

A REVIEW ON ANEMIA IN PREGNANCY CONDITION

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ABSTRACT

Anemia during pregnancy is a global public health challenge facing the world today and it's associated with poor maternal and perinatal outcome. Nearly two-thirds of pregnant and one-half of non-pregnant women in developing countries have anemia. In India about 49.7% pregnant women suffer from anemia (WHO global database) and 20% maternal death's contributed by anemia. Prevalence of anemia in pregnancy varies considerably because of differences in socioeconomic conditions, lifestyles and health seeking behaviors across different cultures. Women of low socio-economic groups and teenagers are more susceptible towards anemia during pregnancy. Anemia is diagnosed by studying the hemoglobin concentration and also a peripheral blood smear for the characteristic red blood cell changes. Iron deficiency anemia (IDA) and folate deficiency anemia (FDA) commonest causes of anemia in pregnancy. To avoid a anemia oral iron and folate supplement are given to a pregnant women.

KEYWORDS: Pregnancy. Anemia, Maternal, Perinatal, Prevalence.

INTRODUCTION

Anemia is the most common nutritional deficiency disorder in the world. WHO has estimated that prevalence of anemia in developed and developing countries in pregnant women is 14 per cent in developed and 51 per cent in developing countries and 65-75 percent in India.^[1] Even among the South Asian countries India has the highest prevalence of anemia. About one third of the global population (over 2 billion) are anemic. Prevalence of anemia and its contributed to maternal mortality in south Asian countries are given in a table 1. Even among the South Asian countries India has the highest prevalence of anemia.^[2]

> World Health Organization (WHO) define anemia as hemoglobin (Hb) level <110g/L in pregnancy and 100 g/L postpartum. Currently, there are no WHO recommendations on the use of different hemoglobin cut-off points for anemia by trimester, but it is recognized that during the second trimester of pregnancy,

hemoglobin concentrations diminish by approximately 5 g/L> US Centers for Disease Control (CDC) has established the lower limit of the normal range of hemoglobin in the latter part of the second trimester is 103 g/L (2 standard deviations [SD] below the mean of 116 g/L)^[3]

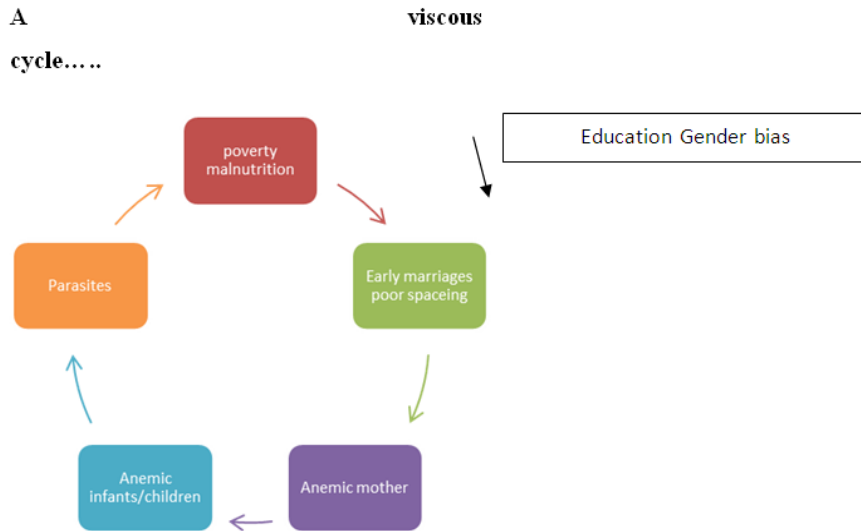
- Hb <110 g/L in first trimester
- Hb <105 g/L in second and third trimesters
- Hb <100 g/L in postpartum period

Women go through a variety of physiological changes during pregnancy^[4] Women with anemia in pregnancy may experience fatigue, reduced energy levels, reduced mental performances, and in cases of severe anemia it is associated with preterm birth, low birth weights, and a small for gestational age fetus. In the postpartum period anemia has been found to be linked to depression, emotional instability, stress and lower cognitive performance tests.^[5]

Table: 1 Prevalence of anemia and its contribution to maternal Mortality.^[1,2]

| Country | Prevalence of anemia in pregnant women % | Maternal deaths from anemia |
|----------------------|--|-----------------------------|
| Afghanistan | - | - |
| Bangladesh | 74 | 2600 |
| Bhutan | 68 | <100 |
| India | 87 | 22,000 |
| Nepal | 63 | 760 |
| S. Asia Region Total | | 25,560 |
| World Total | | 50,000 |

Indian women are anemic to start with.....



- Thus an Indian girl invariably enters her reproductive carrier in an iron depleted state.

MATERNAL AND HAEMATOLOGICAL CHANGES IN DURING PREGNANCY

During pregnancy, the circulating plasma volume increases linearly to reach a plateau in the 8th or 9th month of pregnancy. The increment is about 1000ml, which corresponds to 45% of the circulating plasma volume in non-pregnancy. The plasma volume decreases rapidly after delivery and is then restored to the non-pregnancy level at about 3 puerperal weeks.^[4] Because of hemo-dilution and increasing needs of iron and other nutrients for both the mother and the fetus, hemoglobin (HB) levels decreases progressively in pregnancy, whereas in the third trimester, hem concentration results in higher Hb levels. Although erythrocytes and hemoglobin also increases during pregnancy, their increases are slow in the initial half of the pregnancy period, causing relative hydremia, and the hemoglobin concentration and hematocrit are lowest in the 5th to 7th month of pregnancy. In the latter half of the pregnancy period, erythrocytes and hemoglobin increase markedly, and the hemoglobin concentration and hematocrit tend to increase and finally reach normal levels at 6 puerperal weeks. Pregnancy is associated with normal physiological changes that assist fetal survival and prepares the mother for labor, delivery and breastfeeding. The changes start as early as 4 weeks of gestation and are largely as a result of progesterone and estrogen. The total blood volume increases steadily from as early as 4 weeks of pregnancy to reach a maximum of 35-45% above the non-pregnant level at 28-32 weeks. The plasma volume increases by 40-45% (1000mls). red blood cell mass increases by 30-33 % (approximately 300mg) as a result of the increases in the production of erythropoietin. Thus women who enter pregnancy in an iron deficient state are then unable to meet the demands of pregnancy by diet alone and require supplementation. it takes approximately 2-3 weeks after delivery for these hematologic changes to revert to pre-pregnant status^[19]

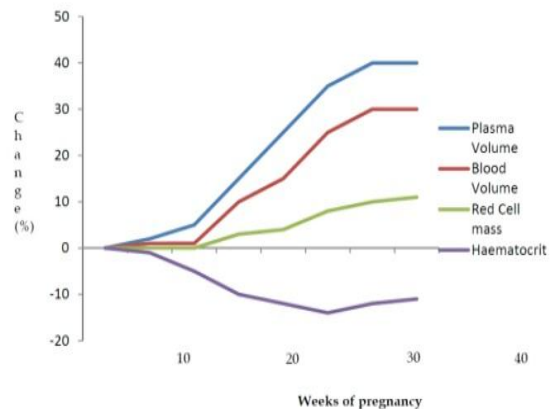


Figure 1: Graphical representation of hematological changes in pregnancy

Classification of anemia in pregnancy

Grossly classified into two types^[10]

- (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. Hemorrhagic

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

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

1. Hereditary: Thalassemia's – Haemoglobinopathies. 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:

A. Deficiency anemia,

B. Hemorrhagic anemia it has been found there is increased prevalence of anemia in Pregnancy in tropical countries. This is due to

1. Faulty dietary habit,
2. Faulty absorption mechanism,
3. More iron loss due to sweating and repeated pregnancy at short interval; prolonged period of lactation,
4. Infection: Chronic malaria, tuberculosis.
5. Excess demand of iron: pregnancy is an iron deficit state.

(B) Physiological Anemia

During pregnancy there is disproportionate increase in plasma volume up to 50%, RBC 33% and Hb 18-20gm% 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 Hem dilution & negative iron balance. Criteria of Physiological Anemia include.

- Hb% - 10 gm% less,
- R.B.C – 3.5 million/mm³,
- P.C.V – 30%,
- PBF – Normal morphology with central pallor.

Iron requirements during pregnancy

Maternal req. of total iron-1000mg

- ✓ 500 mg ~ Maternal Hb. Mass expansion
- ✓ 300 mg~ Fetus and placenta
- ✓ 200 mg~ Shed through gut, urine and skin
- 2.5mg/dl in early pregnancy
- 5.5 mg/day from 20-32 weeks
- 6-8mg/day after 32 weeks

Increase from 1-2mg in 1st trimester to 6-8mg in 3rd trimester

Immune status of anemic pregnant women

Pregnancy is a unique experience in every woman life¹³. In pregnancy, profound changes occur in several laboratory parameters used for the assessment of immune status. Studies undertaken by the National Institute of Nutrition, Hyderabad, showed that there was a fall in T and B cell count with fall in hemoglobin levels below 11 g/dl. The fall in T and B cells was statistically significant in women with hemoglobin levels below 8 g/dl. Immunoglobulin levels showed a progressive rise with decreasing Hb levels. There were no alterations in the phytohemagglutinin induced lymphocyte transformation nor was there any difference in the *in vivo* tests for cell mediated immunity. Available data indicated that humoral immunity as assessed by response to immunogens including tetanus toxoid remains unimpaired. The changes in T and B cells and immunoglobulin were reversed within 6-12 week by

parenteral iron therapy and improvement in hemoglobin levels, indicating that these alterations are due to anemia parse and not due to co-existent undernutrition.^[1]

Influences of Anemia on Pregnancy

Placental weight increases in relation to the severity of maternal anemia. It is presumed that this is because placental growth is promoted to compensate for the lack of oxygen delivered owing to anemia. In contrast, opinion is divided as to the influences of anemia on the maternal body and fetus. No consensus has been reached in spite of years of research on this issue.^[4,10]

Effects of Anemia on Pregnancy

Anemia is an important risk factor for both maternal and fetal morbidity.^[18]

On Mother

1. Abortion
2. Postpartum depression
3. Increased risk of infections
4. Heart and lung problems

On Baby

1. Neural tube defects (a birth defect involving incomplete development of the brain and spinal cord)
2. Mental problems
3. Low birth weight (less than 2500gm)^[6]
4. Pre-term birth
5. Delayed growth in infants and children
6. Neonatal death (within 28 days after delivery)^[6]

Maternal consequences of anemia

Anemic Grades

- Grade 1(mild)=9.5-11gm% HB
- Grade 2(Moderate)=8-9.5 gm% Hb
- Grade 3(severe)=6.5-8 gm% Hb
- Grade 4(Life threatening)= <6.5 gm% Hb

Mild anemia

Work propensity is decreased in women with mild anemia in pregnancy. 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 considerable reduction in work capacity and may find it difficult to cope with household chores and child care. They are more vulnerable 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 labor and may succumb to infections more readily. Substantial proportion of maternal deaths due to antepartum and post-partum

hemorrhage, 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 5.0g/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 edema and death. When Hb is <5g/dl and packed cell volume (PCV) below 14. A blood loss of even 200ml 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.^[14,10]

Symptoms of Anemia during pregnancy

The most common symptoms of anemia during pregnancy usually appears in severe anemia:

- Pale skin, lips, and nails
- Feeling tired or weak
- Dizziness
- Shortness of breath
- Rapid heartbeat
- Headache
- Cold hands and feet

Risk Factors for Anemia in pregnancy

Anemia is an important risk factor for both maternal and fetal morbidity.^[18]

All pregnant women are at risk for becoming anemic. That's because they need more iron and folic acid than usually to feed the fetus. But the risk is higher if:

- Are pregnant with multiples (more than one child)
- Have had two pregnancies close together (in less than a year)
- Vomit a lot because of morning sickness
- Are a pregnant teenager
- No enough iron in the nutrition.
- Had anemia before the pregnancy

Complications of severe anemia

During pregnancy

- Pre-eclampsia,
- Recurrent infection,
- Heart failure,
- Preterm labour,

During labor

- Uterine inertia,
- PIH,
- Cardiac failure,
- Shock.

During puerperium

- Puerperal sepsis,
- Sub-involution,
- Failing lactation.

Management during labor

In 1st stage

- Patient should be in bed and should be in a position comfortable to her,
- Arrangement for oxygen,
- Aseptic condition is to be maintained.

In 2nd stage

- Prophylactic low force/ vacuum delivery.

In 3rd stage

- Active management. Prophylactic antibiotic to prevent infection
- Iron therapy for at least 3 months following delivery.

Risk periods

- At 30-32 weeks of pregnancy,
- During labor,
- Immediately following delivery

Prognosis^[8]

Maternal aspect

1. If detected early & proper treatment is instituted, anemia improves promptly;
2. Substantial chances of recurrence in next pregnancy,
3. Contributes to about 2-% maternal death in developing countries.

Fetal aspects

1. Baby born at term from severely anemic mother will not be anemic at birth. But there is little or no Reserved iron. So anemia develops at neonatal period,
2. Preterm labour,
3. LBW (Low Birth Weight),
4. IUD (Intra-Uterine Death).

Diagnosis^[14]

Knowledge of different hemoglobin cut off levels during pregnancy to differentiate between hydraemia and true anemia is important in the first step of diagnosis. Lower hemoglobin cut off is 11.0 gm% in the first and last trimester and 10.5 gm% in the second trimester? Therefore any level below 10.5 gm% should be regarded as anemia and consequently checked. The next step includes differential diagnosis of anemia. Iron deficiency the major cause of anemia during pregnancy, but others such as infection, abnormal hemoglobin, renal disease or parasites (Malaria, worms) must be ruled out before

therapy starts to guarantee optimal therapeutic effects a trial of oral iron therapy can be both diagnostic and therapeutic. If hemoglobinopathy 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 hemoglobinopathy serum ferritin should be checked first. Ferritin levels below 30 μ /l should prompt treatment and levels below 15 μ /l are diagnostic of established iron deficiency. Traditional therapeutic options of iron deficiency anemia in pregnancy were administration of oral iron or in severe cases administration of blood transfusion. While oral iron shows limited effectiveness in cases of severe anemia due to various factors such as side effects, lack of compliance and often limits intestinal absorption and bioavailability, blood transfusion must be avoided due to considerable transfusion risks such as infections, risk of incorrect transfusion, transfusion reactions and negative impact on the immune system. There are also an increasing number of patients who deny blood transfusion.

Laboratory Parameters

In addition to clinical assessment, laboratory parameters are of major importance for differential diagnosis of anemia. More than 100 years ago first tests including blood smear, red cell being the actual gold standard of iron status testing. However, in certain conditions such as underlying infections, ferritin is not valuable, since it reacts as an acute phase reactant and shows false normal results, e.g. in the postpartum period. During pregnancy, ferritin shows also weak correlations to other iron parameters and then severity of anemia, therefore additional tests are helpful.

Hypochromic Red Cells

Hypochromic red cells are released into the blood in cases of severe anemia, e.g. iron deficiency, or during functional iron deficiency, e.g. erythropoietin stress with insufficient iron supply. Using modern automated red cell analyzer systems it is possible to measure the quantity of hypochromic red cells (HRBC) and the percentage of HRBC of total red cells. These data are helpful to determine the severity of iron deficiency, for differential diagnosis (e.g. thalassemia ><iron deficiency) of anemia, for assessment of functional iron deficiency (e.g. during rhEPO Treatment) and finally the monitoring of therapy and its effects, namely decrease of hypochromic due to efficient iron administration.

Soluble Serum Transferrin Receptors

Serum transferrin receptor (STFR) assay is another important new laboratory test which is increasingly used in obstetrics. STFR are on the surface of every iron incorporating cell and are released into the blood in cases of increased tissue iron needs such as during severe iron deficiency or during forced erythropoiesis. As HRBC,

increased STFR levels indicate functional iron deficiency but also increased erythropoiesis and body iron needs.

COMMON TYPES OF ANEMIA IN PREGNANCY^[15]

Iron-Deficiency Anemia

The majority of all anemias diagnosed during pregnancy are characterized as iron deficiency anemias. And accounts for over 90% cases.^[7] The increased fetal need for iron as well as a number of other factors constitute the iron-deficiency profile of the pregnant woman and the need for supplementation. The factors contributing to that state include poor iron absorption during pregnancy, multiple gestations or successive gestations less than two years apart, adolescent pregnancy, and any associated chronic blood loss, as well as decreased amounts of total body iron before the pregnancy. The most usual clinical symptoms of iron-deficiency anemia are lethargy and fatigue, although they are also seen in normal pregnancy. Other symptoms are headache, paresthesia, burning sensation of the tongue, and pica, which is the ingestion of substances with no dietary value and appears in severe cases of anemia after the twentieth week of gestation. Glossitis, pallor, and inflammation of the lips (cheilitis) are clinical signs of iron deficiency, whereas koilonychia and "spooning" nails are less common findings. In cases of severe anemia, retinal bleeding, conjunctivitis, tachypnea or tachycardia, and splenomegaly may be presented. The expected increase in the red blood cell mass after week 20 of gestation will not be observed if iron stores are depleted. The serum iron levels decline as pregnancy advances for the reasons presented above. Values <30g/dl are usually diagnostic of iron deficiency, but the best indicator for this is the measurement of serum ferritin (normal values in pregnancy: 55–70 μ g/l). Additionally, quite a good indication is the transferrin saturation, which in iron deficiency is <15%. Some authors consider the unsaturated iron-binding capacity (UIBC) an important marker of iron deficiency states, when it takes values > 400 μ g/dl.³⁵ The earliest tissue indicator of an iron-deficient state is decreased iron stores in the bone marrow, but aspiration in pregnancy is usually not indicated.

Therapy of Iron-Deficiency Anemia and Iron Supplementation

Most clinicians advocate iron supplementation in pregnant women. Others believe that supplementation has no value when hemoglobin levels are equal to or greater than 10g/dl. They believe that there is no need for extra therapy, on the grounds that hem dilution during pregnancy is an important physiologic adaptation, important for adequate uteroplacental circulation. In an iron-deficient state, however, iron supplementation must be given, and follow-up is indicated to diagnose iron-unresponsive anemias. Reticulocytosis is normally observed 10 days after the initiation of iron therapy. The increased demand for iron and the hem dilution during pregnancy may mask the response to iron

supplementation. It is self-evident that other causes of anemia have been excluded. In these cases iron supplementation should continue throughout pregnancy, and it can be accomplished with a variety of agents. Oral preparations containing elemental salt are the most commonly employed, whereas ferrous sulfate compounds are the least expensive and have been demonstrated to be efficacious for iron supplementation. It should be taken three or four times daily in a dosage of 30–60mg for a conservative dosage to 200–300mg per day in the iron-deficient state. Nausea, vomiting, diarrhea, and constipation are the most common side effects of the ingestion of oral iron. The sustained release capsules, iron compounds that are slowly absorbed, and syrups may reduce some of the intolerance and increase patient compliance. Patients with severe iron deficiency anemia who cannot tolerate oral administration or who demonstrate noncompliance with the oral administration of iron, can be treated with intramuscular (IM) or intravenous (IV) administration. Additionally, parenteral therapy is preferred when rapid replenishment of iron stores is necessary. However, the hematologic response to the i.m. or i.v. route of therapy is no more rapid than that of the response to oral iron, and adverse effects including fatal anaphylaxis can be observed due to immediate or delayed reactions to iron dextran. It is more likely to appear when oral iron and parenteral iron are given concomitantly; therefore, this combination is not indicated. A test dose is strongly recommended before the first parenteral administration. Side effects of IV iron in the past intravenous iron had been associated with undesirable and sometimes serious side effects and was therefore limited use.^[9]

A formula for the dose of iron needed to restore hemoglobin is the following

Elemental iron (mg) = $0.3 \times \text{weight (lbs.)} \times 100 =$
patient's Hb (gr/dl)*100/14.8

The side effects of such a route of iron administration include discomfort at the injection site, skin staining, malaise, and metallic taste. Moderate reactions of hyperpyrexia, lymphadenopathy, and phlebitis occur in 1–2% of patients, whereas anaphylaxis may occur in about 0.5% of them.

Folic Acid Deficiency Anemia

Folic acid deficiency causes a megaloblastic type of anemia that is second in occurrences a cause for nutritional deficiency anemia of pregnancy after iron deficiency anemia. Folates and especially their derivative formyl FH4 are necessary for appropriate DNA synthesis and amino acid production. Insufficient levels of folic acid may lead to the manifestations noted in megaloblastic anemia. Folic acid must be provided in the diet: common sources are green vegetables, fruits (lemons, melons), and meats (liver, kidney). The absorption happens in the proximal jejunum. The etiology of folic acid deficiency is variable and decreased intake is associated with poor nutrition and

impaired absorption as well as increased folic acid requirements seen in pregnancy because of the increased demands of fetal growth and maternal erythropoiesis. Additionally, the higher levels of estrogen and progesterone during pregnancy seem to have an inhibitory effect on folate absorption. The symptoms of folic acid deficiency are those of general anemia plus roughness of the skin and glossitis. The erythrocyte precursors are morphologically larger (“macrocytic”), and an abnormal nuclear–cytoplasmic appearance as well as normochromic and macrocytic findings are diagnostic criteria for megaloblastic anemia. MCH and MCHC are usually normal, whereas the large MCV is helpful in differentiation of this anemia from physiologic changes of pregnancy or iron-deficiency anemia. For MCV, the presence of increased serum iron and transferrin saturation are also helpful. Neutropenia and thrombocytopenia are the results of abnormal maturation in granulocytes and thrombocytes. A low serum level (<3g/l) may occur early in folic acid deficiency. The daily requirement in a nonpregnant state is at least 0.4 mg. In pregnancy or increased growth states, such as during infancy and adolescence, however, the requirements are increased to 0.8–1.0 mg. It is possible that multiple gestations or short intervals between pregnancies increase folate requirements further. It has been reported that folate deficiency affects about 60 to 95% of untreated women at term. However, true megaloblastic anemia due to folic acid deficiency is uncommon, although megaloblastic changes produced by this state are not uncommon. Half of the pregnant women with this type of anemia present before delivery with the remaining cases being detected puerperal. The majority of folic acid deficiencies during pregnancy appear in the third trimester. Severe folic acid deficiency in experimental animals has been linked to an increased appearance of pregnancy abnormalities such as prematurity, fetal death, hypertension, placental abruption, or fetal malformations. A direct relationship of these outcomes with iron deficiency in humans has not been proven. The fetus seems to have the ability to sustain stable hemoglobin and folate levels even in cases of obvious or severe maternal folate deficiency anemia. It is possible that the fetus removes folic acid from maternal circulation even in her deficit state. Thus, the infants in such cases are not anemic and appear unaffected. However, it has been found that megaloblastic anemia in pregnancy may be accompanied by smaller blood volume and may be related to fetal growth retardation in some cases. On the other hand, when there are no signs of anemia, the effects of folic acid deficiency are controversial or unclear. Nevertheless, the majority of physicians consider folate supplementation useful, especially for those at risk for developing deficiency states. Intake of 0.5 mg to 1 mg two or three times daily orally is generally adequate. A response to therapy within 48–72 hours can be expected as reticulocytes and platelets increase. A neutrophil response can be observed within 2 weeks. If there are low serum iron levels, the existence of concomitant iron

deficiency anemia is possible. In these cases serum iron levels may be elevated and erythropoiesis will not be efficient.

Infections condition.^[16,19]

Malaria

Malaria due to *Plasmodium falciparum* may cause severe anemia in pregnancy. It is estimated that in sub Saharan Africa 23 million pregnant women are exposed to malarial infection annually^[16,19] Women in their first and second pregnancies living in an endemic area are at a higher risk of acquiring malaria than non pregnant women or multi gravidae, due to reduction of an appropriate immune response to the malaria parasite. Anemia associated with malaria is caused by hemolysis of the red blood cells. Hypersplenism, a condition characterized by exaggeration of the inhibitory or destructive functions of the spleen, contributes to the anemia in up to 25% of women who suffer from malaria in pregnancy. Several studies have shown that protection against malaria contributes to the prevention of anemia in pregnancy thus highlighting the importance of chemoprophylaxis and other methods of malaria control. The adverse effects of malaria on maternal and fetal well-being are thought to be for the most part due to the associated severe anemia. There is evidence that malaria can induce iron deficiency by several mechanisms: possibly through immobilizing iron in haemazoin complexes and loss of urinary iron, as well as reducing intestinal iron absorption during the acute illness period 30. However these effects exerted by malaria on body iron status are still poorly understood, in part because biochemical and hematological indices of iron status are confounded by the malaria infection. In the study by Huddle et al 23 152 rural Malawian pregnant women were recruited to study the impact of malarial infection and diet on anemia status. Women were divided in to two groups in the analysis; women with and without malarial parasitaemia. A greater proportion of women (83%) positive for malaria on the test day had anemia (compared to 63% without malaria)^[16]

Hookworm Infection

Hook worm infection is described to be one of the principal causes of iron deficiency anemia in developing countries especially in children. It is prevalent throughout the tropics and subtropics wherever there is fecal contamination of the environment and is acquired mainly by skin contact with contaminated soil or vegetation. Adult hook worms live in duodenum and jejunum of humans attached to the intestinal mucosa and suck blood. Once they leave the attached site this causes chronic blood loss from the mucosa. In people whose dietary intake of iron is low and whose blood iron stores are already depleted, hookworm infection can presumably give rise to iron deficiency anemia in just a few weeks, especially during pregnancy, when iron

Requirements are increased.^[16,19]

Only one study looked at hook worm infestation among the group of 150 anemic women in Blantyre. Out of the total, 6% had hook worm infestation and none had a high density infestation. A maximum worm load of ++ was found in 2 women only. Therefore intestinal parasites are unlikely to have contributed significantly to the presence of anemia in this population. No other study on the prevalence of hookworm infestation among pregnant women was found in the literature.^[16]

Human Immuno Deficiency Virus infection

HIV infection must now be included in the differential diagnosis of anemia in pregnancy. Where anemia is associated with leucopenia and thrombocytopenia, the antenatal health worker should be alerted to the possibility of AIDS. Transmission of HIV infection by blood transfusion is possible in developing countries, where there is a high prevalence of HIV positivity among donors and where the ability to screen for HIV is sub optimal. This further highlights the importance of the antenatal clinic in the prevention of anemia early in pregnancy, which may avoid the need for a blood transfusion later in the pregnancy.^[16,19]

In the study in Chick Wawa (4104 pregnant women attending the antenatal care facilities of two hospitals), it was observed that in prim gravida, anemia prevalence was lower with HIV infection, whereas in multigravida the reverse was observed.^[16]

Side-effects of oral medications and management

The incidence of gastrointestinal side effects was more common with oral iron.^[17] When oral liquid iron is used it should be diluted with water and a straw used to prevent discoloration of the teeth. However, liquid iron supplements should be checked for the content of elemental iron. Side-effects of oral iron supplements include nausea, epigastric pain, constipation, and black discoloration of the faces. Gastrointestinal distress is commonly observed in women consuming high levels of supplemental iron on empty stomach.^[12]

Management for side effects include

- nausea and epigastric discomfort – take iron tablets on an empty stomach 1 hour prior to or 2 hours after a meal, commence tablets on a low dosage and then gradually increase the amount of iron, or take small doses more frequently.
- Constipation

Anemic myths

- Mild anemia does not have any great significance
- Dietary modification is enough for treating mild anemia
- Baby will not be affected by mild anemia. It will take what is necessary from the mother
- Baby will grow BLACK/BIG due to the fe tabs
- Iron injection are very dangerous

- Delayed cord clamping results in increased need for phototherapy

Prevention

- Dietary advice and modification (red meat/poultry/fish)
- Germination and fermentation of cereals and legumes improve the bioavailability of iron in food.
- Green peas/whole wheat/Green vegetables/ jiggery (iron rich foods)
- Iron supplementation of adolescent girls and non pregnant women
- A nutrition diet in a pregnant women should be providing about 40mg elemental iron daily

Food Fortification

1. Fortification of staple food like wheat flour which is technically simple (U S A)
2. Fortification of curry powder, salt and sugar, dried and liquid milk (S A)
3. Fortification of complimentary foods (U S A)
4. Fortification of infant foods (INDIA)

- Treatment of hookworm infestations, malaria, TB
- Avoidance Hypoxia, Acidosis, Infection, Dehydration, Stress, exercise, extreme, temperature
- Avoidance of frequent child birth.
- Supplemental Vitamin-c (250-500 mg/day) with iron
- Adequate treatment for any infection like UTI
- Early detection of falling Hb level, levels should be estimated at 1st A/N visit, 30th and finally 36th week
- Mandatory monthly screening for anemia should be done in all antenatal clinics (especially at booking and at 28 wks. with FBC).
- Screening and effective management of obstetric and systemic problems in all pregnant women.

Iron rich food as follows

- Green leafy vegetables-chana sag, sarson ka sag, chauli, sowa, salgam
- Cereals-wheat, ragi, jowar, bajra.
- Pulses-sprouted pulses.
- Jaggery.
- Dryfruits.
- Animal flesh food-meat, liver.
- Vit c-lemon, orange, guava, amla, green, mango etc.

Prevention and Management of anemia in pregnancy

NICE guidelines recommend that women are screened for anemia 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^[10,14]

India was the first developing country to take up a National Programme to prevent anemia among pregnant women and children. The National Anaemia Prophylaxis Programme of iron and folic acid distribution to all pregnant women in India through the primary health care system was evolved and implemented from 1972, so that the vast majority of pregnant women who never seek health care, could benefit from this outreach programme. It was hoped that this programme will bring about a reduction both in the prevalence and severity of anemia in pregnancy. There were two major components of the anemia prophylaxis programme – pre-school children were to receive 20mg elemental iron and 100mg folic acid and pregnant women to receive 60mg elemental iron and 500µg of folic acid. Of the two components, the coverage under the component for children had always been very poor. Comparatively the component for pregnant women has fared better. At that time antenatal care coverage under rural primary health services was very low and there was no provision for screening pregnant women for anaemia. Therefore an attempt was made to identify all pregnant women and give them 100 tablets containing 60mg of iron and 500µg of folic acid. However all the national surveys⁴⁻⁸ indicated that coverage under all these programmes was very low and there has not been any change either in the prevalence of anaemia or the adverse consequences associated with anaemia. Two decades after the initiation the National Anaemia Prophylaxis Programme, an ICMR study confirmed that most women received 90 tablets without Hb screening. Many did not take tablets regularly. Even among small number of women who took over 90 tablets, rise in Hb was low and mean Hb levels were no more than 9.1g/dl. The study conducted in 1989 by ICMR indicated that coverage under the National Anemia Pregnancy Programme was low and that 60 mg of ferrous sulphate was perhaps inadequate to treat anaemia. The Programme was revised and renamed as National Anemia Control Programme (NACP). The Programme envisaged that all pregnant women will be screened for anemia. Non anemic women would get iron (100mg) and folate (500µg) and those with anemia should get two tablets daily.^[11]

Tenth Plan strategy for combating anaemia in pregnant women

The Tenth Five Year Plan suggested multipronged strategies for the control of anaemia in pregnancy. These include:

- (i) fortification of common food items like salt with iron to increase the dietary intake of iron and improve the hemoglobin status of the entire population, including girls and women prior to pregnancy; nutrition education for dietary diversification to improve the iron and folate intake;
- (ii) Screening of all pregnant women for anemia using a reliable method of hemoglobin estimation;
- (iii) Oral iron folate prophylactic therapy for all non-anemic pregnant women (with hemoglobin more than 11 g/dl);

- (iv) Iron folate oral medication at the maximum tolerable dose throughout pregnancy for women with hemoglobin level between 8 and 11 g/dl;
- (v) Parenteral iron therapy for women with hemoglobin level between 5 and 8 g/dl if they do not have any obstetric or systemic complication;
- (vi) Hospital admission and intensive personalized care for women with hemoglobin less than 5 g/dl;
- (vii) Screening and effective management of obstetric and systemic problems in all anaemic pregnant women;
- (viii) Improvement in health care delivery systems and health education to the community to promote utilization of available care.^[11]

Salient Facts^[2]

- In developing countries, every 2nd pregnant women are estimated to be anemic.
- In developing countries, iron deficiency anemia is aggravated by inadequate intake of iron, dietary deficiency, worm infestations, malaria and other infectious diseases.
- Anemia even today contributes to 20% of all maternal deaths.
- One gm/dl increase in population mean hemoglobin could reduce the risk of maternal mortality by 25%.

Role of pharmacist

There is an urgent need to awareness by the pharmacist by patient counselling among female population about the complication associated with anemia particularly in pregnancy and menstrual cycles.

Summary

- Anemia is most common medical disorder of pregnancy with significant maternal ND fetal implication.
- Iron deficiency is major cause of anemia in pregnancy.
- Diagnosis should be established during and before pregnancy so to treat timely to prevent complications.
- Screening for iron deficiency in pregnancy is simple.

CONCLUSION

Anemia in pregnancy is associated with adverse consequences both for the mother and fetus, it's not only a medical problem .but it is a major public health problem .in country like India ,it is frequently severe and contributes significantly to maternal mortality and reproductive health morbidity, the most common cause of anemia in pregnancy is iron deficiency and less often anemia in pregnancy is caused by folic acid deficiency, and efforts should be geared towards the early detection and treatment of anemia before delivery, and through this review conclude that the anemia control programme needs to be implemented more effectively.

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