.6% in 2010. However, in 2013 the proportion of short toddlers increased again to 37.2%. According to the survey conducted in 2018 revealed that 30.8% of adolescents and 29.9% of toddlers under the age of two had stunting. In addition, stunting was a problem for 27.67% of children in 2019 (Kemenkes RI, 2019). One of the biggest nutritional issues in the world is still the prevalence of stunting. Around 150.8 million children under the age of five, or 22.2%, were stunted in 2017. In 2017, more than half (55%) of young children with stunting
lived in Asia, while more than a third (39%) did so in Africa. North Asia has the biggest percentage of Asia's 83.6 million under-fives (58.7%). Between 2005 and 2017, Indonesia had an average frequency of 36.4% stunted toddlers (Laksono & Kusrini, 2020).

One of the factors that cause stunting and low birth weight babies (LBW) is pregnant women who experience anemia. Anemia is a condition of decreasing blood hemoglobin concentration due to micronutrient deficiencies, especially iron, which affects more than half of the world's population and is widespread over the globe (McKee et al., 2017). Anemia occurs due to non-existent iron deposits as well as signs of impaired iron supply to tissues (Gosdin et al., 2018). Children and women of childbearing age are the most vulnerable groups to anemia (Iqbal et al., 2019).

In addition, the incidence of anemia during pregnancy is one of the factors that can affect the weight of the baby at birth. Severe anemia during pregnancy increases the likelihood of a low birth weight baby, stunting, to bleeding before and during childbirth and even the death of mothers and babies (WHO, 2014). Pregnant women who experience anemia will experience impaired distribution of oxygen and food substances from the mother to the placenta and fetus, so it will affect the function of the placenta. Decreased placental function results in impaired fetal growth and development (Karşahin et al., 2007). Pregnant women who suffer from anemia have the potential to be 4 times greater to cause children to be stunted compared to mothers who do not suffer from anemia during pregnancy (Widyaningrum and Romadhoni, 2018). Based on this, the researcher evaluated previous studies on the correlation of stunting with anemia in pregnant women.

METHOD

This research uses the study literature review method. The study was conducted using the results of research from 2016 – 2022 regarding the correlation of anemia in pregnant women and stunting using PRISMA method. There are 5 steps in this method, namely determining the topic of literature, finding sources, selecting relevant sources, grouping and analyzing, and summarizing. Researchers search through several search engines, namely Google scholar, SAGE journal and PubMed. The article criteria used in this study are based on inclusion criteria made by researchers, namely Indonesian and English articles from various countries, quantitative research, research articles with primary data, full text articles that are available free and accessible, articles published in the 2016-2022 range and articles have conformity with the objectives of the research carried out. The keywords used in article searches on Google Scholar, SAGE journal and PubMed are "Anemia", "Deficiency", "Macronutrients", "Micronutrients", "Pregnancy", "Pregnant Women", and "Stunting".
RESULT AND DISCUSSION

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Stunting

Children 0-59 months old may experience stunting, a growth and development issue. Stunting is experienced by children who experience malnutrition, recurrent infections, and lack of psychosocial stimulation. Children are said to be stunted when high based on their age of more than two standard deviations below the median standard of child growth issued by the World Health Organization (WHO, 2014). The short-term effects of stunting are correlated with a reduction in a child’s cognitive and physical development, while adult productivity and working ability are negatively impacted by stunting’s long-term impacts, which also raise the risk of degenerative diseases in old age (Leroy & Frongillo, 2019).

Infection status and food intake are factors that directly influence stunting. Macronutrient and micronutrient intake in babies plays a significant role in growth and the prevention of growth problems (Savarino et al., 2021). Low protein, carbohydrate, and energy intake is significantly associated with an increase in global DNA methylation of high levels in stunted two- to three-year-olds in Bangladesh (Iqbal et al., 2019).

Additional research has connected children’s fat consumption to stunting. The hormone leptin, which affects bone growth, is one of the numerous hormones that depend heavily on fat for their production. Additional research has revealed that leptin affects bone growth by stimulating fibroblast growth factor 23 (FGF-23) (Tsuji et al., 2010). Leptin also affects and regulates osteocalcin which in turn regulates insulin sensitivity and energy expenditure (Ferron & Lacombe, 2014).

Low protein consumption has been linked to stunting, according to studies. The growth of a child’s length or height is strongly correlated with protein intake (Arsenault & Brown, 2017). Chronic protein deficiency in children under five years of age hinders their growth. Stunting is 1.4 times more likely to occur in children who do not consume protein (Krusevec et al., 2017). Anemia, immunodeficiency, and protein and energy deprivation will induce inflammation and boost cytokine production (Bianchi, 2016). Since macronutrient deficiencies such as wasting and low weight have become public health problems in Indonesia, protein and energy malnutrition affect physiological functions. The lack of nutrients causes growth failure because micronutrients cannot provide maximum benefits based on their function in linear growth (Dewi & Mahmudiono, 2021).
A decrease in protein intake leads to proteolysis due to a decrease in amino acid availability and a decrease in IGF-1 levels. Reduced carbohydrate intake will boosts the secretion of proinflammatory cytokines while decreasing insulin secretion. Both of these substances impair immunological response and macrophage activity. Fats from food encourage the release of hepsidines, which prevent iron absorption. Such mechanisms work together to disrupt the production of herithropoiesis and heritropoietin (Bianchi, 2016).

Anemia caused due to malnutrition of proteins and energy causes the ineffectiveness of erythropoiesis in addition to an increase in the number of erythropoetin. Hemoglobin and hematocrit decreased slightly but significantly after 8 days in a protein diet. As a result, malnutrition is a clinical condition that alters many aspects of the immune response, including decrease in cell migration, stimulation of phagocytosis, bactericidal response, changes in the production of reactive oxygen and nitrogen species, as well as the production of pro-inflammatory cytokines (Bianchi, 2016).

Although the prevalence of stunting globally is high, the pathogenesis underlying the failure of linear growth is less known. Interventions to promote healthy growth remains unclear and no scientific studies have ever normalized linear growth among children in developing countries. From epidemiological studies, it seems that breast milk is less than optimal and the practice of complementary feeding of breast milk, recurrence of infections and micronutrient deficiencies are important determinants in stunting (Dewey & Mayers, 2011).

Anemia

Anemia is a group of diseases characterized by a decrease in either hemoglobin or the volume of red blood cells, thus causing a decrease in the capacity of oxygen carriers to the blood. Anemia in children usually occurs due to primary hematological abnormalities. The risk of iron deficiency anemia increases due to the encouragement of rapid growth and deficiency in food intake (DiPiro
et al., 2017). Anemia is a continuation of macronutrient deficiencies such as carbohydrates, proteins, fats, and micronutrient deficiencies such as vitamins and minerals. Anemia affects the growth and development of children under five years of age. Based on studies conducted in Nigeria, children with crescent anemia have lower IQ, memory, and memory processing speed than healthy children (Oluwole et al., 2016).

Iron deficiency anemia is the type of anemia that most often contributes to global disease (McKee et al., 2017). Iron is needed to form hemoglobin which is an important chemical substance in the process of binding oxygen. Thus, when iron levels decrease, organs and tissues do not get enough oxygen and cause fatigue, decreased performance, and immunity. Untreated iron deficiency will cause serious problems such as delays in growth and development processes (McKee et al., 2017). Iron deficiency anemia in children also have detrimental effects on brain function, metabolism and immune system (Melku et al., 2018).

For the first four to six months after birth, babies who have enough iron deposits to meet their needs must receive iron through food (Gosdin et al., 2018; Rao & Georgieff, 2007). At this time between the ages of one and two years shows the highest risk of anemia. However, in girls, the risk of anemia increases when entering the menarche period (Alvarez-Uria et al., 2014). In infants and children, severe chronic anemia causes growth inhibition and long-term effects on neurodevelopment and behavior, mediated by changes in the neurotransmitter myelin, monoamine metabolism in the striatum, which functions on the hypocampus and energy metabolism (Soliman et al., 2014).

Chronic anemia has a negative effect on linear growth during all stages of growth (infancy, childhood and adolescence). Infants with chronic deficiency anemia will experience cognitive, motor, and developmental delays that may last a long time, mechanisms of growth defects in iron deficiency anemia include defects in the secretion of IGF-I. Correction of anemia is associated with improved growth and a significant increase in IGF-I secretion. Although the use of iron supplementation offers an easy method in the primary prevention of iron deficiency anemia, evidence suggest that iron supplementation is only beneficial in the regions where iron deficiency anemia is common, including those region where endemic to malaria. It may also indicate some risk in people with normal Hemoglobin levels (Soliman et al., 2014).
Both anemia and stunting pose significant challenges to the health system and the survival of children, co-occurrence of anemia and stunting will be more detrimental (Mohammed et al., 2019). Based on research conducted by Gosdin et al. (2018) related to the incidence of co-occurrence of anemia and stunting, it is proven that anemia and stunting must be managed as separate conditions. Targeting one condition will not identify or address another simultaneously, so there is a need for a multistrategic approach to target the anemia and stunting determinants that are most significant because focusing only on one condition will not reveal or address another.

Anemia is determined based on hemoglobin levels, which might change from day to day (Gosdin et al., 2018). On the other hand, stunting is measured using linear growth and changes very slowly (Gosdin et al., 2018). Anemia is characterized by a decrease in hemoglobin levels. The prosthetic group of hemoglobin, known as heme, gives it its distinctive deep red color. Hemoglobin is a conjugated protein. The cytochromes, which are substances that serve as electron carriers and enzymes like catalase and peroxidase, are also found among the heme proteins. (Blanco & Blanco, 2017). Low hemoglobin concentrations are commonly used as an indicator of public health against impaired iron status, although anemia, similar to stunting, is a multifactor problem (Raiten and Bremer, 2020).

Protein deficiency or malnutrition is related to higher rates of morbidity and mortality. Individual assessments of malnutrition include the identification of inflammations such as increased concentrations of C-reactive plasma proteins to determine diagnosis based on etiology, accompanied with proof of decreased food consumption, weight loss, decreased subcutaneous fat, and decreased muscle tone, accumulation of localized fluid or generalizations, and decreased physical status function (White et al., 2012). A decrease in access to food in the long term leads to marasmus, which is also called wasting. Individuals with marasmus appearance are very thin with depletion of muscle mass and adipose tissue. The bones look protruding and the skin is sagging. Malnutrition or protein deficiency indicates insufficient protein intake but sufficient energy consumption. Due to an inadequate amount of protein in the blood and cells from a lack of protein

Table 1. Thalassemia, Growth, and Endocrine Glands: Effects of Iron Deficiency Anemia VS Chronic Hemolytic Anemia (Soliman et al., 2014)
intake from diet, causes water to diffuse out of the blood and out of the cells towards the intercellular, resulting in edema. Edema typically first manifests in the legs, but it can also be found in the face or more commonly throughout the body (Gropper & Smith, 2012).

Myoglobin, a molecule that transports and stores oxygen in the muscles, while hemoglobin is in charge of carrying oxygen throughout the blood. The globin protein, which is abundant in the amino acids lysine, arginine, and histidine, is what creates both myoglobin and hemoglobin (Blanco, 2017). Low protein intake will lead to limited hemoglobin production. Limited protein intake is not capable of producing the normal amount of globin (Hahn & Whipple, 1939).

Myoglobin and hemoglobin, which are involved in metabolism and the transfer of oxygen in the body, require iron as a necessary component. Additionally, iron is necessary for the formation of lymphocytes and Natural Killer (NK) cells to prevent infection, organic compound excretion and energy metabolism. Immunity is weakened when iron levels are low. Heme and non-heme iron can be found in food. Meat, seafood, and poultry meat are contain heme iron, which is best absorbed through the digestive system. Conversely, when consuming a small amount of meat with foods containing non-heme iron, non-heme iron can be absorbed or its absorption will increase. Consumption of foods high in vitamin C can also improved iron absorption (Barrett, 2020).

The Role of Amino Acids and Proteins in Metabolism

Blood Components

Protein is a component of blood transport. For example, hemoglobin in red blood cells is in charge of carrying oxygen. Each hemoglobin subunit contains gugud heme with iron atoms that can bind to oxygen. Other important transport proteins include plasma proteins. Plasma proteins are mostly synthesized and secreted by the liver. Plasma proteins contain simple molecules and also conjugated proteins such as glycoproteins and lipoproteins. Albumin is a transporter of compounds such as fatty acids, bile acids in the portal circulation, and other compounds including some minerals. Other protein transports found in the blood include transferrin, ceruloplasmin, and vitamin D binding protein (DBP), protein containing lipoprotein is a major transporter of fat and fat-soluble compounds (fat-soluble vitamins) (Wildman, 2018).

Blood Clotting

Blood clotting factors are synthesized in the liver and released in the form of zimogen includes factors V, VII (proconvertin), VIII (antihemolytic), IX (natal factor), X (Stuart factor), XI (Thromboplasatin plasma, XII (Hageman factor), and XIII (transaminases); fibrinogen, and prothrombin. The freezing mechanism is simultaneous at each stage. The final reaction of the cascade results in the activation of fibrinogen into fibrin which forms a cross-link structure, which is the basic structure of freezing. The liver also secretes plasminogen which when activated into plasmin works to destroy clots (Wildman, 2018).
Iron and Protein Metabolism

Numerous proteins have been shown to be involved in iron metabolism. The main blood iron transporters are proteins like ferritin or Tf, while peptides like iron regulatory proteins (IRP), hepsidine, and matriptase (Mt2) are crucial regulators of iron at various physiological levels. Iron is transported through cellular membranes by a variety of proteins, primarily divalent metal transporters (DMT1), ferroportin (FPN1), and transferin receptors (Tfrs), which are all ferroxidases. These proteins include duodenal cytochrome B, ceruloplasmin (Cp), and heme transport proteins (HCP1). Since they require iron to work, other proteins such as myoglobin, Hb, and several enzymes are the results of iron metabolism (Waldvogel-Abramowski et al., 2014).

It is impossible to discuss iron metabolism without mentioning the role of hepsidine. Hepcidine is a hormone of 25 amino acid peptides, commonly produced by hepatocytes. Hepcidine production is controlled by a variety of methods. The liver often produces peptides in response to a variety of causes. Inflammation causes more intracellular and extracellular iron to be stored, which raises the level of hepcidine in the blood. Conversely, when the need for iron is high, as in the increase in erythropoesis, hepsidin levels become low. Hepsidin recoups iron production from hepatocytes, macrophages from FPN1 (Waldvogel-Abramowski et al., 2014).

Peptides are produced by the liver. Hepsidin closes the entry of iron from hepatocytes, macrophages of enterocytes, by binding to ferroportin (FPN1) (Waldvogel-Abramowski et al., 2014). In anemic states, hepsidin mRNA is suppressed, but the effect is likely to be indirect, depending on the production of erythropoetin. At least three other proteins also participate in the interaction between BMP and BMP receptors. Hemojuvelin (HJV) is the initial protein, Mt2 controls the amounts of HJV-bound membranes, and neogenin is a transmembrane protein that is ubiquitously produced and has a variety of functions (Enns et al., 2012). Many polymorphisms of Mt2 gene affect iron metabolism characteristics, especially in patients with iron deficiency anemia (Waldvogel-Abramowski et al., 2014).
Hepcidine is found in the blood in both mature and pro-hormone forms (Prohepsidin). Due to the discovery that prohepsidin selectively binds to STAT3 in HAMP gene promoters, it is presumed that prohepsidin influences the expression of its own genes, indicating an autoregulation loop of the hepsidine gene (Pandur et al., 2013).

Iron Regulation Proteins

Different cell types contain different types of iron, which serves a specific purpose as an iron source or a storage for iron. Enterocytes, which accept iron from digested food, macrophages, and hepatocytes are examples of iron export cells. Both of these cells recycle iron as needed. Iron is then transported into the fetal circulation by placental cells. IRP1 and IRP2 maintain cellular iron homeostasis, IRP binds to IRE residing in untranslatable areas and mRNA proteins participating in iron retrieval, utilization storage, and export (Waldvogel-Abramowski et al., 2014).

CONCLUSION

Considering the outcomes of the literature review on the correlation of anemia in pregnant women with stunting incidence, it is known that both macronutrients and micronutrients are correlated with the occurrence of stunting and anemia. It is known that nutrient in infants, both macronutrient and micronutrient have a large role in growth and prevention of growth disorders. It is certainly necessary to make efforts to improve health in both pregnant women and children to prevent anemia, both through cross-program and across sectors.

REFERENCE


Correlation of Anemia in Pregnant Women with Stunting Incidence: A Review


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