Maternal Anemia and Risk of Neonatal Mortality: A Review

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ABSTRACT

Anaemia in pregnancy is a major public health concern all over the world, especially in under developed nations where it contributes significantly to maternal morbidity and mortality. Anemia is of more concern in developing countries since the prevalence of anemia in these countries is significantly higher than in developed countries. Numerous underlying factors can cause anemia in pregnant women, including social, demographic, economic, nutritional, and health factors. Iron deficiency is the most important cause of anemia in pregnant mothers. Maternal anemia in pregnancy represents a common and potentially reversible risk factor associated with antepartum, intra-partum, and postpartum maternal morbidity and perinatal morbidity and mortality. The paper reviewed the concept of maternal anemia, risk factors associated with anemia and the risk of neonatal mortality.

Keywords: Anemia, neonatal mortality, risk factors, maternal anemia

INTRODUCTION

The World Health Organization estimates that over 2 billion people (roughly 30% of the world's population), are affected by anaemia and at least 50% of pregnant women are anemic [1]. Although anaemia has been shown to affect women in both high- and low/middle-income nations, the major burden of disease is found in low/middle-income countries. The association of both the presence of anaemia and its severity to maternal and neonatal outcomes has not been well characterized [2]. Limited data suggest that severe anaemia is associated with an increased risk of low birth weight, but that mild anaemia may protect against low birth weight [3].

Anemia during pregnancy is defined as a hemoglobin concentration of less than 11 g/dL. It is the most prevalent hematologic condition that impairs the normal functioning of the organ system by reducing the amount of oxygen that

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reaches different tissues and organs via blood circulation [4]. Although anemia can develop in any human population, pregnant women and small children are the most common victims of this hematologic disorder. Anemia during pregnancy causes major maternal and fetal problems and can even result in maternal death. Anemia is responsible for 20% of all maternal mortality, according to research [5]. Anemia during pregnancy is caused mostly by nutritional deficiencies (iron, vitamin B12, folate), parasitic diseases (hookworm, malaria, and so on) and acute blood loss [6].

Anaemia in pregnancy is a major public health concern all over the world, especially in under developed nations where it contributes significantly to maternal morbidity and mortality [7]. It's also linked to a higher chance of miscarriage, preterm, stillbirth, low birth weight, and, as a result, perinatal mortality. Iron deficiency, caused by a sustained negative iron balance, is the leading cause of anemia in women of reproductive age worldwide, accounting for 50% of anemia in women [7]. Iron deficiency anemia (IDA) is a condition that causes a large decrease in iron storage in the body as a result of both extrinsic and intrinsic factors [8]. This anemia is hypochromic and microcytic in nature. Pallor, exhaustion, sadness, fainting, dyspnea, emotional instability, palpitation, headaches, and hair loss are all symptoms of iron deficiency anemia during pregnancy, which is caused by decreased oxygen delivery to the tissues.

Furthermore, chronic IDA reduces quality of life, job tolerance, and productivity [8]. Because anaemia is a common medical condition affecting pregnancy, especially in low/middle-income countries, understanding the impact that various levels of anaemia have on pregnant women and their newborns is of paramount importance [9]. If anaemia is found to be associated with poor maternal and neonatal outcomes, meaningful interventions that improve the haemoglobin status of anaemic pregnant women could potentially have a large impact on global health.

ANEMIA IN PREGNANCY

Anemia is one of the most critical health conditions affecting people worldwide [10]. It is estimated that about two billion people worldwide have anemia (WHO). Thus, anemia is a major concern in all countries globally. Anemia is of more concern in developing countries since the prevalence of anemia in these countries (with a prevalence of 43%) is significantly higher than in developed countries (with a prevalence of 9%). Of course, it should be noted that the prevalence of anemia varies according to demographic, economic, and geographical characteristics of the place of residence of the studied populations [11].

Anemia is a silent disease with a slow progression and a few physical symptoms, which may cause the patient not to be able to feel the condition until they are in an advanced state of the illness [10]. A person with anemia is considered to have lower than normal hemoglobin levels in the bloodstream, followed by a decrease in the oxygen-carrying capacity of red blood cells to the tissues [11]. Anemia can be classified into three categories: mild anemia (hemoglobin concentration 10–10.9 g/dl), moderate anemia (hemoglobin concentration 9–9.9 g/dl), and severe anemia (hemoglobin concentration less than 8 g/dl) [1].

Acquired anemia may be caused by iron deficiency anemia, folate, vitamin B12 anemia, anemia due to blood loss, chronic disease, hemolytic and aplastic anemia. Hereditary anemia includes sickle cell anemia, thalassemia, and Fanconi anemia [12]. Although the "mild/moderate/severe" anemia classification has historically been used to indicate severe levels of anemia and, to some extent, is still present, such classification can be a little misleading, especially for those whose specialty is outside of global health nutrition. "Mild" could connote that this level of anemia is not that serious of a public health issue, when in fact, iron deficiency-related "mild anemia" occurs only at the 3rd stage of iron deficiency when iron stores are low enough to cause decreased hemoglobin concentration [13]. The cutoffs listed are specific to pregnant women and children, and non-pregnant people have different cutoffs as per WHO guidelines [14]. The most common type of anemia worldwide is nutritional anemia mainly due to iron deficiency yet may also be due to the deficiency of folate, vitamin B12, vitamin C, and other micronutrients [15]. Anemia can occur in individuals at any age; nevertheless, it is more common in pregnant women and children [12,14]. Often, the cause of anemia in children is insufficient iron in the diet, while the causes of anemia in pregnant women can also be due to the loss of large amounts of blood during menstruation and pregnancy due to poor nutrition and not consuming iron [14].

Numerous underlying factors can cause anemia in pregnant women, including social, demographic, economic, nutritional, and health factors [16]. Iron deficiency is the most important cause of anemia in pregnant mothers. The mother's body requires iron to increase blood flow and the growth of tissues in her body and meet the fetus's physiological needs in the first months of life [6]. Maternal iron demand during this

period increases from 1 to 2.5 mg per day in early pregnancy to 6.5 mg per day in the third trimester [17]. Anemia can also develop during chronic diseases such as tuberculosis, malaria, HIV, and diabetes, and genetic factors may also increase susceptibility to anemia [2]. It should be noted that the contribution of each of these factors in the development of anemia in pregnant women varies according to social, economic, lifestyle, and health-seeking behaviors in different geographical areas and under the influence of specific cultures of different communities [10].

Mothers with anemia may experience fatigue, dizziness, decreased energy levels and decreased cognitive ability. On the other hand, anemia in pregnancy increases the risk of preterm birth (PTB), low birth weight (LBW), fetus malformations, low fetal age, low Apgar score, maternal mortality, and perinatal mortality. Recent studies indicate the presence of mental disorders among children who have had anemia from the beginning of life [18]. Anemia can also impose additional costs on the family and society by reducing women's productivity, imposing treatment costs, and reducing the health of the community's young workforce.

RISK FACTORS ASSOCIATED WITH ANEMIA IN PREGNANCY

Age

In a study conducted by Loy et al. [19] that the age of pregnant women <25 years can increase the occurrence of anemia by 2 times and is statistically significant (p = 0.04) compared to those aged> 25 years. This has the same results as research conducted by Ammalia et al. [20] high risk age in pregnant women has a tendency to 2 times greater and statistically significant (p = 0.03) to experience anemia than pregnant women with age at risk. The high risk ages referred to in the study were <20 years and> 35 years. Age can cause anemia because the age of the mother during pregnancy who is not in a healthy reproductive period (<20 years or> 35 years) is a risk factor for anemia in pregnancy, similar to research conducted by Ademuyiwa [21], it was found that age was statistically significant (p = 0.033). Research conducted by Astuti [22] refers to age <20 years which statistically significant (p = 0.004) can cause anemia. Similar to research conducted by Gedefaw [23], 15-24 year olds have nine times the risk of experiencing anemia. When the age is <20 years, the reproductive organs are not mature enough to perform their functions and the hormonal system is still unstable compared to those aged> 20 years, with this unstable hormone system it is prone to anemia.

Parity

Parity is the number of mothers who have given birth to live children [24]. Pregnant women with a history of pregnancy more than three or multi-parity can cause anemia risk as much as two times and statistically significant (p = 0.046) compared with the new pregnant women pregnant with her first to the third [19]. This is also reinforced by research conducted by Ammalia et al., [20] that multi-parity can cause the risk of anemia in pregnant women 4 times and it is statistically significant (p = 0.05). Pregnant women who give birth to their third to fifth children have a risk of anemia 2 times compared to mothers who give birth to six and over have a 3 times higher risk of anemia [23]. Research by Derso et al. [25] also showed that multi-parity> 5 had 5 times the risk of anemia and was statistically significant (P = 0.02). Multi-parity reflects a reduced iron intake as the number of pregnancies increases. Parity is also closely related to pregnancy spacing, if the pregnancy is too close or <2 years, then the body's organs are not ready for pregnancy [24]. Pregnancy status can affect the degree of anemia, the more often a mother gives birth, the greater the risk of blood loss and an impact on reducing HB [26].

Economic Status

Economic status was found where pregnant women with low economic status can cause anemia in pregnant women as much as 4 times higher than pregnant women with high economic status, it is confirmed by the existence of a significant statistical test p = 0.002 [27] as well as the research of Lebso [28] that low economic conditions have a double risk of experiencing anemia. Low economic status has a higher prevalence of anemia than pregnant women with low economic status. Maybe pregnant women who have a low economy cannot buy food with good quality and sufficient quantity [28]. Bahan foods rich in iron found in food sources that contain good protein animal (chicken liver, fish, milk, eggs, and meat) or vegetable (tofu, tempeh, and legumes) and derived from green vegetables. The food sources that contain the most iron are those derived from animal protein which are quite expensive, the high cost of these foods makes it impossible for people with low family income to reach them [27]. So that pregnant women cannot meet their nutritional needs during pregnancy more than before pregnancy.

Compliance with Fe

Pregnant women who do not adhere to taking Fe tablets will increase the risk of anemia by 7 times compared to pregnant

women who are compliant in consuming Fe tablets [27]. Lack of intake of Fe tablets has four times the risk of experiencing anemia and statistically significant (p = 0.003; 0.01) [19,29]. Another study conducted by Astuti Dwi [26] was statistically significant (p = 0.000) and had 14 times the risk of experiencing anemia if they did not comply with Fe tablets. Research is reinforced by Lebso [28] that pregnant women who do not take Fe tablets 2 times have a risk of up to 6 times the risk of experiencing pregnancy anemia. In the research above, it is explained that pregnant women need to consume Fe tablets during pregnancy, because the iron needs of pregnant women increase during pregnancy. Pregnant women experience dilution of red blood cells, so they need additional iron to increase the number of maternal and fetal blood cells. Iron is needed for hemopobesis (blood formation), which is in the synthesis of hemoglobin and can be conjugated with protein in the form of ferrous or ferric in the body, so it is needed especially pregnant women whose iron needs are increasing [27].

Nutritional Status of Pregnant Women

Several studies showed that nutritional status during pregnancy has a statistical effect (p = 0.00 0) on the occurrence of anemia in pregnant women [30] and this is strengthened by research conducted by Tanziha et al. [31] where mothers have nutritional poor status or experiencing chronic energy deficiency will experience a risk of 2 times compared to pregnant women with normal nutritional status. Based on Derso's research [17], the nutritional status of pregnant women can be measured through the upper arm circumference where Lila is measured <23cm at risk of anemia and has 4 times statistical significance (p = 0.02).

Trimester in Pregnancy

Gebreweld [29] reported that pregnancy in the second trimester has a risk of 6 times and the third trimester 8 times the incidence of anemia compared to the initial trimester. This may be due to a 40-50% higher increase in maternal plasma volume against the red cell mass by 20-30% and to a decrease in hemoglobin concentration. This is similar to research by Lebso [28] which states that second and third trimester pregnancies have a risk of anemia 3 times higher than the initial trimester, this is because calories and nutrients are increased to support increased metabolism of pregnant women, blood volume and nutrients to the fetus, this demanded most during the second and third trimesters of pregnancy. Meanwhile, in the early trimester, there is a decrease in iron absorption due to lower iron requirements. However, the second trimester of pregnancy iron absorption from food with iron availability increases by 1.9mg / day and the final trimester up to 5, mg / day. Anemia in the third trimester of pregnancy can cause the mother to become weaker and the iron in the blood is divided for fetal growth, thereby reducing the iron-binding capacity of the mother's blood [24].

RESIDENCE

Derso et al. [25] with a significance level (p = 0.02) and pregnant women who live in rural areas are at 3 times the risk of pregnant women living in urban areas. The possibility of anemia living in rural areas is due to not having adequate latrines so that PHBS is less and anemia is easy. And in a study conducted by Derso et al. [25] pregnant women who live in rural areas are still affected by public trust in bad food, access is difficult and the majority of rural communities receive education and counseling. Similar to Ullah Azmat's research, there was a significant relationship between pregnant women living in rural areas with anemia (p = 0.001). In rural areas, pregnant women who do not get information about pregnancy nutrition have an effect on the health of the mother and the fetus, including anemia. Pregnant women who routinely carry out prenatal care come from urban areas so that the prevalence of disease is more due to the increasing number of pregnant women who are conducting consultations [32].

ANEMIA IN PREGNANCY AND NEONATAL MORTALITY

Individual studies, including a very recent secondary analysis of data from an international trial comprising 11,976 women, [33] have reported that maternal anemia is associated with adverse fetal, neonatal and childhood outcomes such as perinatal mortality, neonatal mortality, low-birth weight, preterm birth, and small for-gestational age newborns. Maternal anemia has also been associated with behavioral and neurodevelopmental abnormalities [34].

Seven recent systematic reviews and meta-analyses of fetal, neonatal, and childhood consequences of maternal anemia found an association between maternal anemia and some adverse fetal and neonatal outcomes, a causal relationship has not been established. Anemia is present in multiple conditions that increase the risk of adverse outcomes such as hemoglobinopathies, infections, and autoimmune disease. Anemia may be a contributor to adverse fetal and neonatal outcomes or may merely accompany these conditions that negatively affect fetal and neonatal well-being. At a minimum,

maternal iron deficiency anemia is correlated with lower cord-blood serum ferritin levels [35]. Studies in animals underscore the essential role of iron in normal brain development [36] and individual studies in humans report an association between maternal iron deficiency anemia and behavioral and neurodevelopmental abnormalities in children [37]. In theory, if iron deficiency anemia causes such adverse outcomes, iron supplementation should reduce the risk of behavioral and neurodevelopmental abnormalities. One randomized trial, which examined the outcomes of IQ and behavior at 4 years of age, did not find a benefit of iron supplementation [38]. Other studies, however, as well as assessments other than IQ and behavior, would be required to support or refute a benefit of iron supplementation.

Based on a systematic review of randomized trials commissioned by the United States Agency for Health Care Quality and Research in preparation for updating the U.S. Preventive Services Task Force recommendations regarding iron deficiency anemia in pregnant women, there is limited evidence that iron supplementation has any effect on fetal, neonatal or childhood outcomes [39].

Smith et al. [40] estimate the incidence of anemia in pregnancy and compare the maternal and perinatal outcomes of women with and without anemia in British Columbia who had a live birth or stillbirth at or after 20 weeks of gestation between 2004 and 2016. Finding showed that anemia was associated with preterm birth, small for-gestational-age live birth, neonatal death, and perinatal death

A study of 421 pregnant women in India indicated that there is a high prevalence of anaemia (85%) in this population as well as a correlation between anaemia severity and low birth weight as well as earlier gestational age at delivery [41]. Other studies have reported conflicting data on the effect of anaemia on preterm birth. A met a-analysis reported in the year 2000 showed an increased risk of preterm birth among women who experienced anaemia in the first trimester with an overall odds ratio of 1.32 [42].

CONCLUSION

The available evidence suggests that iron deficiency anemia contributes substantially to the women's health even today. Severe anemia during pregnancy is an important contributor to maternal mortality and morbidity. The review showed that maternal anemia in pregnancy represents a common and potentially reversible risk factor associated with antepartum, intra-partum, and postpartum maternal morbidity and perinatal morbidity and mortality.

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