ANEMIA IN PREGNANCY

Dr. Saadia Bano
Assistant Professor
Department of Gynae & Obs.
Independent University Hospital,
Faisalabad.

Correspondence Address:
Dr. Saadia Bano
Assistant Professor
Department of Gynae & Obs.
Independent University Hospital,
Faisalabad.

Article received on:
23/02/2015
Accepted for Publication:
23/02/2015
Received after proof reading:
10/03/2015

Article Citation: Bano S, Anemia in pregnancy. Indep Rev Jan-Mar 2015;17(1-3): 053-059.

Key Concepts
• Definition of anemia in pregnancy
• Classification of anemia in pregnancy
• Consequences of anemia in pregnancy
• Management of anemia in pregnancy

Abstract: The term anemia refer to reduction in the oxygen carrying capacity of the blood due to fewer circulating red blood cells than normal or reduction in concentration of hemoglobin. Anemia is the most common nutritional deficiency disorder in the world. WHO has estimated that prevalence of anemia in pregnant women is 14% in developed and 51 percent in developing countries and 65-75% in India? According to etiology and red blood cell morphology, anemia can be classified as physiological (e.g. pregnancy), according to the aetiology (Table 1) and red blood cell morphology (Table 2). Effective management of iron deficiency relies on (i) the appropriate management of the underlying cause (for example, gastrointestinal or menstrual blood loss) and (ii) iron replacement therapy.

Key words: Anemia, Folic Acid, Blood Transfusion, Iron deficiency anemia.

The term anemia refer to reduction in the oxygen carrying capacity of the blood due to fewer circulating red blood cells than normal or reduction in concentration of hemoglobin. The deficiency may occur as a result of reduction in the production or an increased destruction of erythrocytes. Pregnancy is physiological condition and usually has no effect on general health of pregnant women. However pregnancy results in hormonal hemodynamic and hematological changes.

The lowest normal hemoglobin in the healthy non-pregnant women is defined as 12g/dl. The world health organization recommends that hemoglobin ideally should be maintained at or above 11g/dl, and should not be allowed to fall below 10.5 g/dl in the second trimester. However in most of developing countries the lower limit is often accepted as 10g/dl because a large percentage of pregnant women in this setting with hemoglobin level of 10g/dl tolerate pregnancy, labour and delivery very well and with good outcome.¹

Epidemiology:
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% in developed and 51 percent in developing countries and 65-75% in India? About one third of the global population (over 2 billions) is anemic.

Prevalence of anemia in all the groups is higher in India as compared to other developing countries. Prevalence of anemia in south Asian countries. India contributes to about 80% of the maternal morbility due to anemia in south Asia.

**Classification of Anemia**

Anemia can be classified as physiological, according to etiology and red blood cell morphology.

Classification based on red cell morphology classifies anemia based on the size and shape of the red blood cell,(normocytic MCV 80-100fl, macrocytic MCV>100fl, microcytic MCV<80fl), as well as pigmentation (hypochromic, normochromic, hypochromic) (Table 2 )

**Table 1. Classification of anemia based on aetiology.**

<table>
<thead>
<tr>
<th>A. Blood loss</th>
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<tbody>
<tr>
<td>a. Acute</td>
</tr>
<tr>
<td>i. Antepartum haemorrhage (eg placent praevia, abruptio placenta)</td>
</tr>
<tr>
<td>ii. Intrapartum haemorrhage</td>
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<tr>
<td>b. Chronic</td>
</tr>
<tr>
<td>i. Hookworm infestation</td>
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<tr>
<td>ii. Bleeding hemorrhoids</td>
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<td>iii. Peptic Ulcer Disease</td>
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<table>
<thead>
<tr>
<th>B. Nutritional Anaemia</th>
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<tbody>
<tr>
<td>i. Iron deficiency</td>
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<tr>
<td>ii. Folate deficiency</td>
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<tr>
<td>iii. B12 deficiency</td>
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<th>C. Bone marrow failure</th>
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</thead>
<tbody>
<tr>
<td>a. Aplastic anaemia</td>
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</tbody>
</table>

b. Isolated secondary failure of erythropoiesis

c. Drugs (eg Chloramphenicol, Zidovudine)

**D. Haemolytic**

<table>
<thead>
<tr>
<th>a. Inherited</th>
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<tbody>
<tr>
<td>i. Haemoglobinopathies (eg Sickle cell disorders, Thalassemia)</td>
</tr>
<tr>
<td>ii. Red cell Membrane defects (eg Hereditary spherocytosis, elliptocytosis)</td>
</tr>
<tr>
<td>iii. Enzyme deficiencies (eg G6PD deficiency, Pyruvate kinase deficiency)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>b. Acquired</th>
</tr>
</thead>
<tbody>
<tr>
<td>i. Immune Haemolytic anaemias (eg autoimmune, alloimmune, drug induced)</td>
</tr>
<tr>
<td>ii. Non- Immune Haemolytic anaemias</td>
</tr>
<tr>
<td>a. Acquired membrane defects (eg Paroxysmal nocturnal Haemoglobinuria)</td>
</tr>
<tr>
<td>b. Mechanical damage (eg Microangiopathic haemolytic anaemia)</td>
</tr>
<tr>
<td>iii. Secondary to systemic disease (eg renal diseases, liver disease)</td>
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<tr>
<td>iv. Infections (Malaria, Sepsis, HIV)</td>
</tr>
</tbody>
</table>

**Table 2. Morphological Classification of Anemia and causes.**

**Hypochromic Microcytic**

- Iron deficiency
- Thalassemia
- Sideroblastic anemia
- Anaemia of chronic disorders
- Lead poisoning

**Macrocytic**

- Folic acid deficiency
- Vitamin B12 deficiency
- Liver disease
- Myxoedema
- Chronic Obstructive Pulmonary Disease
• Myelodysplastic syndromes
• Blood loss anemia

**Normocytic Normochromic**
• Autoimmune haemolytic anaemia
• Systemic Lupus Erythematosus
• Collagen vascular disorders
• Hereditary spherocytosis
• Haemoglobinopathies
• Malignancies
• Myelodysplasia
• Blood loss anemia

**Anemia of chronic disease**
The classifications are not necessarily independent of each other as the cause of the anaemia could be multifactorial.

**Degree of Severity**
Anaemia can be classified according to severity as mild, moderate, severe and very severe (Table 3). Following the diagnosis and possible cause(s) of anaemia in the pregnant woman, management as regards the need for blood transfusions or not will depend on the severity as well as rapidity of development of anaemia.

<table>
<thead>
<tr>
<th>Degree of Severity</th>
<th>Haemoglobin level (g/dl)</th>
</tr>
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<tbody>
<tr>
<td>Normal haemoglobin level</td>
<td>&gt;11g/dl</td>
</tr>
<tr>
<td>Mild Anemia</td>
<td>9-11g/dl</td>
</tr>
<tr>
<td>Moderate</td>
<td>7-9g/dl</td>
</tr>
<tr>
<td>Severe</td>
<td>4-7g/dl</td>
</tr>
<tr>
<td>Very severe</td>
<td>&lt;4g/dl</td>
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**Maternal consequences of anaemia**

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

**Moderate anaemia**
Women with moderate anaemia 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. They are more susceptible to infections and recovery from infections may be prolonged. Premature births are more common in women with moderate anaemia. They deliver infants with lower birth weight and perinatal 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 ante-partum and post-partum haemorrhage, pregnancy induced hypertension and sepsis occur in women with moderate anaemia.

**Severe anaemia**
Three distinct stages of severe anaemia 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 further restricting work output. Untreated, it leads to pulmonary oedema and death. When Hb is <5 g/dl...
dl and packed cell volume (PCV) below 14, cardiac failure is seen in a third of cases. 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 decompensated 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. Anaemia directly causes 20 per cent of maternal deaths in India and indirectly accounts for another 20 per cent of maternal deaths.6

**Foetal consequences of anaemia**

Studies to define the effect of maternal anaemia on the foetus indicate that different types of decompensation occur with varying degrees of anaemia. Most of the studies suggest that a fall in maternal haemoglobin below 11.0 g/dl is associated with a significant rise in perinatal mortality rate.7 There is usually a 2 to 3-fold increase in perinatal mortality rate when maternal haemoglobin levels fall below 8.0 g/dl and 8-10 fold increase when maternal haemoglobin 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 haemoglobin levels were below 8.0 g/dl.8

**Investigations**

Investigations for anaemia are general and specific. A full blood count is required as part of the general investigation and includes the haemoglobin levels, packed cell volume, white cell and platelet counts. Red cell indices include mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC). These indices will classify anaemia into either microcytic (MCV <80 fL), macrocytic (MCV >100 fL) and normocytic (MCV80-100 fL) or hypochromic or normochromic (MCH and MCHC). A peripheral blood smear and reticulocyte count are also mandatory. While peripheral blood smear provides information about red cell morphology, variations in size, and shape, the reticulocyte count provides information on the marrow response. In the presence of anaemia a reticulocyte count less than 2-3 times normal indicates inadequate bone marrow response. Elevated neutrophil counts may suggest an infection and peripheral smears that reveal pancytopenia is suggestive of marrow failure. Stools should also be examined for colour, consistency, occult blood, ova and parasites. It is also important to note that in the tropics most of the causes may coexist. Other specific tests are often dictated by suspected cause of the anaemia. In the tropics, it is usual to screen for malaria as it is a well documented cause of anaemia in pregnancy. Some specific tests necessary to confirm some common causes and features of anemia are shown in Table4.
Management:
Iron Deficiency Anemia
Effective management of iron deficiency relies on (i) the appropriate management of the underlying cause (for example, gastrointestinal or menstrual blood loss) and (ii) iron replacement therapy.

Oral iron replacement therapy, with gradual replenishment of iron stores and restoration of haemoglobin, is the preferred treatment. Oral ferrous salts are the treatment of choice (ferric salts are less well absorbed) and usually take the form of ferrous sulphate 200 mg three times daily (providing 65 mg × 3 = 195 mg elemental iron/day). Alternative preparations include ferrous gluconate and ferrous fumarate. All three compounds, however, are associated with a high incidence of side effects, including nausea, constipation and diarrhoea. These side effects may be reduced by taking the tablets after meals, but even milder symptoms account for poor compliance with oral iron supplementation. It is worth noting that these lower gastrointestinal symptoms are not dose related. Modified release preparations have been developed to reduce side effects, but in practice prove
expensive and often release the iron beyond the sites of optimal absorption Effective iron replacement therapy should result in a rise in hae-moglobin concentration of around 0.1 g/dL per day (about 2 g/dL every 3 weeks), but this varies from patient to patient. Once the haemoglobin concentration is within the normal range, iron replacement should continue for 3 months to replenish the iron stores.

**Failure to respond to oral iron therapy**
The main reason for failure to respond to oral iron therapy is poor compliance. However, if the losses (for example, bleeding) exceed the amount of iron absorbed daily, the haemoglobin concentration will not rise as expected; this will also be the case in combined deficiency states.

The presence of underlying inflammation or malignancy may also lead to a poor response to therapy. Occasionally, malabsorption of iron, such as that seen in coeliac disease, may lead to a failure to respond. Finally, an incorrect diagnosis of iron deficiency anemia should be considered in patients who fail to respond adequately to iron replacement therapy.

**Intravenous and intramuscular iron preparations**
Parenteral iron may be used when the patient cannot tolerate oral supplements, for example, when patients have severe gastrointestinal side effects or if the losses exceed the daily amount that can be absorbed orally. The rise in haemoglobin concentration are no faster with parenteral iron preparations than with oral iron therapy.

Intramuscular iron sorbitol (a complex of iron, sorbitol and citric acid) injection was used as a parenteral iron replacement for many years, but was discontinued in the UK in 2003. Generally, around 10–20 deep intramuscular injections were given over 2–3 weeks. However, side effects were common and included pain, skin staining at the site of injection and arthralgia. Newer intravenous iron preparations include iron hydroxide sucrose (Venofer) and iron dextran (Cosmofer®, may also be given IM) for use in selected cases and under strict medical supervision, for example, on a haematology day unit (risk of anaphylaxis or other reactions).

**Blood Transfusion**
Blood transfusion is not indicated unless the patient has decompen-sated due to a drop in haemoglobin concentration and needs a more rapid rise in haemoglobin, for example. In cases of iron deficiency with serious ongoing acute bleeding, blood transfusion may be required.

**Folic acid deficiency anemia**
The treatment of established folate deficiency is by giving 5mg oral folic acid per day, which should be continued for at least 4 wk post partum. Parenteral folate in only rarely indicated.

**Vitamin B<sub>12</sub> deficiency**
The patients suffering from megaloblastic anemia due to vitamin B12 deficiency are treated with parenteral cyanocobalamine 250mg 1/m every month during pregnancy.

**Beta Thalassemia minor (Thalassemia trait)**
The women with beta Thalassemia minor should be advised iron and folate supplement in usual dosage but parental iron should be avoided. If anemia does not respond to the
oral iron then blood transfusion be required to correct anemia.

Other kinds of anemia’s like
- Sickle cell disease
- Hemolytic anemia’s
- Anemia with auto immune diseases
- Drugs induced anemia
- Aplastic anemia
- Leukemia’s
Should be managed in collaboration with physician and hematologist.

Prevention
To Prevent anaemia in pregnancy the following are necessary. Routine Screening for anaemia in adolescence, nutritional education about foods rich in iron (meat, liver, leafy green vegetables, legumes) and folate (liver, egg yolk, yeast and leafy green vegetables) to encourage consumption, early as well as regular antenatal clinic attendances, iron, folate supplementation in pregnancy and early treatment of concomitant infections. In areas of high malaria endemicity, intermittent prophylactic therapy with pyrimethamine- Sulfadoxine for malaria should also be given at 16-17 wks and 4 wks later.

Conclusion:
Anaemia in pregnancy is a major public health problem in developing countries and is associated with an increased risk of maternal and perinatal morbidity and mortality. Fortification of foods with iron and folate, routine screening for anaemia from adolescence, health education and prompt treatment of infections and attendance of antenatal facilities by pregnant women can reduce this burden.

References: