



ANEMIA IN PREGNANCY

Hematology

Miss. Imnasena W	M.Sc. MLT (Pathology), Medical Laboratory Technology, Nims College Of Paramedical Technology
Dr. Atul Khajuria	Professor & H.O.D. Medical Laboratory Technology, Nims College Of Paramedical Technology, Nims University Rajasthan, Jaipur

ABSTRACT

The most common hematological disorder in pregnancy is anemia. Anemia is defined as having a Hemoglobin (Hb) concentration in the peripheral blood of 11 gm/dl or less, according to the most recent WHO standard. Iron deficiency is the most common cause of anaemia during pregnancy. A less common cause is a lack of folic acid. In some communities, up to 80% of pregnant women are anemic. Women from low socioeconomic groups and teenagers are the most vulnerable. Anemia is diagnosed by measuring hemoglobin concentrations and examining a peripheral blood smear for red blood cell changes. Iron and folate supplementation is recommended during pregnancy to avoid complications.

KEYWORDS

INTRODUCTION

Anemia, defined as a decrease in blood hemoglobin concentration, is one of the most common nutritional deficiency diseases observed globally, affecting more than a quarter of the global population [1–8]. It is a major public health issue that affects people of all ages, with the highest prevalence among children under the age of five and pregnant women [2, 3]. Anemia affects 1.62 billion people worldwide (25%) of whom 56 million are pregnant women [1, 2].

Anemia is defined as a lack of functioning red blood cells (RBCs), which results in a lack of oxygen-carrying ability and unusual complications during life [4]. RBCs are created in the bone marrow. They have a lifespan of about 120 days. For erythropoiesis, the body requires iron, vitamin B12, and folic acid, among other things. Anemia develops when one or more of these ingredients are deficient or there is an increase in RBC loss. Anemic patients have hemoglobin levels of less than 11 gm/dl to 11.5 gm/dl at the start of pregnancy. The reason for this is that as the pregnancy progresses, the woman's blood becomes diluted, and she will eventually become anemic. [5]

There are two contrasting medical philosophies protecting this problem. According to the first, it is preferable to stop pregnant women from developing too low hemoglobin concentrations. According to any other point of view the “physiologic anemia” is of outstanding significance for normal fetal growth and should be passively observed. Moreover, the relationship between a successful result of being pregnant and this normal growth in maternal plasma quantity has been noted. [6] This controversy is reflected in the guidelines from the World Health Organization on the optimal hemoglobin (Hb) concentrations or hematocrit (Hct) level. Thus, in 1965 a WHO specialist committee advised that 10 gm/dl need to be accepted as the lower limit of the physiologic changes made throughout pregnancy. [7] However, three years later some other WHO scientific team encouraged that when Hb values are lower than 11 gr/dl anemia should be regarded to exist in pregnant women, and diets must be supplemented with medical iron. [8]

Anemia is underreported in most growing countries even though it is one of the most well-known public health problems and has serious consequences for national development.[9] Iron deficiency causes approximately 50% of all anemia (but the proportion varies amongst population groups and in unique areas), and almost a million deaths a year; three-quarters of the deaths occur in Africa and Southeast Asia.[10,11] Although extra prevalent in less-resourced countries, women from developed countries are also affected. Women in both rural and urban areas are at risk. [12] A massive number of women from less-resourced countries embark upon pregnancy with frank iron deficiency anemia and/or depleted iron stores. Anemia is the main contributory or sole reason in 20–40% of maternal deaths. [13]

Iron deficiency anemia is the most frequent and significant nutritional deficiency in the world. The research carried out in South Asian countries have proven that iron deficiency is the main cause of anemia.

Recently, recognized more than 70% of the pregnant women have vitamin B12 deficiency in contrast to International guidelines.[14] In India, the prevalence of anemia is excessive due to the fact of fewer intakes of iron, folic acid and food sources that stop iron absorption, coupled with poor bioavailability of iron is the major aspect accountable for prevalence of anemia.[15] More than iron deficiency, zinc, vitamin B12 and folate deficiency was fairly prevalent due to ascariasis infestation.[16] A study in rural Bangladesh discovered the elevated prevalence of anemia was associated to vitamin B12 and zinc deficiency.[17,14] Moreover, poor nutritional reputation affected by low body mass index (BMI) in the women was once discovered to be related with anemia,[18] which necessitates intervention through health care providers in order to stop complications that may occur as an end result of these dietary inadequacies. The different contributing factors are younger age, grand multiparity and ethnicity. [18]

Etiology

Because of the regular physiologic changes in pregnancy that have an effect on the hematocrit and certain different parameters, such as hemoglobin, reticulocytes, plasma ferritin, and unsaturated iron-binding capacity, diagnosing real anemia, as well as determining the etiology of anemia, is challenging. The most frequent anemia are iron-deficiency anemia and folate deficiency megaloblastic anemia. These anemia are more common in women who have insufficient diets and who are no longer receiving prenatal iron and folate supplements. Other less frequent causes of acquired anemia in pregnancy are aplastic anemia and hemolytic anemia. In addition, anemia such as thalassemia and sickle cell disease can have an impact on the health of the mother and fetus.

As was referred to above, the most familiar reasons of true or absolute anemia are nutritional deficiencies. Frequently, these deficiencies are multiple, and the clinical presentation may additionally be problematic by attendant infections, usually poor nutrition, or hereditary disorders such as hemoglobinopathies. [19, 20] However, the fundamental sources of nutritional anemia embody inadequate intake, inadequate absorption, elevated losses, elevated requirements, and inadequate utilization of hemopoietic nutrients. Approximately 75% of all anemia recognized throughout pregnancy are due to iron deficiency. A significant iron deficiency results in hypochromic, microcytic erythrocytes on the peripheral blood smear. Other reasons of hypochromic anemia, even rare, need to be considered, such as hemoglobinopathies, inflammatory processes, chemical toxicity, malignancy, and pyridoxine-responsive anemia. However the increased percentage of the remaining cases of anemia in pregnancy other than the iron-deficiency type consists of the megaloblastic anemia of pregnancy due to folic acid deficiency. Anemia caused through deficiencies of different vitamins or elements does no longer often take place in humans.

Nutritional anemia is no longer a broad-based problem in the populations of developed countries. It is despite the fact that a problem for many people in these countries, and it is certainly a major health

problem in poor, underdeveloped countries. Pregnant women as well as menstruating women and children make up the section of the population in third-world countries—and even in the United States and Europe—that is affected through nutritional deficiency, every now and then accompanied by frank anemia.[22]

In conclusion, the investigation of obtained anemia throughout pregnancy is very important, considering that insufficient nutrition and nutritional deficiencies have an adverse effect on pregnancy outcome, without excluding a priori other, much less frequent types of anemia.

Pathophysiology

A healthy woman's plasma volume begins to increase around 6 weeks of pregnancy. [23]The physiologic fall in Hb concentration during pregnancy is accounted for by this increase, which is disproportionately greater than the corresponding changes in red cell mass. As a result, despite the drop in Hb, there is a significant reduction in arteriovenous oxygen extraction at the heart and a significant increase in the pregnant woman's oxygen carrying capacity.

At term, the increase in plasma volume is approximately 1,250 ml, representing a total increase of approximately 48 percent over the nonpregnant state. This is due to a rapid rise at first, followed by a slower rise after the 30th week of pregnancy. Several studies show a positive relationship between newborn weight and an increase in plasma volume. [24]The increase in plasma volume appears to be an indication of normal fetal growth and one of the hallmarks of a successful pregnancy.

As regards the red cell mass, it also will increase although, in distinction to the plasma volume, it does so more slowly. The complete increase is about 18% or 250 ml at term. After stimulation with iron supplements, however, the red cell mass may additionally reach 400ml—a complete increase of about 30% compared with the non-pregnant state. Similar to the plasma volume, the elevated red cell mass is linked to fetal growth, although probably to a lesser degree.

Clinical Features

There may also be no symptoms, especially in mild and moderate anemia. Patient may also complain of feeling of weakness, exhaustion and lassitude, indigestion and loss of appetite. Palpitation, dyspnea, giddiness, edema and, rarely, generalized anasarca and even congestive cardiomyopathy can appear in extreme cases. There can also be signs and symptoms of unique conditions causing anemia like bleeding from the rectum.

- There might also be no symptoms especially in mild anemia.
- There may be signs and symptoms specifically in mild anemia.
- There may also be pallor, glossitis and stomatitis.
- Patients may have signs due to hypoproteinemia.
- Soft systolic murmur may also be seen.[25]

Differential Diagnosis

Hemoglobin estimation is the most practical method of analysis as it is value effective and can be easily carried out by means of trained technician. The Tallquist's method of Hb estimation has simplicity and effortless applicability, however is now not very accurate. The copper sulfate method additionally has many drawbacks and is no longer reliable. Sahil's method is dependable and correct when carried out through expert, and is the most normally used, though the cyanmethemoglobin method appears to be the most accurate. Although the WHO put of point of countries (11 g/dl Hb) seems to be too high by means of the standard of non-industrialized world countries, it should be used through all to assist in comparison of information from one center to another. Peripheral blood film is another bedside indicator for the diagnosis of anemia which will additionally differentiate between IDA, megaloblastic anemia and hemolytic anemia. In IDA, the blood film contains microcytosis, hypochromia, anisocytosis, poikilocytosis, and target cells.

Serum iron varies from 60-120 ug/dl while total iron binding capacity (TIBC) is 300-350 ug/dl, (increased to 300-400 mg/dl in pregnancy). Serum iron of much less than 60 ug/dl, TIBC of more than 350 ug/dl and transferrin saturation of less than 15% indicates deficiency of iron for the duration of pregnancy.

Free erythrocyte protoporphyrin (FEP) is the third estimation of iron status rising with faulty iron supply to the growing red cells and takes 2-3 weeks to become abnormal after depletion of iron stores. It

additionally helps in differentiating between IDA and thalassemia. Serum transferrin receptor seems to be unique and sensitive marker of iron deficiency in pregnancy. Its stages are increased in IDA. Although it is the first-class indicator, its amenities are no longer but routinely available.

Bone marrow examination by staining with potassium Ferro cyanide to see characteristic blue granules of stainable iron in erythroblasts is the most correct method for iron stores, however is now not practical in most instances as the test is invasive. Bone marrow examination is only dated in cases where there is no response to iron remedy after four weeks or for analysis of Kala-azar or in suspected aplastic anemia (Antonelli). As worm infestation is frequent cause of anemia, stool examination for ova and cysts should be done consecutively for three days in all cases. In areas where schistosomiasis is prevalent, urine examination for occult blood and schistosomes must be performed. As malaria is an essential cause of anemia peripheral blood need to be done, renal function tests in suspected renal disease and serum proteins in hypoproteinemia. [25]

Lab Diagnosis:

Investigations Of Iron Deficiency Anemia

The following investigations are carried out to verify the diagnosis of iron deficiency anemia:

- Hemoglobin estimation to determine the severity of anemia. Ideally, hemoglobin should be estimated by semi-auto analyzer or by the calorimetric method. Sahli's hemoglobinometer is no longer regarded as a right method to estimate hemoglobin.
- Peripheral blood smear in iron deficiency anemia is characteristic with smaller size than normal, Change in size of RBC, abnormal shape of RBC and pale color staining (hypochromic) vacuolated red cells in plenitude. Mean corpuscular volume is beneath 80 cu and the mean corpuscular hemoglobin concentration (MCHC) is less than 30%. Serum ferritin levels will be low, while total iron binding capacity will be high, indicating iron deficiency.
- Stool examination may also reveal Ancylostoma duodenal ova which are typical, with a obvious outer membrane with 4 blastomeres and are non-bile stained, occult blood, ova, parasites and cysts. Urinalysis, blood urea, serum creatinine, serum proteins and liver function tests may also be accomplished to rule out systematic causes of anemia.
- When patients do not respond to therapy, hemoglobin electrophoresis can be used to rule out thalassemia and sickle mobile disease.
- Bone marrow test biopsy is not performed during pregnancy.[28]

Investigation Of Vitamin B12

Findings are the same as in folate deficiency. Vitamin B12 levels are decrease in blood (< 90 ug/l).Serum methylmalonic acid is increased in vitamin B12 deficiency. Serum homocysteine is increased in both folate and vitamin B12 deficiency. The deoxyuridine suppression test can differentiate between vitamin and folate deficiency. Schilling test is carried out to diagnose pernicious anemia. [25]

Treatment

Vitamin B12:

Pernicious anemia caused by lack of intrinsic issue resulting in lack of absorption of vitamin B12 is uncommon during pregnancy as it generally causes infertility. Acquired vitamin B12 deficiency causing megaloblastic anemia is additionally uncommon, as the day by day requirement of vitamin B12 is only 3.0 ug during pregnancy which is easily met with a regular diet. Only vegans who do not consume any animal-derived substance may have a deficiency of vitamin B12, and they should have their diet supplemented during pregnancy. Infestations with Diphyllobothrium latum in some countries can cause megaloblastic anemia due to competitive utilization of ingested vitamin B, by the parasite.

Treatment: Parenteral cyanocobalamin (250 g) is given intramuscularly every month. [25]

Folic Acid Deficiency

Deficiency can be due to more than one pregnancy, poor diet, and adverse social circumstances and may also occur secondary to drug

therapy such as antiepileptic drugs (AEDs). The average daily folate necessities rise in pregnancy from 50 to 400 ug (Addo et al 2013). Although this can typically be met via a healthy diet, women are inspired to take prophylactic folic acid 400 ug/day (0.4 mg) routinely the first trimester, which need to be elevated to 5 mg if the woman is also taking AEDs or different drugs affecting folate metabolism. Chronic maternal folate deficiency can lead to megaloblastic anaemia (Greer et al 2007). [26]

Prophylactic:

- Avoidance of frequent child births
- Supplementary iron therapy
- Dietary prescription
- Adequate treatment
- Early detection

Curative

Anaemia is not a disease, but rather a symptom of another condition. Treatment must begin with an accurate diagnosis of the cause and type of anaemia.

Hospitalization:

- Associated obstetrical-medical complication even with moderate anaemia
- If the haemoglobin level is less than 7.5 g/dL.
- Treatment in general:

Diet:

- A sensible, well-balanced diet high in proteins, vitamins, and iron.
- To increase appetite and aid digestion.
- To eliminate
- Curve therapy that works [27]

CONCLUSION

The accessible proof suggests that iron deficiency anemia contributes extensively to the women's fitness even today. Severe anemia in the course of being pregnant is an vital contributor to maternal mortality and morbidity. Eleven research posted between yr. 2007 and 2012 located that anemia incidence in south Asian international locations is nevertheless persisting. The estimated occurrence of anemia ranged from 18 to 80%, and the incidence of extreme anemia ranged from 2.7 to 20%. The overview confirmed that anemia effects from insufficient consumption of bioavailable dietary iron, malaria, hook worm infestation. Moreover, the nations face challenges in enhancing the socioeconomic status, instructional stage and health conduct modifications.

REFERENCES

1. WHO/CDC, Worldwide Prevalence of Anemia 1993–2005: WHO Global Database on Anemia, WHO Press, Geneva, Switzerland, 2008.
2. Y. Balarajan, U. Ramakrishnan, E. Ozaltin, A. H. Shankar, and S. V. Subramanian, "Anaemia in low-income and middle-income countries," *The Lancet*, vol. 378, no. 9809, pp. 2123–2135, 2011.
3. S. Salhan, V. Tripathi, R. Singh, and H. S. Gaikwad, "Evaluation of hematological parameters in partial exchange and packed cell transfusion in treatment of severe anemia in pregnancy," *Anemia*, vol. 2012, Article ID 608658, 7 pages, 2012
4. Centres for Disease Control and Prevention. Recommendations to Prevent and Control Iron Deficiency in the United States. Morbidity and Mortality Weekly Report. 1998;47(No. RR-3)
5. Breyman C, Bian X, Blanco-Capito LR, et al. Expert recommendations for the diagnosis and treatment of iron-deficiency anemia during pregnancy and the postpartum period in the Asia-Pacific region. *Journal of Perinatal Medicine*. 2010;38:1-8
6. GOODLAND, R.D. et al. 1983. Clinical science of normal plasma volume expansion during pregnancy. *Am. J. Obstet. Gynecol.* 145: 1001.
7. WORLD HEALTH ORGANIZATION. 1965. Nutrition in pregnancy and lactation. WHO Tech. Rep. Ser. 302.
8. WORLD HEALTH ORGANIZATION. 1968. Nutritional anemias. WHO Tech. Rep. Ser. 405.
9. Balarajan Y, Ramakrishnan U, Ozaltin E, Shankar AH, Subramanian SV. Anaemia in low-income and middle-income countries. *Lancet* 2011;378:2123-35.
10. Stoltzfus RJ, Mullany L, Black, RE. Iron deficiency anaemia. In: M Ezzati, Lopez AD, Rodgers A, Murray CJL, editors. Comparative Quantification of Health Risks: Global and Regional Burden of Disease Attributable to Selected Major Risk Factors. Geneva: World Health Organization; 2004. p. 163-210. Available from: <http://www.who.int/publications/cra/chapters/volume1/0163-0210.pdf?ua=1>. [Last accessed on 2018 Jul 20].
11. World Health Organization. The Prevalence of Anaemia in Women: A Tabulation of Available Information. 2nd ed. Geneva: WHO; 1992 (WHO/MCH/MSM/92.2).
12. Obasi IO, Nwachukwu N. Comparative iron related anaemia at pregnancy in Ebonyi State, South-east Nigeria. *J Med Sci* 2013;13:425-31.
13. Daru J, Zamora J, Fernandez-Felix BM, Vogel J, Oladapo OT. Risk of maternal mortality in women with severe anaemia during pregnancy and post-partum: A multilevel analysis. *Lancet* 2018;6:E548-54.
14. WHO 2008. World prevalence of Anemia 1993–2005.
15. Stoltzfus RJ, Mullany, et al. Iron deficiency anemia. Comparative quantification of health risks: Global and regional burden of disease attributable to selected major risk factors 2004;1:163-209.
16. Seshadri S. Prevalence of micronutrient deficiency particularly iron, zinc and folate in

- pregnancy women in South East Asia. *Br J Nutr* 2001;85(2):87-92.
17. Lindstrom E, Hossain MB, Lommerdal B, Raqib R, Arifeen SEL, Ekstrom EC. Prevalence of anemia and micronutrient deficiencies in early pregnancy in rural Bangladesh. *Acta Obstet Gynecol Scand* 2011;90:47-56.
18. Liabsuetrakul T, Chaikongkeit P, Korvittanagarn S, et al. Preterm births among Thai population? An observational study. *Journal of Health, Population, and Nutrition* 2011;29(3):218-28.
19. BAKER, S.J. 1983. Nutritional anemias. Part 2: Tropical Asia. *Clin. Haematol.* 10: 843.
20. WILLIAMS, M.D. et al. 1992. Anemia in pregnancy. *Med. Clin. N. Am.* 76(3): 631–647.
21. Ziauddin Hyder SM, Persson LA, Chowdhury M, Lommerdal B, Ekstrom EC. Anemia and iron deficiency during pregnancy in rural Bangladesh. *Public Health Nutrition* 2004;7(8):1065-70.
22. COOK, J.D. 1983. Nutritional anemia. *Contemp. Nutr.* 8: 366.
23. LUND, C.J. et al. 1967. Blood volume during pregnancy. Significance of plasma red cell volumes. *Am. J. Obstet. Gynecol.* 98: 393.
24. GOODLAND, R.D. et al. 1983. Clinical science of normal plasma volume expansion during pregnancy. *Am. J. Obstet. Gynecol.* 145: 1001.
25. Narendra Malhotra, Randhir Puri, Jaideep Malhotra, Donald School Manual of Practical Problem in Obstetrics, Jaypee Brothers Medical Publishers (P)LTD, Ch.9, page 144-145.
26. Jayne E Marshall, Maureen D Raynor, Myles Textbook for Midwives, CHURCHILL LIVINGSTONE ELSEVIER, Ch.13, Page No.274.
27. D.C.DUTTA, Text Book Of Obstetrics, New Central Book Agency (P)LTD Calcutta, Ch.19, Page No. 270.
28. A L Mudaliar, M K Krishna Menon, Clinical Obstetrics, Universities press (India) Private Limited , Hyderabad, Ch.20, Page 164