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Review Article

An Overview of Anemia in Pregnancy

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Abstract

Anemia is the commonest hematological disorder that occurs in pregnancy. According to the recent standard laid down by 'WHO', anemia is present when the Hemoglobin (Hb) concentration in the peripheral blood is 11 gm/dl or less. The most common cause of anemia in pregnancy is lack of iron. Less often, it is caused by folic acid deficiency. In some populations, 80% of pregnant women are anemic. Those most at risk are women from low socio-economic groups and teenagers. Anemia is diagnosed by estimating the hemoglobin concentration and examining a peripheral blood smear for the characteristic red blood cell changes. Iron and folate supplementation is indicated during pregnancy to prevent the complications. Even in normal pregnancy, the hemoglobin concentration becomes diluted according to the increase in the volume of circulating blood. Since iron and folic acid in amounts necessary for the fetus are preferentially transported to the fetus, the mother is likely to develop iron deficiency anemia and folic acid deficiency anemia. An adult woman has about 2 g of iron in her body. When a woman becomes pregnant, the demand for iron increases, necessitating an additional 1 g.

Key words: Anemia pregnancy, RBC Hb, iron, vitamin B12 & folic acid

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1. Introduction

Women go through a variety of physiological changes during pregnancy. Changes in the blood circulatory system are particularly notable, permitting normal fetal growth. Even in normal pregnant women, the hemoglobin concentration decreases with dilution according to the increase in the volume of circulating blood. Since iron and folic acid in amounts necessary to the fetus are preferentially transported to the fetus, the mother is likely to develop iron deficiency anemia and folic acid deficiency anemia. About 20% of pregnant women suffer anemia, and most of the cases are iron deficiency, folic acid deficiency, or both [1] Anemia is the most common nutritional deficiency disorder in the world. WHO has estimated that prevalence of anemia in developed and developing countries in

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pregnant women is 14 per cent in developed and 51 per cent in developing countries and 65-75 percent in India. Prevalence of anemia in all the groups is higher in India as compared to other developing countries [2] Anemia is a lack of functioning red blood cells (RBCs) that leads to a lack of oxygen-carrying ability, causing unusual complications during life time. These RBCs are produced in the bone marrow. They have a life expectancy of about 120 days. Among other things, the body needs iron, vitamin B12 & folic acid for erythropoiesis. If there is a lack of one or more of these ingredients or there is an increased loss of RBCs, anemia develops. Any patient with a Hb of less than 11 gm/dl to 11.5 gm/dl at the start of pregnancy will be treated as anemic. The reason is that as the pregnancy progresses, the blood is diluted and the woman will eventually become anemic. The dilution of blood in pregnancy is a natural process and starts at approximately at the eighth week of pregnancy and progresses until the 32nd to 34th week of pregnancy [3].

Classification of anemia in pregnancy [3, 5]

Grossly classified into two types:

(A) Pathological anemia in pregnancy.

(B) Physiological anemia in pregnancy.

(A) Pathological Anemia is further sub-classified into

1. Deficiency Anemia, e. g.
   -Iron deficiency
   -Folic acid deficiency
   -B12 deficiency
   -Protein deficiency
2. Hemorrigic:

Acute hemorrhagic: Following bleeding in early month of pregnancy or APH

Chronic hemorrhagic : as by hookworm infestation, GI (gastrointestinal) bleeding.

1. Hereditary : Thalassemias – Haemolobinopathies.

Hereditary hemolytic anemia – RBCs defects.

2. Bone Marrow insufficiency: as by radiation, marrow suppressant drugs.
3. Anemia of infection – as by malaria tuberculosis
4. Chronic diseases: as in nephropathies & neoplastic disorders.

It is noteworthy that obstetricians are concerned with two common types of anemia. They are:

5. Deficiency anemia,
6. Hemorrhagic anemia

It has been found there is increased prevalence of anemia in pregnancy in tropical countries.

This is due to

a. Faulty dietary habit,

b. Faulty absorption mechanism,

c. More iron loss due to sweating and repeated pregnancy at short interval; prolonged period of lactation,

d. Infection: Chronic malaria, tuberculosis,

e. Excess demand of iron: pregnancy is an iron deficit state.

(B) Physiological Anemia

During pregnancy there is disproportionate increase in plasma volume upto 50%, RBC 33% and Hb 18-20% mass. In addition there is marked demand of extra iron during pregnancy especially in the second half of pregnancy. So, physiological anemia is due to combined effect of hemodialution & negative iron balance.

Criteria of Physiological Anemia include [6]

- Hb% - 10 gm or less,
- R.B.C – 3.5 million/mm^3,
- P.C.V – 30%,
- PBF – Normal morphology with central pallor.

Clinical features of iron deficiency Anemia depends more on the degree of anemia.

Symptoms of anemia include lassitude, feeling of exhaustion, weakness, anorexia, indigestion, palpitation; swelling legs Signs of anemia include pallor,
glossitis, Stomatitis, edema legs, soft systolic murmur in mitral area. Investigations are done to detect the degree of anemia, the type of anemia the cause of anemia.

To ascertain the degree of anemia one must look for Hb%, RBC count, PCV (Packed Cell Volume). Mild anemia means Hb- 8-10 gm%; Moderate- less than 7-8 gm%; Severe – Less than 7 gm%. To determine type of anemia one must examine the PBF (Peripheral Blood Film), hematological indices like MCV, MCH, MCHC, etc.

A typical iron deficiency anemia shows the flowing blood values:

- Hb-less than 10 gm%
- RBC – less 4 million/ mm^3
- PCV – less than 30%
- MCHC – Less than 30%
- MCV – less than 75% micro mole m^3 (meter cube)
- MCH- less than 25 pg.

Serum iron is usually below 30 micro gram/ 100 ml. Total iron binding capacity increases to 400 micro gram/100ml. Serum ferritin falls below 15 micro gm/L. To find out the cause of anemia, the physician should carefully follow the basic protocols.

- History taking,
- Physical examination,
- Routine examination of stool to detect helminthes or occult blood,
- Urine is examined for the protein, sugar and pus cells,
- X ray chest in suspected cases of pulmonary tuberculosis; but in case not responding to therapy, bone marrow study should be undertaken.
- Blood for PBF & malarial parasites,
- Kidney function tests like BUN & s. creatinine, etc.

Maternal consequences of anemia

Mild anemia

Women with mild anemia in pregnancy have decreased work capacity. They may be unable to earn their livelihood if the work involves manual labour. Women with chronic mild anemia may go through pregnancy and labour without any adverse consequences, because they are well compensated.

Moderate anemia

Women with moderate anemia have substantial reduction in work capacity and may find it difficult to cope with household chores and child care. Available data from India and elsewhere indicate that maternal morbidity rates are higher in women with Hb below 8gm/dl [11]. They are more susceptible to infections and recovery from infections may be prolonged. Premature births are more common in women with moderate anemia. They deliver infants with lower birth weight and prenatal mortality is higher in these babies. They may not be able to bear blood loss prior to or during labour and may succumb to infections more readily. Substantial proportion of maternal deaths due to antepartum and post-partum haemorrhage, pregnancy induced hypertension and sepsis occur in women with moderate anemia.

Severe anemia

Three distinct stages of severe anemia have been recognized - compensated, decompensated, and that associated with circulatory failure. Cardiac decompensation usually occurs when Hb falls below 5.0 g/dl. The cardiac output is raised even at rest, the stroke volume is larger and the heart rate is increased. Palpitation and breathlessness even at rest are symptoms of these changes. These compensatory mechanisms are inadequate to deal with the decrease in Hb

levels. Oxygen lack results in anaerobic metabolism and lactic acid accumulation occurs. Eventually circulatory failure occurs restricting work output. Untreated, it leads to pulmonary oedema and death. When Hb is <5 g/dl and packed cell volume (PCV) below 14[12]. A blood loss of even 200 ml in the third stage produces shock and death in these women. Even today women in the remote rural areas in India reach to the hospital only at this late decompensate stage. Available data from India indicate that maternal morbidity rates are higher in women with Hb below 8.0 g/dl. Maternal mortality rates show a steep increase when maternal Hb levels fall below 5.0 g/dl. Anemia directly causes 20 percent of maternal deaths in India and indirectly accounts for another 20 per cent of maternal deaths [24].

Foetal consequences of anemia

Studies to define the effect of maternal anemia on the foetus indicate that different types of decomposition occur with varying degrees of anemia. Most of the studies suggest that a fall in maternal hemoglobin below 11.0 g/d1 is associated with a significant rise in perinatal mortality rate18, 19, and 25. There is usually a 2 to 3-fold increase in perinatal mortality rate when maternal hemoglobin levels fall below 8.0 g/d1 and 8-10 fold increase when maternal hemoglobin levels fall below 5.0 g/dl. A significant fall in birth weight due to increase in prematurity rate and intrauterine growth retardation has been reported when maternal hemoglobin levels were below 8.0 g/d1. [8, 10]

Effects of Anaemia on Pregnancy

Maternal effects [13]

Mild, anemia may not have any effect on pregnancy and labour except that the mother will have low iron stores and may become moderately to- severely anemic in subsequent pregnancies. Moderate anemia may cause increased weakness, lack of energy, fatigue and poor work performance. Severe anemia, however, is associated with poor outcome. The woman may have palpitations, tachycardia, breathlessness, increased cardiac output leading on to cardiac stress which can cause de-compensation and cardiac failure which may be fatal[14,15]. Increased incidence of pre-term labour (28.2%), pre-eclampsia (31.2%) and sepsis have been associated with anemia [14].

Fetal effects [13, 14]

Irrespective of maternal iron stores, the fetus still obtains iron from maternal transferrin, which is trapped in the placenta and which, in turn, removes, and actively transports iron to the fetus. Gradually, however, such fetuses tend to have decreased iron stores due to depletion of maternal stores. Adverse perinatal outcome in the form of pre-term and small-for-gestational-age babies and increased perinatal mortality rates have been observed in the neonates of anemic mothers. Iron supplementation to the mother during pregnancy improves perinatal outcome. Mean weight, Apgar score and haemoglobin level 3 month after birth were significantly greater in babies of the supplemented group than the placebo group.

Clinical Signs and Symptoms:

Pregnancy anemia can be asymptomatic and may be diagnosed following routine screening. The signs and symptoms are often non-specific with tiredness being the most common. Women may also complain of weakness, headaches, palpitations, dizziness, dyspnoea and hair loss. Signs of anemia can occur in the absence of a low Hb.

Line of treatment

Sr. No.	**Drug Content**	**Brand**	**Use**
1	**Carbonyl Iron**	Abonyl | Carboron Capsule | Cario | Cario(200ml) | Evaglow | HB Fast Susp | Hemic-C | IroonC | Mediron |	Carbonyl Iron is a dietary supplement, prescribed for iron deficiencies and iron deficiency anemia.
2	**Cyanocobalamin (Vitamin B12)**	Shytone (200ml) | Abiron (200ml) | Adfe (250mg+1.5mg+10mcg) | Adfe Syrup(200ml) | Agiron F | Anemi Z (200ml) | Angel | Aniron (200ml) | Aniron (300ml) | Aristo Neurol | Benevital (200ml) | Blush XT (33mg+5mg+15 mcg) | Cal De Ce (10ml) | Calcid (200ml) | Calcidol M (15ml) | Calid (200ml) | Calstar (100ml) | Carb-I SR | Carboriv (30ml) | CarfolZ (100ml)	Cyanocobalamin (Vitamin B12) is a vitamer (varied chemical substances) of vitamin B12, used in treating anemia, folic acid deficiency, neuropathies (damage in the nerves of peripheral nervous system), prophylaxis, and psychiatric disorders. Recommended for patients with the condition of pancreatic tumor.
3	**Darbepoetin alfa**	Cresp (40 mcg) | Cresp PFS (40 mcg) |	Darbepoetin alfa is an erythropoiesis-stimulating agent, prescribed for anemia due to chronic kidney disease.
4	**Epoetin beta-methoxy polyethylene glycol**	Ceriton | Ceriton (10000i.u) | Ceriton (3000 i.u) | Ceriton (4000i.u) | Epofer | Epofe r (2000 i.u) | Epofer (3000i.u) | Epofer (4000i.u) | Eposis | Eposis (10000 i.u) | Eposis (4000i.u) | Epotop | Epox	Epoetinbeta-methoxy polyethylene glycol is an erythropoiesis-stimulating agent, prescribed for anemia in people with chronic kidney failure.

		| Epox (1 ml) | Eprex | Eprex (0.4 ml) | Eprex (0.6ml) | Eprex (1ml) | Eprex (1000u) | Eprex (10000 u) |	
5	**Ferrous Fumarate**	AF12 | FeronXT | Ferroge n | Ferrous Fumarate | Hb ACT | Irobin | Livogen | Livogen Tonic | Oshofol |	Ferrous Fumarate is an essential body mineral, used to treat iron deficiency anemia. It replaces iron in the body when the body does not produce enough on its own.
6	**Iron Dextran**	FERRI INJ amp® | IMFERON F-12 inj® | IMFERON MD vial® | SUPRAL amp® |	Iron Dextran is an essential mineral, prescribed for anemia or iron deficiency, megaloblastic anemia as an astringent.
7	**Iron-III Hydroxide Polymaltose Complex - IPC** Iron-III Hydroxide Polymaltose Complex-IPC is an iron preparation, prescribed for iron deficiency anemia.		Iron-III Hydroxide Polymaltose Complex - IPC is an iron preparation, prescribed for iron deficiency anemia.
8	**Iron Sucrose**		Iron Sucrose is a mineral iron, prescribed for iron deficiency anemia especially for kidney failure patients.

9	**Nandrolone**	Abonic | Alanbol | Alanbol (50 mg) | Alandec | Aldec (50mg) | Alidec(100mg) | Alidec(50mg) | Amdec(50 m) | AND(50mg) | Andy | Arbol | Avillin25,Avobol25 | Axidrol50 | Axydec(50mg) | BCVit | BDec(50mg) | Betabolin | Betalobin | Bevodec |	**Nandrolone** Nandrolone is an anabolic steroid, prescribed for anemia caused by kidney problems.
10	**Oxymetholone**	BC -Vit |	**Oxymetholone**
11	**Lenalidomide**		Lenalidomide is an immunomodulatory agent, prescribed for certain types of myelodysplastic syndrome and multiple myeloma either alone or with other medications.
12	**L-methylfolate**		L-methylfolate is a vitamin (medical food), prescribed for dietary management in patients with low plasma or low red blood cells.
13	**Multivitamin**		Multivitamin is an essential nutrient, prescribed for patients with vitamin deficiency.

In this instance it would be diagnosed by a full blood count with a reduced MCV (Mean Cell Volume) and MCHC (Mean Corpuscular Haemaglobin Concentration). In these patients, a ferritin needs to be checked and if it is <30µ/l iron therapy should be commenced.

Diagnosis

A trial of oral iron therapy can be both diagnostic and therapeutic. If haemaglobinopathy status is unknown, then it is reasonable to start oral iron therapy whilst screening is carried out. A trial of oral iron should demonstrate a rise in Hb within 2 to 3 weeks. If there is a rise then this confirms the diagnosis of iron deficiency. If there is no rise, further tests must be carried out. In patients with a known haemaglobinopathy serum ferritin should be checked first. Ferritin levels below 30µ/l should prompt treatment and levels below 15µ/l are diagnostic of established iron deficiency.

Management

NICE guidelines recommend that women are screened for anaemia at booking and again at 28 weeks gestation. All women should be given advice regarding diet in

pregnancy with details of foods rich in iron along with factors that may promote or inhibit the absorption of iron. This should be backed up with written information. Dietary changes alone are not sufficient to correct an existing iron deficiency in pregnancy and iron supplements are necessary [7].

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