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Relationship between Anemia and Obesity with Women's Reproductive Health: A Review

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ABSTRACT

The most common anemia is related to problems with nutritional status. Obesity increases the risk of anemia because of the accumulation of fat in adipose tissue that triggers inflammation which can lead to anemia. Hepcidin is a small peptide hormone that negatively regulates intestinal iron absorption. The absorption of iron in the body is disturbed, it will affect the hemoglobin level in the body, leading to anemia.

KEYWORDS: *Anemia, Hepcidin Level, Hemoglobin Level, and Obesity*

INTRODUCTION

Anemia is a severe global public health problem that occurs in adolescents and women of childbearing age. According to the World Health Organization (WHO), the prevalence of anemia worldwide in 2021 is 29.9%. Southeast Asia is ranked first in the world with anemia incidence. According to Riskesdas data for 2018, the prevalence of anemia in Indonesia is 23.7%, with a proportion of 32% occurring in women of childbearing age in the age group 15-24 years [1-2].

The most common risk factors for anemia are related to problems with nutritional status. Nutritional status can be calculated by measuring BMI (Body Mass Index). Several previous studies have shown that dietary deficiencies and excesses are risk factor for anemia [3]. Obesity also increases the risk of anemia due to fat accumulation, which triggers inflammation. Several studies have shown that inflammatory mediators such as Interleukin-6 will induce excessive expression of the acute phase reactant, the hormone hepcidin. Hepcidin is a peptide hormone synthesized and secreted by the liver that regulates systemic iron homeostasis. Hepcidin binds and induces internalization and degradation of ferroportin (the sole exporter of iron from cells to plasma). If it is excessive, it will cause hypoferremia and hyperferritinemia, thereby reducing the amount of iron that enters the blood plasma [4]. A lack of iron will limit the production of hemoglobin; a further decrease in iron in the body will result in iron deficiency anemia [5].

A young adult woman is a prospective mother who should have sufficient iron reserves in her body. Iron comes from food intake and the breakdown of red blood cells that are used again. So it is essential to examine food intake, hepcidin levels, and hemoglobin levels in young adult women to detect anemia early in the pre-conceptional period [6].

DISCUSSION

Anemia

Anemia is a hemoglobin concentration less than the fifth percentile for age. Normal hemoglobin levels vary with age. Therefore, the patient's hemoglobin level should be compared with age-based norms to diagnose anemia [7]

A person's normal limit for hemoglobin levels is difficult to determine because each ethnic group varies. Here are various opinions about the normal limit for hemoglobin levels. The normal limits for hemoglobin levels according to WHO (Fahmi, 2021) are as follows: [8]

Subject	Normal value (gr%)	Anemia		
		Mild (gr%)	Moderate (gr%)	Severe (gr%)
Children 6-59 month	≥11,0	10,0-10,9	7,0-9,9	<7,0
Children 5-11 year	≥11,5	11,0-11,4	8,0-10,9	<8,0
Children, 12-14 year	≥12,0	11,0-11,9	8,0-10,9	<8,0
Man	≥13,0	11,0-12,9	8,0-10,9	<8,0
Non-pregnant adult women	≥12,0	11,0-11,9	8,0-10,9	<8,0
Pregnant adult women	≥11,0	10,0-10,9	7,0-9,9	<7,0

Obesity

Obesity is an excessive or abnormal accumulation of fat in adipose tissue which can impair health. Obesity is also defined as a pathological condition which is a metabolic disorder (metabolic disorder) with excessive fat accumulation than the body needs, which can result in disease (multifactorial disease) [9,10].

Obesity Pathophysiology

Obesity occurs as a result of disturbances from homeostatic mechanisms that control the balance of energy in the body, an imbalance in the input and output of calories from the body, and a decrease in physical activity (sedentary lifestyle), which causes accumulation of fat in several parts of the body. Control of one's appetite and satiety level is governed by neural and humoral mechanisms influenced by genetics, nutrition, environment, and psychological signals [11].

The hypothalamus regulates energy balance through 3 physiological processes, namely controlling hunger and satiety, influencing the rate of energy expenditure, and regulating hormone secretion. The process of handling energy storage occurs through efferent signals (which are centered in the hypothalamus) after receiving afferent alerts from the periphery (adipose tissue, intestine, and muscle tissue) [11].

These signals are anabolic (increase hunger and reduce energy expenditure). They can also be catabolic (anorexia increases energy expenditure) and are divided into two categories, namely short signals and long signals. Temporary signs affect meal portions and meal times and are related to gastric distention factors and gastrointestinal peptides, played by cholecystokinin (CCK) as a stimulator in increasing hunger. The long signal is played by the fat-derived hormones leptin and insulin, which regulate energy storage and balance [11].

If energy intake exceeds what is needed, then adipose tissue increases, accompanied by increased leptin levels in the blood circulation. Leptin stimulates the anorexigenic center in the hypothalamus to reduce the production of Neuro Peptide Y (NPY), resulting in decreased appetite. Vice versa, if energy demand is more significant than energy intake, adipose tissue is reduced, and stimulation of the orexigenic center in the hypothalamus occurs, which causes an increase in appetite. In most obese people, there is leptin resistance, so high leptin levels do not cause a decrease in appetite [11].

Obesity Impact

Obesity can cause social, economic, and health impacts. Obesity can cause various diseases such as coronary heart disease, type 2 diabetes mellitus, dyslipidemia, deep vein thrombosis, pulmonary embolism, osteoarthritis, gastroesophageal reflux disease (GERD), asthma, cirrhosis of the liver, cancer, and so on [3].

Two classifications of BMI are widely used, namely the classification according to WHO and Asia-Pacific. The World Health Organization (WHO) categorizes average weight with a BMI of 18.5 – 24.9, while the Asia Pacific classification uses a range of 18.5 – 22.9, as shown in the Table below.

Relationship Between Anemia and Obesity

Obesity occurs due to an imbalance between food intake and energy expended, in which food intake is too much, but too little energy is expended. Unbalanced food intake can affect iron intake. In obese people often occurs iron deficiency anemia. Because an increase in body weight will increase the body's need for iron. For every kilogram of weight gain, an increase in body iron is required by 35–45 mg. The habit of eating foods containing iron with low bioavailability often occurs among young women who generally consume foods derived from carbohydrates and fats [12]. Research by Lestari et al., 2020 found that the density of iron intake in respondents with excess body weight was higher than normal [13].

Obesity is also associated with anemia because fat deposition and chronic inflammation in adipose tissue can reduce iron absorption, the concentration of which decreases early in the development of iron deficiency. Research by (Rasyid et al., 2021) at the Faculty of Medicine, Hasanuddin University, was conducted on 72 subjects. The median value of hepcidin levels in obese women was 244 pg/mL; in non-obese women, it was 200 pg/mL. This shows an increase in hepcidin levels based on the median value in obese subjects compared to non-obese. Increased hepcidin levels in obesity are caused by stimulating liver cells by inflammatory mediators such as IL-6 release due to an inflammatory process 14. Another research conducted by (Wisnusanti et al., 2022) showed that there is no difference in hepcidin levels in obese and normal with statistical test results p value > 0.05 (p = 0.511). In obesity, there is chronic inflammation. However, inflammation did not affect hepcidin levels, as shown by the analysis of the relationship between hepcidin levels between the obese nutritional status and normal nutritional status groups, which did not differ significantly [14-15].

If inflammation occurs, hepcidin production increases so that hepcidin will bind to ferroportin found on the cell surface and trigger tyrosine phosphorylation resulting in ferroportin degradation. Internalization of ferroportin can occur both on the surface of enterocytes and macrophages and hepatocytes. This can cause the supply of iron to stop resulting in a decrease in iron levels. Consequently, the absorption and mobilization of stored iron from the liver and macrophages are decreased. Hepcidin synthesis will increase when transferrin saturation is high (when the capacity of transferrin to bind to serum iron is maximal). Conversely, hepcidin synthesis decreases when iron saturation is low [16].

Based on WHO standards, the diagnosis of anemia is carried out by laboratory examination of hemoglobin levels in the blood using the Cyanmethemoglobin method. This is by the Minister of Health Regulation Number 37 of 2012 concerning the Organization of Public Health Central Laboratories. Adolescent girls and WUS suffer from anemia if the blood hemoglobin level is less than 12 g/dL. Anemia can be grouped into three categories, namely, it is said to be mild anemia if the hemoglobin level in the blood ranges from 11-11.9 g/dL, moderate anemia if the hemoglobin level in the blood ranges from 8-10.9 g/dL, and severe anemia if the hemoglobin level < 8 g/dL [17].

Research conducted by (Nisa et al., 2019) showed that hemoglobin levels in obese subjects were lower than in the non-obese group. So the majority of the obese group experienced anemia [6]. However, this differs from the results of a study conducted (Elmugabil, 2017), which found that hemoglobin levels and white blood cell counts were significantly higher in the obese group than in the non-obese group [18].

Mechanistically, low hemoglobin levels in obesity are caused by excess fat accumulation, which can interfere with the work of hepcidin as the primary hormone regulating iron homeostasis resulting in an increase in hepcidin which will inhibit iron

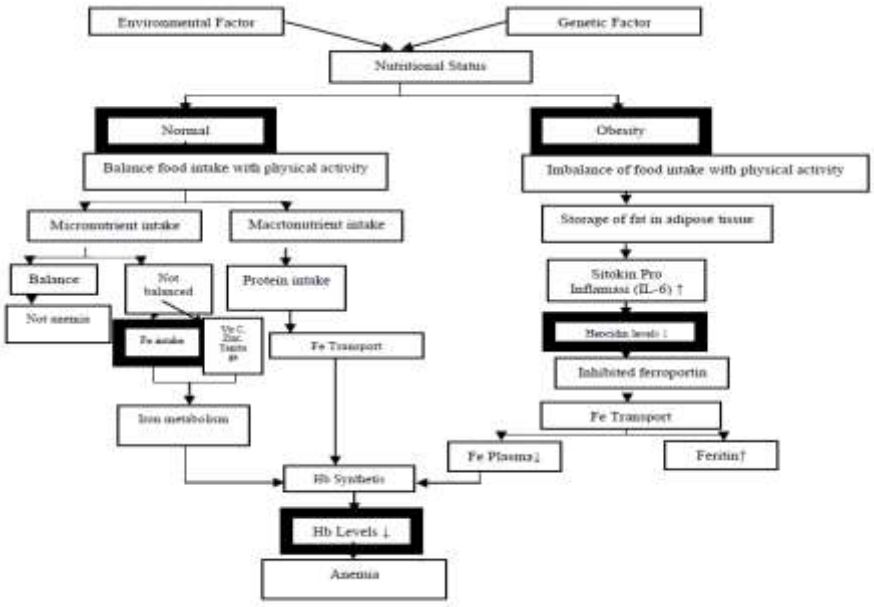
absorption and limit iron for erythropoiesis. If erythropoiesis is disturbed, the following process will automatically be disrupted. Disturbances in iron binding to form hemoglobin will form erythrocytes with small cytoplasm and less hemoglobin content. The failure of the cytoplasm of nucleated erythrocytes to bind Fe for the construction of hemoglobin can be caused by low levels of Fe in the blood so that the hemoglobin level in the respondent decreases [19].

Physiologically, young adult women experience menstruation every month. A research result in Indonesia shows a decrease in women's hemoglobin levels after menstruation. The thing that affects the reduction of hemoglobin levels is the decrease in iron stores during menstruation. If menstruation ends and iron stores are sufficient, the reduction in hemoglobin may occur only temporarily during menstruation. This was one of the factors considered in this study because the subjects had different menstruation durations, so it is possible that menstrual factors also affected the decrease in hemoglobin levels in the two groups of respondents [20].

The mechanism of low hemoglobin levels in obesity is caused by excess fat accumulation, which can interfere with the work of hepcidin as the primary hormone regulating iron homeostasis resulting in an increase in hepcidin which will inhibit iron absorption and limit iron for erythropoiesis. Physiologically, young adult women experience menstruation every month. A research result in Indonesia shows a decrease in women's hemoglobin levels after menstruation. The thing that affects the reduction of hemoglobin levels is the decrease in iron stores during menstruation. If menstruation ends and iron stores are sufficient, the decrease in hemoglobin may be only temporary during menstruation. This was a factor to consider in this study because the subjects had different menstruation durations, so it is possible that menstrual factors also affect the decrease in hemoglobin levels in obese subjects [6].

However, in the group of female students with normal nutritional status, anemia occurred due to a lack of RDA for Fe intake and the habit of consuming other substances that could inhibit the absorption of non-heme iron, including phenolic compounds found in tea and coffee, calcium, and phytate. In high-fiber foods. Suppose a person has a habit of consuming high non-heme iron accompanied by increased consumption of substances that inhibit iron absorption. In that case, this condition will lead to low iron intake, impacting low hemoglobin levels [6].

Theoretical Framework



Environmental and genetic factors influence nutritional status. In the nutritional status of obesity, there is an imbalance between food intake and physical activity, resulting in fat accumulation in adipose tissue. Then there is subclinical inflammation. The inflammatory process that occurs in the fat tissue of obese people causes an increase in the proinflammatory cytokine Interleukin-6 (IL-6). This increase in proinflammatory cytokines stimulates the liver to increase hepcidin secretion, inhibiting iron absorption in erythrocytes and ferroportin. This causes inhibition of iron absorption in erythrocytes and iron release in reticuloendothelial macrophages resulting in decreased plasma iron (hyperemia) and impaired iron metabolism [17].

Obesity is also associated with anemia because fat deposition and chronic inflammation in adipose tissue can reduce iron absorption, the concentration of which decreases early in the development of iron deficiency. Obesity is associated with inflammatory changes, which increase iron storage in tissues and reduce Fe in the blood circulation resulting in reduced iron for the hematopoietic process. He is the most abundant macro mineral in human and animal bodies, with as much as 3-5 grams in the adult human body. In iron deficiency anemia, the following occurs: When iron reserves decrease, this condition is called a negative iron balance, namely the stage of iron depletion (iron-depleted state). If iron deficiency continues, the supply of iron for erythropoiesis decreases, causing disturbances in the shape of erythrocytes, causing an increase in total iron binding capacity and an increase in transferrin receptors in serum. Suppose the decrease in the amount of iron continues to occur. In that case, erythropoiesis is increasingly disrupted, so the hemoglobin level decreases, resulting in microcytic hypochromic anemia, known as iron deficiency anemia [17].

In normal nutritional status, there is a balance between food intake and physical activity. Anemia can also occur in normal dietary status due to a lack of information on Fe, so it affects iron metabolism and affects hemoglobin levels which cause iron deficiency anemia.

CONCLUSION

In this review, anemia will probably be very susceptible to occurring in obese people. So, it is necessary to carry out routine examinations and management in this population. Physicians who treat or manage the health of obese adolescents in early adolescence should be aware that anemia may be present.

Declaration by Authors

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