REVIEW OF LITERATURE
Chapter - II

REVIEW OF LITERATURE

The literature pertaining to the study on “Effect of maternal anaemia on the outcome of pregnancy in Trivandrum” is reviewed under the following headings.

I. Anaemia
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   (b) Causes of anaemia
   (c) Symptoms of anaemia.

II. Pregnancy and Anaemia

III. Prevalence of anaemia among pregnant women.
   (a) International anaemia prevalence.
   (b) National anaemia prevalence.
   (c) Prevalence of anaemia in Kerala.

IV. Requirement of iron for pregnant women to overcome anaemia.

V. Effect of anaemia on the outcome of pregnancy.

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      (b) Low birth weight,
      (c) Infections
      (d) Elevated risk of death.
      (e) Physical and cognitive developments in later life.
      (f) Cardiovascular diseases in later life.
      (g) Diabetes in later life.
2. Health consequences in mother.

(a) Maternal haemorrhage.

(b) Maternal anaemia and gestational diabetes.

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VI. National prophylaxis programme on anaemia.

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IX. Anaemia screening tests.

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(b) Stool test for hookworm infestation.
Anaemia

The term anaemia is derived from ancient Greek word for "bloodlessness". It is a condition involving abnormal reduction in haemoglobin content.

Red blood cells (containing haemoglobin) are the means by which oxygen is carried to the various parts of the body.

Anaemia is defined as a state in which the blood haemoglobin level is below the normal range for patient’s age, sex and altitude of residence (Mathew et al., 1999).

Anaemia is defined by the presence of an Hb level that is below the normal range of values for the population (Allen, 2000).

Lack of iron leads to lack of haemoglobin, which in turn leads to lack of oxygen for burning up of fuel from foods to provide energy. This explains the listlessness characteristics of anaemia, which is sometimes described as the occupational disease of the housewife (Kar et al., 2001).

Anaemia is a condition that occurs when the red blood cells do not carry enough oxygen to the tissues of the body. Anaemia affects all population groups. However the most susceptible groups are pregnant women and young children. In the milder form, anaemia is “silent”, without symptoms. In the more severe form, anaemia is associated with fatigue, weakness, dizziness and drowsiness (Department of Nutrition for Health and Development (NHD)/WHO, 2001).

Anaemia is a condition in which there is a diminished oxygen-carrying capacity of the blood as a result of a reduction in total circulating haemoglobin/or a reduction in red cell mass (Antia, 2002).
Nutritional anaemia may be defined as the condition that results from the inability of the erythropoietic tissues to maintain a normal haemoglobin concentration on account of inadequate supply of one or more nutrients leading to reduction in the total circulating haemoglobin (Srilakshmi, 2003).

Anaemia occurs when the number of red blood cells or the amount of haemoglobin (the oxygen-carrying protein) in them is lower than expected (Dhmc, 2004).

Anemia (American English) or anaemia (British English), which literally means "without blood," is a lack of red blood cells and/or haemoglobin. This results in a reduced ability of blood to transfer oxygen to the tissues. Haemoglobin (the oxygen-carrying protein in the red blood cells) has to be present to ensure adequate oxygenation of all body tissues and organs (Encyclopedia, 2004).

Anaemia is a condition in which the blood cannot carry enough oxygen, either because there is a low number of red blood cells or because each red blood cell is able to carry less oxygen than normal (BUPA, 2004).

The WHO (2005) has defined nutritional anaemia as a condition in which the haemoglobin content of the blood is lower than normal as a result of deficiency of one or more essential nutrients, regardless of the cause of such deficiency.
(a) Types and causes of anaemia.

The three main causes of anaemia include excessive blood loss (hemorrhage), excessive red blood cell destruction (hemolysis) or deficient red blood cell production.

Anaemia is the most common disorder of the blood. There are several kinds of anaemia, produced by a variety of underlying causes. Anaemia is classified according to the size of the red blood cell: decreased (*microcytic*), normal (*normocytic*) or enlarged (*macrocytic* or *megaloblastic*) (Raymond, 1999) (Conrad, 2004).

According to Swaminathan (2005) Anaemia is a broad term applied to the condition in which there is inadequate or defective formation of haemoglobin and defective maturation and formation of red blood cells. People who are anaemic develop symptoms caused by the inadequate delivery of oxygen to their body tissues. This can vary from simple fatigue to death according to the nature and severity of the anaemia. The distinction between anaemia and iron deficiency is important. They often go hand in hand, but people can be anaemic without being iron deficient and iron deficient without being anaemic. Anaemia is a symptom of a wide variety of disorders, some unrelated to nutrition and some related to nutrients other than iron, such as folate and vitamin B12.

In iron deficiency anaemia new red blood cells are smaller and lighter than normal. The depleted cells cannot carry enough oxygen from the lungs to the tissues, so energy release in all the cells is hindered. The entire body feels the effect.
Immediate Deficient Nutrition intakes Iron (Bio availability) Folate Vitamin B complex Vitamin C Protein

Interfering factors
- Phytates
- Tea
- Coffee

Conditions as respiratory infections and diarrhoea

Increased blood loss with inadequate iron take

Underlying Inadequate diet in quantity/ quality

Poor Environment
- Water
- Sanitation
- Food hygiene

Poor health care, e.g. on no immunization

Excessive menstruation, child birth, malaria parasitism - hook worm Schistosomiasis Trauma

Basic

Lack of Awareness of food values
Inadequate food security
Inadequate carrying capacity
Poverty
Inadequate health policy/ programme security

Figure 1 gives Multi-factorial causes of anaemia
UNICEF – WHO Joint Committee on Health Policy, 1994
Nutritional anaemia is caused by the absence of any dietary essential that is involved in haemoglobin formation or by poor absorption of these dietary essentials. Some anaemia's are caused by lack of either dietary iron or high quality protein, by lack of pyridoxine (vitamin B6) which catalyses the synthesis of the haem portion of haemoglobin molecule, by lack of vitamin C, which influence the rate of iron absorption into the tissues; or by lack of vitamin E, which affects the stability of red blood cell membrane. Copper is not part of haemoglobin molecule but acids in its synthesis by influencing the absorption of iron, its release from the liver or its incorporation into haemoglobin molecule (Srilakshmi, 2003).

<table>
<thead>
<tr>
<th>Nutritional Causes of Anaemia</th>
<th>Non Nutritional Causes of Anaemia</th>
</tr>
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<tbody>
<tr>
<td>1. Inadequate intake of iron</td>
<td>1. Hookworm infestation</td>
</tr>
<tr>
<td>2. Inadequate intake of folate</td>
<td>2. Excessive losses of iron from the body (loss during accidents, menstruation in women)</td>
</tr>
<tr>
<td>3. Inadequate intake of Vit B12</td>
<td>3. Degree of urbanisation</td>
</tr>
<tr>
<td>4. Inadequate intake of iron, folate and Vit B12 together</td>
<td>4. Socio economic status</td>
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<tr>
<td>5. Malnutrition</td>
<td>5. Educational background</td>
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<td>6. Accessibility to health care facilities</td>
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(Sulabha, 1999)
Types of Anaemia (Anaemia, 2005)

- Anaemia Of B12 Deficiency
- Anaemia Of Chronic Disease
- Anaemia Of Folate Deficiency
- Drug-Induced Immune Haemolytic Anaemia
- Haemolytic Anaemia
- Haemolytic Anaemia Due To g6pd Deficiency
- Idiopathic Aplastic Anaemia
- Idiopathic Autoimmune Haemolytic Anaemia
- Immune Haemolytic Anaemia
- Iron Deficiency Anaemia
- Megaloblastic Anaemia
- Pernicious Anaemia
- Secondary Aplastic Anaemia
- Sickle Cell Anaemia

Microcytic anaemia.

The most common type of anaemia overall is iron deficiency anaemia, which is most often microcytic. Much rarer causes (apart from communities where these conditions are prevalent) are hemoglobinopathies such as sickle cell anaemia and thalassemia (Conrad. 2004).

Normocytic anaemia

Normocytic anaemia can be caused by acute blood loss, chronic disease ("anaemia of chronic disease") or failure to produce enough red blood cells (as opposed to haemoglobin, which causes microcytic anaemia). Chronic renal
failure or liver failure cause normocytic anaemia; in renal failure this is due to decreased production of the hormone erythropoietin (American Family Physician, 2000).

Normocytic anaemia’s may be thought of as representing any of the following: a decreased production of normal-sized red blood cells (e.g., anaemia of chronic disease, aplastic anaemia); an increased destruction or loss of red blood cells (e.g., hemolysis, posthemorrhagic anaemia); an uncompensated increase in plasma volume (e.g., pregnancy, fluid overload); or a mixture of conditions producing microcytic and macrocytic anaemia’s (John et al., 2000).

**Macrocytic anaemia**

The most common cause of macrocytic anaemia is megaloblastic anaemia due to a deficiency of either vitamin B12 or folate acid (or both) due either to inadequate intake or insufficient absorption. Folate deficiency normally does not produce neurological symptoms, while B12 deficiency does. Pernicious anaemia is an autoimmune condition where the body lacks intrinsic factor, required to absorb vitamin B12 from food. Alcoholism can cause macrocytic anaemia (Hoffbrand et al., 1997).

There are specific anaemia like Fanconi anaemia - a hereditary disease featuring aplastic anaemia and various other abnormalities (Akiko et al., 2002).

Hemolytic anaemia is a separate constellation of symptoms (also featuring jaundice and elevated LDII levels) with numerous potential causes. It can be autoimmune, hereditary or mechanical (e.g. heart surgery). It can result
(because of cell fragmentation) in a microcytic anaemia, a normochromic anaemia, or (because of premature release of immature red blood cells from the bone marrow), a macrocytic anaemia (Butturini, 1994) (Robert et al., 2004).

**Iron deficiency anaemia** is a state of depletion in iron stores, Anaemia resulting from iron deficiency is a haematological state which points to (i) a severe depletion of iron stores and (ii) a drop of haemoglobin (Hb) concentration (UNESCO, 2006).

Iron deficiency is the most common nutritional disorder in the world. The numbers are staggering: as many as 4-5 billion people, 66-80% of the world’s population, may be iron deficient; 2 billion people – over 30% of the world’s population – are anaemic, mainly due to iron deficiency, and in developing countries, frequently exacerbated by malaria and worm infections. Approximately 20% of women, 50% of pregnant women, and 3% of men are iron deficient. Iron is an essential component of haemoglobin, the oxygen carrying pigment in the blood. Iron is normally obtained through the food in the diet and by the recycling of iron from old red blood cells (WHO, 2005).

The causes of iron deficiency are too little iron in the diet, poor absorption of iron by the body, and loss of blood (including from heavy menstrual bleeding). It is also caused by lead poisoning in children.

Iron deficiency anaemia is caused when the dietary intake or absorption of iron is insufficient. Iron is an essential part of haemoglobin, and low iron levels result in decreased incorporation of haemoglobin into red cells. In the United States, 20% of all women of childbearing age have iron deficiency anaemia, compared with only 2% of adult men. The principal cause of iron
deficiency anaemia in premenopausal women is blood lost during menses. Studies have shown that iron deficiency without anaemia causes poor school performance and lower IQ in teenage girls. In older patients, iron deficiency anaemia of often due to bleeding lesions of the gastrointestinal tract: faecal occult blood testing, upper and lower endoscopy are often performed to identify bleeding lesions, which can be malignant (Breymann, 2002).

Iron deficiency is the most prevalent deficiency state on a worldwide basis. Iron deficiency affects women from different cultures and ethnicities. In countries where meat consumption is not as common, iron deficiency anaemia is six to eight times more prevalent than in North America and Europe. This is due to the importance of meat in the diets of North Americans and Europeans (Viteri, 1994).

Iron deficiency anaemia does occur during pregnancy, but its true prevalence is difficult to determine. There are many problems in accurately diagnosing iron deficiency in pregnancy, there are several different criteria for defining iron deficiency and iron deficiency anaemia, and the prevalence will vary at different times over the 40 weeks of gestation. Iron status and iron stores play a major role in whether women are likely to become anaemic in pregnancy. Data from Australian surveys for non pregnant women of childbearing age indicate that: 8% of 20-69 year-old women have serum ferritin concentrations (SF) < 10 µg/L (National Heart Foundation Risk Factor Prevalence Study, 1989) 14.1% of 15-30 year old women have SF < 16 µg/L. 5.5% of 17-65 year old women have SF < 10 µg/L (Legget et al., 1990).

Anaemia develops slowly after the normal stores of iron have been depleted in the body and in the bone marrow. Women, in general, have smaller stores of iron than men and have increased loss through menstruation, placing them at
higher risk for anaemia than men. In men and postmenopausal women, anaemia is usually due to gastrointestinal blood loss associated with ulcers or the use of aspirin or nonsteroidal anti-inflammatory medications (NSAIDs) (Agarwal, 1996).

Fig 2: Note the washed out appearance of the red blood cells in the slide above Source: Atlas of haematology 1996

High-risk groups include, Women of childbearing age who have blood loss through menstruation. Pregnant or lactating women who have an increased requirement for iron. Infants, children, and adolescents in rapid growth phases. People with a poor dietary intake of iron through a diet of little or no meat or eggs for several years. Risk factors related to blood loss are peptic ulcer disease, long term aspirin use, colon cancer, uterine cancer, and repeated blood donation. The incidence is 2 out of 1000 people (Theresa et al., 2000).

Dietary sources of iron are red meat, liver, and egg yolks. Flour, bread, and some cereals are fortified with iron. If the diet is deficient in iron, iron should be taken orally. During periods of increased requirements such as pregnancy
and lactation. Increase dietary intake or take iron supplements (Beegum, 2005) (Eileen et al., 2005).

Symptoms are pale skin colour (pallor), Fatigue, Irritability, Shortness of breath, Low blood pressure with position change from lying or sitting to standing (orthostatic hypotension), Sore tongue, Brittle nails, Unusual food cravings (called pica). Decreased appetite (especially in children), Headache – frontal. There may be no symptoms if anaemia is mild. Signs and tests to identify are Low haematocrit and haemoglobin in a CBC, Low serum ferritin (serum iron) level, Transferrin saturation, Stool for occult blood (stool guaiac) that reveals blood loss, Higher than normal TIBC levels (Blumberg, 1994) (Raymond, 1999).

Identification of the cause of the deficiency is essential. Iron deficiency cannot be overcome by increasing dietary intake alone. Iron supplements are always required.

Oral iron supplements are in the form of ferrous sulphate. The best absorption of iron is on an empty stomach, but many people are unable to tolerate this and may need to take it with food. Milk and antacids may interfere with absorption of iron and should not be taken at the same time as iron supplements. Vitamin C can increase absorption and is essential in the production of haemoglobin (Kleigman et al., 2004).
Table 2: Dietary iron requirements per 24 hours
(Frewin et al., 1997)

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<table>
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<tbody>
<tr>
<td>Male</td>
<td>1 mg</td>
</tr>
<tr>
<td>Adolescence</td>
<td>2-3 mg</td>
</tr>
<tr>
<td>Female (reproductive age)</td>
<td>2-3 mg</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>3-4 mg</td>
</tr>
<tr>
<td>Infancy</td>
<td>1 mg</td>
</tr>
<tr>
<td>Maximum bio availability from normal diet about</td>
<td>4 mg</td>
</tr>
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</table>

Supplemental iron is needed during pregnancy and lactation because normal dietary intake cannot supply the required amount.

The haematocrit should return to normal after 2 months of iron therapy, but the iron should be continued for another 6 to 12 months to replenish the body's iron stores, contained mostly in the bone marrow. Intravenous or intramuscular iron is available for patients when iron taken orally is not tolerated. Iron-rich foods include raisins, meats (liver is the highest source), fish, poultry, eggs (yolk), legumes (peas and beans), and whole grain bread. With treatment, the outcome is likely to be good. In most cases the blood counts will return to normal in 2 months (Meier et al., 2003).

There are usually no complications; however, iron deficiency anaemia may recur, so regular follow-up is encouraged. Children with this disorder may have an increased susceptibility to infection.

Sickle-Cell Anaemia. also sickle-cell disease is a hereditary condition in which haemoglobin, an oxygen-carrying protein in the blood is altered. This leads to periodic interruptions in blood circulation. Preventive administration
of penicillin to affected children by the age of four months greatly decreases mortality from infections. For this reason, routine screening of new-borns for sickle-cell anaemia is currently carried out in most developed countries (Buchanan et al., 2004).

![Image of a blood sample from a patient suffering from Sickle cell anaemia](image)

**Fig 3. Blood sample from a patient suffering from Sickle cell anaemia**

*Source: Atlas of haematology 1996*

**Thalassaemia**, inherited form of anaemia in which there is reduced synthesis of one or more of the four globin chains, usually $2\alpha$ (alpha) and $2\beta$ (beta), which make up haemoglobin in red blood cells. The function of haemoglobin is to carry oxygen between the lungs and the tissues of the body; in anaemia this is insufficient to meet the oxygen requirements of the tissues (for example, the muscles and the brain) (Douglas, 2004).
Homozygous Thalassaemia (Cooley’s Anaemia)

Homozygous thalassaemia, where both copies of the gene for a haemoglobin chain are defective, occurs when no chains are synthesised. The symptoms develop after birth during the first few months of life. If affected patients are correctly diagnosed when babies and treated with regular blood transfusions, they will develop normally during childhood until puberty. However, at puberty a variety of liver, heart, and glandular problems can result from the iron overload caused by the transfusions. Death normally occurs before the age of 30 from cardiac damage. In the absence of transfusion, children die within the first year of life. If they receive insufficient blood transfusions, they tend to develop deformities of the skull and the bones, leading to a characteristic mongoloid appearance; they have enlarged spleens, severe anaemia, and are subject to repeated infections and a tendency to bleed. They also fail to thrive and if they survive to adolescence they run the risk of the same complications of iron overloading as those who are sufficiently transfused (Weatherall et al., 2001).

Fig 4: Blood sample from a patient suffering homozygous thalassaemia
Source: Atlas of haematology 1996
Heterozygous thalassaemia occurs when only one copy of the gene for the chain is affected. Sufferers are normally free from symptoms except during pregnancy, when they may become anaemic (Steinberg et al., 2001).

**Anaemia of chronic disease** is an anaemia that develops as a result of long-term infection or disease. Certain chronic infections and diseases cause several changes in the blood production (haematopoietic) system. These include a slightly shortened red blood cell life span, decreases in the amount of iron that is available in the fluid portions of blood, and decreases in the activity of the bone marrow. In the presence of these three effects a low to moderate grade anaemia develops. The symptoms of the anaemia often go unnoticed in the face of the primary disease (Higgins, 2005).

The most common cause of anaemia is iron deficiency. A disturbance of iron metabolism, though not a deficiency, is a feature of the mild to moderate anaemia that often complicates the course of many common chronic conditions including carcinoma, chronic inflammatory conditions such as rheumatoid arthritis, and longstanding infectious diseases like tuberculosis. These chronic conditions are numerous and common, so anaemia of chronic disease (ACD) is also very common. Indeed, after iron deficiency, chronic disease is the most common cause of anaemia. Iron deficiency anaemia (IDA) and ACD share common features that can make distinction difficult. Results of a recent study by Greek researchers that looked at bone marrow recovered from patients suffering from rheumatoid arthritis now provides convincing evidence that the cytokine tumour necrosis factor-a plays a key role in the pathogenesis of ACD (Rivera et al., 2005).

Conditions associated with the anaemia of infection and chronic diseases include such diverse diseases as chronic bacterial endocarditis, osteomyelitis,
juvenile rheumatoid arthritis, rheumatic fever, Crohn's disease, and ulcerative colitis. Chronic renal failure may produce a similar anaemia because it causes reduced levels of erythropoietin, the hormone that stimulates the production of red blood cells in the bone marrow (Sood, 1988)(Grover et al., 2004).

Treatment of the underlying disease can prevent or reverse the anaemia. Chronic diseases such as Crohn's disease are difficult to treat and patients may exhibit intermittent anaemia that varies with their condition. Symptoms include: Presence of a chronic disease or infection, Pallor, Fatigue, Tiredness, Headache, Lethargy, Shortness of breathe on exertion, Dizziness. This type of anaemia responds to treatment of the primary disease and with successful treatment of the primary disease the anaemia will resolve (Andrews, 1999) (Weiss, 1999).

**Anaemia of b₁₂ deficiency** is a decrease in the red cells in the blood caused by a vitamin deficiency. Vitamin b₁₂ is essential for normal nervous system function and normal red cell, white cell and platelet production. All sources of vitamin b₁₂ come from the diet in animal products, including dairy and eggs. For vitamin b₁₂ to be absorbed by the body, it must become bound to an intrinsic factor, a protein secreted by cells in the stomach (Beers et al., 1999).

Causes of vitamin b₁₂ deficiency include Dietary (a strict vegetarian diet excluding all meat, fish, dairy products, and eggs), Chronic alcoholism. Abdominal or intestinal surgery that eliminates the site of intrinsic factor production or absorption, Crohn's disease intestinal malabsorption disorders Crohn's disease intestinal malabsorption disorders, Fish tape worm, and Pernicious anaemia, which is caused by an inherited intrinsic factor deficiency (Areekul et al., 1990).
Anaemia of b\textsubscript{12} deficiency that is caused by a poor diet can be prevented through a well-balanced diet. Prophylactic (preventative) use of vitamin b\textsubscript{12} injections can prevent deficiency after surgeries known to result in vitamin B\textsubscript{12} deficiency. Anaemia resulting from other causes cannot be prevented, but early diagnosis can limit the severity of the anaemia (Andres \textit{et al.}, 2004).

Pernicious anaemia requires life long therapy with vitamin B\textsubscript{12} injections. Anaemia caused by dietary insufficiency of vitamin B\textsubscript{12} can be corrected by oral (by mouth) vitamin replacement in combination with a more balanced diet. Initially it may be treated with vitamin B\textsubscript{12} (Zimhony \textit{et al.}, 1998).

Anaemia caused by malabsorption (inadequate absorption of nutrients from the intestinal tract) is treated with vitamin B\textsubscript{12} injections until the condition improves. Prognosis for this form of anaemia is generally that it is corrected by therapy. Central nervous system signs and symptoms may be irreversible if treatment is not initiated within 6 months of the onset of these symptoms. Vitamin B\textsubscript{12} affects the maturation of all epithelial cells (cells that form injections the outer surface of the body and line inner passageways) and a deficiency may cause a false positive pap smear (Ban-Hock \textit{et al.}, 1998).

Anaemia of folate deficiency is a decrease in the red cells in the blood caused by folate (folic acid) deficiency. Folate or folic acid is necessary for red blood cell formation and growth. Dietary sources of folate are found in green leafy vegetables and liver. Some medications such as Dilantin interfere with the absorption of this vitamin. Because folate is not stored in the body in large amounts, a continual dietary supply of this vitamin is needed. In folate deficiency anaemia, the red cells are abnormally large and are referred to as megalocytes and in the bone marrow as megaloblasts. Subsequently, this anaemia may be referred to as megaloblastic anaemia (Joshi, 2000) (Klee, 2000).
Megaloblastic anaemia is also frequently caused by folic acid deficiency. It is usually a result of dietary lack of folic acid. Alcoholics and women in late pregnancy are especially likely to have such a diet. Adequate dietary intake in high-risk individuals and folic acid supplementation during pregnancy may help prevent the onset of this anaemia. Symptoms include tiredness, headache, sore mouth and tongue pallor or jaundice. Signs and tests are a folate – test, low red blood cell folate level, a CBC and a bone marrow examination (Sarma, 1987) (Swaminathan, 2001).

Symptoms of anaemia can cause discomfort. In a pregnant woman, folate deficiency has been associated with neural tube defects (such as spina bifida) in the infant (Nair, 2001).

**Haemolytic anaemia** refers to any condition causing inadequate number of circulating red blood cells caused by premature destruction of red blood cells. Haemolytic anaemia occurs when the bone marrow is unable to compensate for premature destruction of red blood cells by increasing their production. When the marrow is able to compensate, anaemia does not occur. There are many types of haemolytic anaemia, which are classified by the location of the defect. The defect may be in the red blood cell itself (intrinsic factor) or outside the red blood cell (extrinsic factor) (Dhaliwal et al., 2004).

G-6-PD deficiency is an inheritable x-linked recessive disorder whose primary effect is the reduction of G-6-PD in the red blood cell, with resultant haemolysis of the cell. The ultimate effect of the disease is to produce anaemia, either acute haemolytic or a chronic spherocytic type. People with the disorder are not normally anaemic and display no evidence of the disease until the red cells are exposed to an oxidant or stress (Kaplan et al., 2002).
Symptoms arise as the consequence of bone marrow failure. Anaemia (low red blood cell count) leads to fatigue and weakness. Low white blood cell counts, or neutropaenia, cause an increased risk of infection. Low platelet counts, or thrombocytopenia, results in bleeding of mucus membranes and skin. The disease may be acute or chronic, and is always progressive. Risk factors are unknown. The incidence is 2 out of 1 million people. There is no known prevention for idiopathic anaemia. (Scrimer, 2001)

Fig 5: Slide shows a sample of blood from a patient suffering acute autoimmune haemolytic anaemia. Source: Atlas of haematology 1996

There is no known prevention for idiopathic autoimmune haemolytic anaemia, because the cause is unknown. Adults commonly have long-term disease, but in children the anaemia is usually short-lived. Complications include bleeding and infection.
Megaloblastic anaemia is a blood disorder characterised by red blood cells that are larger than normal, low white blood count, and low platelet count resulting from a deficiency of folic acid or vitamin B-12. Deficiencies of vitamin B₁₂ and folic acid are the most common causes of megaloblastic anaemia. Other causes are leukaemia, myelofibrosis, multiple myeloma, certain hereditary disorders, drugs that affect nucleic acid metabolism such as chemotherapy agents (methotrexate), and other causes. Risk factors relate to the causes (Thomas, 2004).

Fig 6: Note the large size of the red blood cells when compared to the white blood cells in this slide showing a blood sample taken from a patient with megaloblastic anaemia. Source: Atlas of haematology 1996.

Pernicious anaemia is a form of anaemia caused by a lack of intrinsic factor, a substance needed to absorb vitamin B₁₂ from the gastrointestinal tract. A person with pernicious anaemia loses their ability to make intrinsic factor, a
substance that enables vitamin $B_{12}$ to be absorbed from the intestine. This condition may result from hereditary factors. Congenital pernicious anaemia is inherited as an autosomal recessive disorder (Carmel, 1996).

Pernicious anaemia usually does not appear before the age of 30, although a juvenile form of the disease can occur in children. Juvenile or congenital pernicious anaemia is evident before the child is 3 years old. Risk factors are a history of autoimmune endocrine disorders, a family history of pernicious anaemia, and Scandinavian or Northern European descent. The incidence is 1 out of 1,000 people. (Zimhony et al., 1998)

II. Pregnancy and Anaemia
Adequate nutrition before and during pregnancy has greater potential for a long-term health impact that it does at any other time. Maternal health is a complex, influenced by various genetic, social and economical factors, infections and environmental conditions, many of which may affect the foetal growth. Physiological adaptations result in improved utilisation of nutrients either through increased absorption, decreased excretion or alternations in metabolism (Geelhoed et al., 2006).

According to WHO (2005) anaemia in adults causes fatigue and reduced work capacity and may cause reproductive impairment.

Maternal iron deficiency is thought to have a negative effect on pregnancy outcomes through impaired haemoglobin transport of oxygen to the uterus, placenta and foetus. However, while there is noteworthy consistency among studies demonstrating this negative effect, there is still much data, which is conflicting, not least because only very large study samples can hope to control all the possible sources of variation that can influence pregnancy
outcome. Iron deficiency anaemia in pregnancy is often associated with low socioeconomic status, multiple pregnancies, and extremes of maternal age, and smoking, all of which may independently account for the poor pregnancy outcomes (Scholl and Hediger, 1994).

Most of the studies do not control for these and other factors that may affect birth weight and prematurity making it unclear whether iron deficiency and anaemia have a direct influence on pregnancy outcomes. The more cynical view is that, given how common both iron deficiency and iron supplementation during pregnancy are, the ill effects of the former and the positive effects of the latter should be clearer cut (Walker, 1996).

Non-nutritional causes of fetal growth retardation include hemorrhage, multiple births, uterine and placental abnormalities, parental size and genetics, and major congenital malformations. These explain up to 50% of the variance in birth weight in both developed and developing countries (Villar and Belizan 1982).
RELATIONSHIP BETWEEN MATERNAL AND FOETAL NUTRITION

Inadequate food intake and poor nutrient utilisation

→

Maternal malnutrition

→

Reduced blood volume expansion

→

Inadequate increase in cardiac output

→

Decreased blood and nutrient supply to the foetus

→

Reduced placental size

→

Reduced nutrient transfer

→

Foetal growth retardation

Fig 7: Schematic diagram of Relationship between Maternal and Foetal Nutrition. (Srilakshmi, 2003)
In developing countries, more IUGR is due to low maternal weight and height (under nutrition during the mother’s development). low pregnancy weight gain (which is influenced by energy intake during pregnancy) and maternal infection. Low maternal weight at conception and low weight gain during pregnancy are independent predictors of poor fetal growth and IUGR. Low maternal height also plays a role independently of low body mass index (Allen, 2000).

**Fig 8: Maternal anaemia and outcome of pregnancy (Rasmussen, 2001)**

Supplementation with iron is generally recommended during pregnancy to meet the iron needs of both mother and foetus. When detected early in pregnancy, iron deficiency anaemia (IDA) is associated with a > 2-fold increase in the risk of preterm delivery. Maternal anaemia when diagnosed before midpregnancy is also associated with an increased risk of preterm birth (Scholl, 2005).
Table 3. Components of weight gain during pregnancy – 28 – 40 weeks (Arafa et al., 1998).

<table>
<thead>
<tr>
<th>Components</th>
<th>Weight g</th>
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<tbody>
<tr>
<td>Foetus</td>
<td>3000</td>
</tr>
<tr>
<td>Placenta and amniotic acid</td>
<td>1500</td>
</tr>
<tr>
<td>Maternal tissues and blood</td>
<td>7000</td>
</tr>
<tr>
<td>Total</td>
<td>11500</td>
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</tbody>
</table>

Poor maternal nutrition may also lead to poor child survival, which increases the overall fertility. The other causes of anaemia in pregnancy include – hookworm infestation, repeated pregnancy inter-current infection, ante- and post-partum haemorrhages, persistent vomiting and spontaneous abortion. Premature labour, low birth weight babies, premature births, puerperal sepsis, thromboembolic phenomenon and high perinatal mortality are associated with anaemia in pregnancy (Mahajan and Gupta, 1995) (Park, 2000).
Table 4. Recommended weight gains for pregnant women based on body mass Index (Fowles, 2004):

<table>
<thead>
<tr>
<th>Weight category Based on BMI gain (Kg)</th>
<th>Total weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight (BMI&lt;19.8)</td>
<td>12.5-18</td>
</tr>
<tr>
<td>Normal weight (19.8-26)</td>
<td>11.5-16</td>
</tr>
<tr>
<td>Overweight BMI&gt;26-29</td>
<td>7-11.5</td>
</tr>
<tr>
<td>Obese&gt;29</td>
<td>6.0</td>
</tr>
</tbody>
</table>

Low availability and poor absorption of iron and repeated and closely spaced pregnancies place a constant drain on the iron stores of the pregnant women. The increased iron requirement during pregnancy often outstrip the availability supply of iron and induces low level of haemoglobin and haematocrit values resulting in decreased oxygen carrying capacity and impairment in fetal growth. Thus iron deficiency anaemia during pregnancy may be an important risk factor contributing to the high incidence of low birth weight (Baron et al., 2005).

Anaemia is estimated to affect 3.5 billion individuals in the developing world and more than 320 million people in India with the highest prevalence among women and children (40 to 80 per cent pregnant women, 60 to 70 per cent children and 50 per cent adolescent girls (Vijayalakshmi, 2004).
Table 5: Causes of Anaemia During Pregnancy (Scholl, 2000)

<table>
<thead>
<tr>
<th>Causes of Anaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acquired</strong></td>
</tr>
<tr>
<td>Iron deficiency anaemia</td>
</tr>
<tr>
<td>Anaemia associated with acute blood loss</td>
</tr>
<tr>
<td>Anaemia caused by infection</td>
</tr>
<tr>
<td>Megaloblastic anaemia</td>
</tr>
<tr>
<td>Acquired haemolytic anaemia</td>
</tr>
<tr>
<td>Aplastic or hypoplastic anaemia</td>
</tr>
<tr>
<td><strong>Hereditary</strong></td>
</tr>
<tr>
<td>Thalassaemia</td>
</tr>
<tr>
<td>Sickle-cell anaemia</td>
</tr>
<tr>
<td>Sickle-cell-haemoglobin C disease</td>
</tr>
<tr>
<td>Sickle-cell-thalassaemia disease</td>
</tr>
<tr>
<td>other haemoglobinopathies</td>
</tr>
<tr>
<td><strong>Other</strong></td>
</tr>
<tr>
<td>Spurious laboratory error</td>
</tr>
</tbody>
</table>

In developing countries, the most common cause of anaemia in pregnancy is nutritional. An inverse type of relationship indirectly exists between maternal nutritional status and fertility levels. Virtually, in societies where women are well fed, the fertility levels are low, while societies where women are not well fed, the fertility levels are high (Park 2000).

The nutritive value of diet of pregnant women is probably one single factor, which would directly affect the outcome of pregnancy (Devadas, 2001) (Zhou et al., 2005).
Closely spaced pregnancies are especially likely to cause anaemia. Iron is transferred to the new growing foetus before the mother has had time to replace the iron stores used up during her previous pregnancy. During pregnancy their bodies make red blood cells faster than normal (King, 2003).

Parasitic infection are often involved in the causality of iron deficiency anaemia in many developing countries (UNESCO, 2006).

The rationale for building iron stores before the first and subsequent pregnancies derives from the process by which iron deficiency anaemia develops, and the pattern of iron needs during pregnancy.

---

Fig 9. Detailed conceptual framework used to guide interpretation of the literature. Hb, haemoglobin concentration. (Rasmussen, 2001)
Iron stores and vulnerability to anaemia

Iron deficiency anaemia develops through three steps indicating increasing severity of deficit in the supply of iron relative to needs:

1. **Depletion of iron stores**: Iron stores can be understood as buffer stocks. This iron—held in the form of two compounds, hemosiderin and ferritin—is mobilised when the supply of dietary iron is inadequate relative to iron needs. Pregnancy is a period of relatively high iron needs. During pregnancy, iron stores are low or absent even among women who are not iron deficient. Depletion of iron stores is technically not termed iron deficiency, but is a good indicator of impending deficiency.

2. **Impaired haemoglobin production**: This is a stage of iron deficiency characterised by an insufficient supply of iron to developing red blood cells. Haemoglobin concentration, however, remains in the normal range.

3. **Iron deficiency anaemia**: This is the stage of iron deficiency at which biochemical processes are affected. The cut-off point for anaemia for non-pregnant women is 12.0 gm/dl. However, plasma volume expansion during pregnancy necessitates different standards for anaemia during pregnancy to distinguish iron deficiency anaemia from pregnancy-induced anaemia. The World Health Organisation standards (Lale *et al.*, 2004) are as follows:

   - First trimester: 11.0 gm per dl
   - Second trimester: 10.5 gm/dl
   - Third trimester: 11.0 gm/dl
When women lack iron stores any increase in iron requirements needs to be matched immediately with an increase in iron absorbed from dietary sources if iron sufficiency is to be maintained. An absence of iron stores therefore implies increased vulnerability to iron deficiency anaemia (Harding, 2001).

There is no data on the prevalence rates for iron deficiency anaemia amongst pregnant women in India disaggregated by gestational age, or on iron stores of women prior to entering pregnancy. However, on the basis of iron deficiency anaemia prevalence amongst adolescent girls and adult women, one can safely estimate that the proportion of women who enter pregnancy without any iron stores must be significant (UNICEF, 2000).

**Pattern of iron needs during pregnancy**

Iron supplementation during pregnancy cannot maintain iron sufficiency during the first trimester for iron deficient women or women without iron stores.

As mentioned above, iron supplementation during pregnancy is a well-established practice in public health. 100 Iron and Folic Acid tablets are routinely delivered during Ante Natal Care to pregnant women by the public health system. Supplementation should ideally commence during the second trimester (in practice, as a result of late registration for Ante Natal Care supplementation commences only in the mid-second or in the third trimester). This pattern of supplementation to maintain iron sufficiency matches the standard pattern of increase in iron needs during pregnancy. The calculations below are of iron need during pregnancy and do not account for pre-pregnancy iron deficits (ICMR, 1989)(Rao, 1991)(National Family Health Survey, 1998).

<table>
<thead>
<tr>
<th>Severity of anaemia</th>
<th>Cut off level of Haemoglobin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>19g/dl and above but below 11g/dl</td>
</tr>
<tr>
<td>Moderate</td>
<td>7g/dl and above but below 10g/dl</td>
</tr>
<tr>
<td>Severe</td>
<td>Below 7g/dl</td>
</tr>
</tbody>
</table>

**First trimester**

Net iron requirements do not increase during the first trimester. Menstruation stops. The only iron losses are the basal losses through the gut, urine and skin. There is also some evidence that erythropoietic activity may be reduced during this period with a slight reduction in red blood cell mass, a reduction in the number of reticulocytes and a rise in the serum ferritin concentration levels. The average iron requirement in the first trimester is 0.8-mg/ day, which is equivalent to daily basal losses. It follows that no increase in iron available to the body is required to maintain iron sufficiency in the first trimester (Rasmussen 2001).

**Second trimester**

Iron requirements begin to increase in the second trimester. As the foetus grows there is an increase in the oxygen consumption by both the mother and the baby. This is associated with major haematological changes. The total blood volume is found to increase in most studies by 45%. The various contributors to this increase include a 50% increase in plasma volume, a 35% increase in red blood cell mass and a 30% increase in haemoglobin mass. The result of this increase in plasma is a decline in haemoglobin concentration by
around 1 g/dl. These changes begin in the second trimester. The average iron requirement in the second trimester is 4-5 mg/day (Kazmierczak et al., 2004).

**Third trimester**

As pregnancy progresses, iron requirements for fetal growth rise in proportion to the increasing weight of the fetus. Foetal weight gain is maximum in the third trimester.

The average iron requirement in the third trimester is > 6 mg per day. It may reach as much as 10 mg per day during the last 6-8 week of pregnancy. Clearly, the pattern of iron needs across pregnancy for iron sufficient (at conception) pregnant women is such that the savings of iron normally lost during menstruation are adequate to meet the increased iron needs during the first trimester. For these women iron needs outstrip supply only from the second trimester onwards, which is, when iron supplementation can be commenced (Scholl, 2005).

Women who enter pregnancy in an iron deficient state or without adequate stores present a different pattern of iron deficits during pregnancy. The reason is that iron savings from absence of menstrual blood losses are not sufficient to meet iron needs in the first trimester given that the starting point is one of iron insufficiency (i.e. anaemia) or near-insufficiency. Iron supplementation can only commence in the second trimester (Strauss & Dietz, 1999).

**Dietary compensation**

A fall in appetite due to nausea in the first trimester makes it unlikely that the iron deficit can be compensated for through increased food intake. Poorly
bioavailable iron in developing country diets renders compensation through diets more difficult. Vegetarian diets contain non-heme iron. This form of iron is more difficult to absorb physiologically relative to heme iron found in meat, fish and eggs. Its absorption is also particularly vulnerable to the effects of absorption inhibitors such as tannin (in tea). The average amount of iron absorption required per day for women who begin pregnancy with minimal iron stores is 6 mgs per day. Even diets containing large quantities of bioavailable iron enable absorption of between 3 and at most 5 mgs a day. When diets consumed have poorly bio-available iron, absorption is much lower (FAO/WHO, 1988) (Leeuw et al., 1996) (Halberg, 1998) (Patra et al., 2005).

**Iron Requirements in Pregnancy**

Iron requirements are increased in pregnancy, especially in the last trimester when they may be several times higher than at other stages of the life cycle. This iron covers normal basal losses from the gastrointestinal tract, the skin, and the urinary tract, and the additional demands of the placenta, cord and the growing foetus, as well as the increased maternal red blood cell mass. The expansion of the red cell mass will be determined by the supply of iron from body iron stores and the diet. If iron stores are adequate, 300-500 mg of iron [450 mg often quoted] (Hytten & Leitch, 1971) will be required; this will depend on body size. At term, the foetus has accumulated 200-370 mg (mean = 270 mg) of iron (Widdowson and Spray, 1951). Foetal blood in the placenta and cord may account for a further 30-170 mg (mean = 90 mg) of iron (Bothwell, 2000).
Table 7: The iron cost of pregnancy (a)

<table>
<thead>
<tr>
<th>Iron costs</th>
<th>Amount of iron (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foetal Iron</td>
<td>270</td>
</tr>
<tr>
<td>Umbilical cord and placental iron</td>
<td>90</td>
</tr>
<tr>
<td>Maternal blood loss</td>
<td>150 510</td>
</tr>
<tr>
<td>Obligatory losses</td>
<td>230</td>
</tr>
<tr>
<td>Expansion of maternal red cell mass</td>
<td>450</td>
</tr>
<tr>
<td><strong>Total Net cost</strong></td>
<td>1190</td>
</tr>
<tr>
<td>Contraction of maternal red cell mass postpartum</td>
<td>450</td>
</tr>
<tr>
<td><strong>Net total (b)</strong></td>
<td>740</td>
</tr>
<tr>
<td><strong>Total requirement (c)</strong></td>
<td>1040</td>
</tr>
</tbody>
</table>

a. Adapted from AMA (1968), (Bothwell, 1979, 1995)
b. Expansion of red cell mass not included
c. Blood loss at delivery not included

Table 7 indicates that the total iron requirements during pregnancy are between 800-1000 mg (Bothwell, 1995). There are blood losses at parturition (representing 100-275 mg iron), which are sometimes added to the requirements of pregnancy, although they are strictly post-partum requirements. The 450 mg or so of iron required for red cell mass expansion is returned to iron stores after delivery. It must nevertheless be obtained from the diet if it is not present in the stores at the start of pregnancy. If the woman does have a 450 mg iron reserve there is still a mean of about 740 mg of iron, which must be absorbed from the diet. If the woman has no iron stores she must absorb about 1000 mg if the red cell mass is to expand fully. The increase in iron demand is offset by the iron-sparing effect of amenorrhoea, which may save, 250-500 mg of iron (Beard et al., 2005).
The recommended dietary allowances in the daily diet of pregnant women according to ICMR 2001 is,

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Energy</td>
<td>2400 kcals,</td>
</tr>
<tr>
<td>Protein</td>
<td>78 gm</td>
</tr>
<tr>
<td>Calcium</td>
<td>2200 mg</td>
</tr>
<tr>
<td>Iron</td>
<td>56 mg</td>
</tr>
<tr>
<td>Carotene</td>
<td>2400 mg</td>
</tr>
<tr>
<td>Ascorbic acid</td>
<td>40 mg.</td>
</tr>
</tbody>
</table>

**The significance of the first trimester for the fetus- placental formation**

The placenta is an important link in the maternal-foetal nutrient supply chain, through its role in nutrient transfer and metabolism of key nutrients. It also regulates foetal growth by secreting hormones. The placenta’s transfer capacity during pregnancy is influenced by factors such as placental surface area and the availability of specific nutrient transmitters on the placenta. Placental formation may be influenced, in turn, by maternal nutritional environment. The first trimester is critical for placental formation (Lone et al., 2004).

There is documented evidence of attempted placental compensation for poor maternal nutrition, including iron deficiency, which directly affects haemoglobin formation and oxygen supply. This compensation takes the form of an increase in size to optimise transfer of oxygen and nutrients to the foetus. The implications of this may be increased metabolic demands by the placenta for its own nutrient needs. This results in relatively greater claims on available nutrient supply by the placenta for its metabolic needs. Moreover, in times of severe shortfall there could be a reverse transfer of nutrients from the
foetus to the placenta- this transfer would be higher for a larger placenta as compared to a smaller placenta (Taylor, 1979) (Nair, 2001).

Optimal placental formation is key to optimising foetal growth, thereby reducing Intra Uterine Growth Retardation incidence. Maintaining iron sufficiency in early pregnancy may be critical to achieving this goal.

**Iron availability from Kerala diet**

According to Prema (2002) most foods included in the diets of keralites, in general contain a small amount of iron which very often is not in the form that easily passes through the gut wall, this means that the body absorbs only a small part of the iron that is present in the food, the amount of iron that a person absorbs depends on the total amount of iron in the meal, the type of iron in the food, the other foods in the meal and the amount of the iron that the person needs. The proportion of dietary iron absorption can increase 3 to 5 fold, if iron stores depleted in the body. Conversely the proportion absorbed is found to decrease in conditions of iron overloaded in the body.

Some of the serious limiting factors in fulfilling the iron requirement in Kerala diet are as following.

1. Quantity wise diet in predominated by cereals, the phosphorus and Phytate components of which form staple, poorly absorbs complexes with iron.

2. Food, which is capable of counteracting the negative effects of phytates, pulses are also found in negligible amounts.

3. Regular consumption brand rice parboiled may induce changes in the intestine or its microflora leading to reduction in iron absorption.
4. Vitamin C rich foods like green leafy vegetables and fruits which enhances of iron absorption are not included in adequate amounts in the diets.

5. Milk and milk products, after digestion may form a complex with iron called lactoferrin in habitting iron absorption.

6. Vegetable s forming 16% of the diet contain ligands (chlorogenic acids) in abundance inhibiting iron absorption.

7. Inclusion of tea and coffee beverages in large quantities and also several times in a day significantly reduces iron availability.

8. Cooking procedure like germination, which may cause concomitant reduction in the tannin content of food, inhibitor of iron absorption: fermentation, causing enzymatic hydrolysis of phytic acid and use of thermal process soaked and milled grains are not common in Kerala cuisines.

Advantages of Kerala diet

1. Fish, a food rich in easily absorbable in haem iron and which enhances the non-haem iron after digestion form 3.2% of the diet.

2. Habit of simmering low pH vegetables helps the integration of released iron in to the haem iron pool.

Hookworm infestation

Anaemia is a major problem among pregnant women in Jabalpur Anaemia is a major problem among pregnant women in this region. The mean haemoglobin level was lower in primigravidae infected with P. falciparum, as reported in other malarious areas (Brabin et al., 1998)
Anaemia usually increases in vivax-infected women and in non-infected pregnant women with parity, with primigravidae being the least anaemic group. This is presumably because iron deficiency tends to increase as gravidity increases (Isah et al., 1985) (Nayak et al., 1992).

It is unfortunate that the haemoglobin data from our pregnant and non-pregnant study subjects were incomplete because many women feared the discomfort of blood sampling; we therefore do not have a more precise picture of the effect of anaemia in the infected and non-infected groups. Furthermore, since the etiology of anaemia in pregnancy is multifactor, i.e. due to iron deficiency, folate deficiency and hookworm infection (WHO 1986), the effect of malaria on this condition is difficult to ascertain. Quantification of the relative contributions of malaria, hookworm and malnutrition to anaemia is thus an important step in selecting appropriate control measures to prevent the adverse perinatal outcomes associated with anaemia in pregnancy (Brabin, 1991).

Hookworm infection was associated with severe but not moderate anaemia among women receiving antenatal care at a hospital in Kathmandu, Nepal (Bondevik et al., 2000).

Familial distribution of Ascaris lumbricoides, anaemia resulting in low birth weight babies during pregnancy because of hookworm infection, higher incidence of intestinal taeniasis in pig rearing than in non pig rearing communities, negative effects on growth and development particularly in malnourished children and economic consequences on the family and community, higher prevalence among children under five years in rural and semi urban slums and recent detection of some of these helminths in human immunodeficiency virus (HIV) positive patients are some of the reported facts
which indicate the magnitude of the problem and need for control of these soil transmitted helminths particularly targeting the children and pregnant women (Mahajan, 2003).

Hookworm infestation causes chronic blood loss and depletion of body iron stores leading to iron deficiency anaemia. This has implications for child health in terms of retarded physical growth and development; for the health of the mothers in terms of increased morbidity, low birth weight babies, abortion, still births and impaired lactation; and for the health of adults in terms of diminished capacity for sustained hard work (Park2008).

![Diagram of Hookworm Infestation Cycle](Fig 10. Hookworm infestation cycle (Srilakshmi 2003))
III. Prevalence of anaemia among pregnant women.

Nutritional divide is increasing between the rich and the poor within and among nations. The situation is particularly alarming in developing countries. The nutritional paradox of South Asia lies in the coexistence of grain mountains and hungry millions. This is largely due to inadequate purchasing power, arising from the lack of sustainable livelihood opportunities. Famine of income is becoming the most important cause of a famine of food at the household level. Pregnant and nursing mothers and children belonging to the families living below the poverty line (the World Bank poverty line is an income of one US dollar per capita per day or below) suffer the worst. For example, severe anaemia during pregnancy is associated with very high relative risk of maternal death. Maternal mortality rates are as low as 3 to 4 per 100,000 births in industrialised countries, while in many developing countries they are at least 100 to 200-fold higher. Protein-energy malnutrition (PEM) affects nearly 30 per cent of children under five years of age in countries in Sub-Saharan Africa (Swaminathan, 2005).

Worldwide, iron deficiency is the most common nutrient deficiency affecting more than one billion people. In developing countries, one-third of the children and women of childbearing age suffer from iron-deficiency anaemia. In United States, iron deficiency anaemia is less prevalent but still affects about 10% of toddlers, adolescent girls and women of childbearing age (West, 1996) (Lockwood et al., 1999) (Cornett et al., 1998).

Iron deficiency anaemia is probably the most common cause of anaemia in the world today. A study on the prevalence and etiology of nutritional anaemia in early childhood in an urban slum area of east Delhi indicated a high
prevalence (76%) of anaemia and iron deficiency in 41% children (Gomber et al., 1998).

In population where the prevalence of iron deficiency anaemia is high, casualty is generally attributed to the interaction of low bioavailability of dietary iron (i.e., non haem iron) and other chronic blood loss due to helminth infections and schistosomiasis. An anaemic woman is more likely to bleed severely or to become ill and die during delivery. Variations in the prevalence rates of anaemia are seen within the country with the lowest prevalence of 33% being reported from Andhra Pradesh to the highest of 98% in Rajasthan (Seshadri, 1997) (WHO, 1998).

Pre-school-age children and adolescent girls, along with women of child bearing age, are especially prone to iron deficiency anaemia, which affects over 2000 million people worldwide. Iodine deficiency disorder is also widespread, with 1500 million people in the world at risk (FAO, 2000).

Anemia is a substantial public health problem in many developing countries and has been associated with a range of adverse consequences including poor mental development, reduced productivity, maternal mortality, and low birth weight (Lozoff et al., 2001) (Ramakrishnan, 2001).

Iron deficiency is considered the main cause of anemia, especially among young children and pregnant women, who are at increased risk due to their increased requirements (Allen, 2000). Anemia during pregnancy, however, remains a problem in many settings despite the fact that routine provision of iron supplements has been recommended for pregnant women. The failure of iron supplementation programs to reduce anemia in pregnant women has been attributed to various factors that influence program delivery. These include lack of availability of supplements, poor coverage, inadequate provider
knowledge, and poor compliance due to lack of motivation and/or side effects. However, more recently the efficacy of iron supplements has been questioned given the complex etiology of anemia (Mason et al., 2001) (Ekstrom, 2001).

The early stages of anaemia in pregnancy are often without symptoms. However, as the haemoglobin concentration falls, oxygen supply to vital organs declines and the expectant mother begins to complain of general weakness, tiredness, dizziness, and headaches. Pallor of the skin and of the mucous membranes, as well as the nail beds and tongue, becomes noticeable when the haemoglobin drops to 70 g/l. With a further fall in haemoglobin concentration to 40 g/l, most tissues of the body become starved of oxygen, and the effect is most marked on the heart muscles, which may fail altogether if there is severe anaemia. Death from anaemia is the result of heart failure, shock, or infection that has taken advantage of the patient’s impaired resistance to disease (Allen, 2000).

Some group of people are more likely to be iron or folate deficient than other. They are “at risk” of anaemia. High-risk group are Women especially during pregnancy or soon after delivery, Babies who were low birth weight or not breastfed, Young children especially if they are malnourished, Adolescent who are growing fast, especially girls, Older men and women especially if they are poor (Sachdev, 1997).

Women are at risk of nutritional anaemia because they lose blood with menstruation. Anaemia is especially likely if menstruation is heavy. During pregnancy, they must provide the growing foetus with a store of iron. Iron is transferred to the baby even if the mother’s stores are low. The baby gets a good store of iron, even if the mother becomes anaemic (Christian et al., 2003).
International anaemia prevalence

Anaemia associated with pregnancy is a public health problem all over the world. It is significantly higher in the third trimester than in the first and the second trimester of pregnancy. Anaemia in pregnancy continues to be a common clinical problem in many developing countries, and prevalence rates of 35–75% are reported. In cases in which the anaemia is severe and not corrected, blood transfusion may become necessary. Anaemia has been reported to contribute significantly to maternal mortality and to both maternal and foetal morbidity (Nynke et al., 2000).

Nutritional anaemia is another serious public health problem affecting women in reproductive age group and young children. Anaemia impairs physical capacity hence productivity. Prevention and control strategies thus assume great importance in the content of national economy and development. Nutritional anaemia due to iron and folic acid deficiency is either responsible for about 20% of maternal deaths (WHO, 2005).

The worldwide prevalence of anaemia in pregnant women is estimated at 51% (Roodenburg, 1995). In industrialised countries the most common cause of anaemia in pregnancy is iron deficiency (Dallman, 1989). The prevalence of iron deficiency in women has decreased over past several decades and this has been variously attributed to iron fortification, prophylactic iron supplements, better health care and public health programs aimed at women and children (Ramakrishnan, 2004).

There is little data on risk factors for iron deficiency in pregnancy. Iron deficiency is more common among certain high risk groups, such as multiparous women and those with multiple foetuses, blood donors, persons with diets low in meat/vegetarians, women with diets high in calcium and, presumably, dairy foods, adolescents (because of their lower body iron stores). Aboriginal/African-
American/Hispanic women and immigrants from countries in South-East Asia. More information is required to determine accurate prevalence and risk factors for iron deficiency in pregnancy (Scholl et al., 1994).

Iron deficiency is the most common nutritional disorder in the world. The numbers are staggering: as many as 4-5 billion people, 66-80% of the world's population, may be iron deficient; 2 billion people – over 30% of the world’s population – are anaemic, mainly due to iron deficiency, and in developing countries, frequently exacerbated by malaria and worm infections. Iron deficiency and anaemia reduce the work capacity of individuals and entire populations, bringing serious economic consequences and obstacles to national development. Conversely, treatment can raise national productivity levels by 20%. Overall, it is the most vulnerable, the poorest and the least educated that are disproportionately affected by iron deficiency, and it is they who stand to gain the most by its reduction. (WHO, 2005).
Table 8. Estimated anemia deaths (in thousands) in women of reproductive age

<table>
<thead>
<tr>
<th>Region</th>
<th>15–29 y</th>
<th>30–44 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Developed (all)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Developing (all)</td>
<td>9.0</td>
<td>7.1</td>
</tr>
<tr>
<td>EME</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FSE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>India</td>
<td>3.5</td>
<td>1.0</td>
</tr>
<tr>
<td>China</td>
<td>1.5</td>
<td>3.0</td>
</tr>
<tr>
<td>OAI</td>
<td>1.6</td>
<td>0.0</td>
</tr>
<tr>
<td>SSA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MEC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>World</td>
<td>9.3</td>
<td>7.5</td>
</tr>
</tbody>
</table>

2 A dash (—) indicates <1000 deaths.
3 Abbreviations: EME, established market economies; FSE, formerly socialist economies; OAI, other Asia and islands; SSA, sub-Saharan Africa; LAC, Latin America and Caribbean; MEC, Middle Eastern crescent.

In developing countries, more IUGR is due to low maternal weight and height (under nutrition during the mother’s development), low pregnancy weight gain (which is influenced by energy intake during pregnancy) and maternal infection. Low maternal weight at conception and low weight gain during pregnancy are independent predictors of poor fetal growth and IUGR. Low maternal height also plays a role independently of low body mass index (Allen, 2001).

The prevalence of iron deficiency is far greater than the prevalence of anaemia and iron deficiency (low serum ferritin and sparse or absent stainable iron in bone marrow) often develops during the later stages of pregnancy even in
women who enter pregnancy with relatively adequate iron stores (Meier et al., 2003).

**National anaemia prevalence.**

India has made a slow and steady progress in human development ever since independence. Severe and florid forms of malnutrition have declined substantially, infant mortality has declined from 146 per 1000 live births (1951) to 69 per 1000 live births (2000), life expectancy has risen from 37 years to 63 years and we have achieved self sufficiency in food production1-3. In spite of all these impressive developments on records, one third of newborns start their life with low birth weight, more than half of young children below five years of age continue to suffer from moderate and severe malnutrition, over 60% of women are anaemic and this figure rises to 85% during pregnancy state. 40-60% of adolescent girls tend to be anaemic. Malnutrition is thus wide spread in rural, tribal and urban slum areas and it is a significant public health problem described as silent killer, silent emergency, invisible enemy affecting those who cannot express, their voice and have to depend upon others for their advocacy (GOI, 2004).

Iron deficiency anaemia (IDA) is a significant public health problem in India. National and regional surveys indicate that the prevalence of anaemia could be as high as 74 percent in children below three years of age, 85 percent in expectant mothers and 90 percent among adolescent girls in some population groups (MOHFW, 1998-1999; ICMR, 2001).

In the slums of Bombay anaemia was found to be present in 70 percent of women over the age of 70, 52 percent of women over the age of 60 and 38 percent of men. The prevalence of anaemia was highest among those with
severe malnutrition (ACC/SCN, 2000). IDA in infants and children is associated with impaired physical and cognitive development, and in adults with reduced work capacity and hence productivity, overall lowered resistance to disease and increased morbidity and mortality. In women, IDA is also associated with adverse pregnancy outcome. It has been estimated that iron deficiency costs India about 5 percent of its gross national product annually from loss of lives, resources and productivity (Sanghvi, 1996).

Though anaemia is more prevalent among women belonging to lower socio-economic strata of society, it is not uncommon among the well-to-do sections of society (Mahajan and Gupta, 1995). Surveys in different parts of India have revealed that about 50-60% women belonging to lower socio-economic groups are anaemic in the last trimester of pregnancy (Park, 2003).

In India, the incidence of anaemia among expectant mothers is alarmingly high. Nutritional anaemia is a serious problem in pregnancy, which affects 60 to 70 percent of pregnant women with haemoglobin levels less than 10gms. 15 to 30 percent of all maternal deaths are due to anaemia. Anaemia may develop if the diet does not provide enough iron, protein, vitamin B_{12} and other vitamins and minerals needed in the production of haemoglobin and the formation of erythrocytes. The combination of poor diet and chronic loss of blood makes for particular susceptibility to severe anaemia. In pregnancy, anaemia has a significant impact on the health of the foetus as well as that of the mother. Anaemia, especially if severe, may impair the oxygen delivery to placenta and foetus and interfere in normal intrauterine growth (Thangaleela and Vijayalakshmi, 1994) (Burrows, 2003).
Table 9. Comparison among selected Indian states – percentage prevalence of malnutrition and female literacy (NFHS-2, 1999) (Bamji, 2003)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Maharashtra</th>
<th>Andhra Pradesh</th>
<th>Kerala</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malnutrition in &lt;3 years children</td>
<td>49.6</td>
<td>37.7</td>
<td>26.9</td>
</tr>
<tr>
<td>Anaemia in 6–35 months children</td>
<td>76</td>
<td>72.3</td>
<td>43.9</td>
</tr>
<tr>
<td>Women with BMI &lt; 18.5</td>
<td>39.7</td>
<td>37.4</td>
<td>18.7</td>
</tr>
<tr>
<td>Women with anaemia</td>
<td>48.5</td>
<td>49.6</td>
<td>22.7</td>
</tr>
<tr>
<td>Female literacy</td>
<td>55.4</td>
<td>36.2</td>
<td>88.4</td>
</tr>
</tbody>
</table>


In India >90% of anaemia cases are estimated to be due to iron deficiency, because high iron requirements during pregnancy are not easily fulfilled by dietary intake, especially when iron bioavailability is poor. Because of religious reasons, poverty, or both, the Indian population observes dietary patterns that are largely vegetarian. Diet alone cannot supply the 30–40 mg Fe that is required for absorption of the 4–6 mg Fe/d needed during the latter stages of pregnancy. Iron supplementation is strongly recommended for all pregnant women in developing countries. Oral iron intake is the treatment of choice, and almost all women can be treated effectively with oral preparations (Letsky, 1991) (Galan, 1991) (Sharma, 1998) (Sharma, 2003).
Table 10. ANAEMIA AMONG PREGNANT WOMEN, MARRIED (15 - 44 YEARS), (PERCENTAGE), 2002

<table>
<thead>
<tr>
<th>S.No.</th>
<th>State/UTs</th>
<th>Severe</th>
<th>Moderate</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>India</td>
<td>3</td>
<td>33</td>
<td>36</td>
</tr>
<tr>
<td>2.</td>
<td>Andhra Pradesh</td>
<td>3</td>
<td>31</td>
<td>34</td>
</tr>
<tr>
<td>3.</td>
<td>Bihar</td>
<td>1</td>
<td>35</td>
<td>36</td>
</tr>
<tr>
<td>4.</td>
<td>Chhattisgarh</td>
<td>5</td>
<td>41</td>
<td>46</td>
</tr>
<tr>
<td>5.</td>
<td>Gujarat</td>
<td>1</td>
<td>39</td>
<td>40</td>
</tr>
<tr>
<td>6.</td>
<td>Haryana</td>
<td>3</td>
<td>52</td>
<td>55</td>
</tr>
<tr>
<td>7.</td>
<td>Himachal Pradesh</td>
<td>2</td>
<td>32</td>
<td>34</td>
</tr>
<tr>
<td>8.</td>
<td>Jharkhand</td>
<td>0</td>
<td>31</td>
<td>31</td>
</tr>
<tr>
<td>9.</td>
<td>Karnataka</td>
<td>2</td>
<td>24</td>
<td>26</td>
</tr>
<tr>
<td>10.</td>
<td>Kerala</td>
<td>1</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>11.</td>
<td>Madhya Pradesh</td>
<td>2</td>
<td>38</td>
<td>40</td>
</tr>
<tr>
<td>12.</td>
<td>Maharashtra</td>
<td>2</td>
<td>56</td>
<td>58</td>
</tr>
<tr>
<td>13.</td>
<td>Orissa</td>
<td>4</td>
<td>30</td>
<td>34</td>
</tr>
<tr>
<td>14.</td>
<td>Punjab</td>
<td>4</td>
<td>50</td>
<td>54</td>
</tr>
<tr>
<td>15.</td>
<td>Rajasthan</td>
<td>3</td>
<td>36</td>
<td>39</td>
</tr>
<tr>
<td>16.</td>
<td>Tamil Nadu</td>
<td>1</td>
<td>24</td>
<td>25</td>
</tr>
<tr>
<td>17.</td>
<td>Uttar Pradesh</td>
<td>3</td>
<td>37</td>
<td>40</td>
</tr>
<tr>
<td>18.</td>
<td>Uttaranchal</td>
<td>1</td>
<td>26</td>
<td>27</td>
</tr>
<tr>
<td>19.</td>
<td>West Bengal</td>
<td>8</td>
<td>16</td>
<td>24</td>
</tr>
</tbody>
</table>


The FOGSI study found the common causes to be anaemia, PET/eclampsia, sepsis, haemorrhage and abortion related in that order. These together contributed to over 80% of the deaths. The SRS has estimated the causes of death (estimated through verbal autopsy conducted by lay enumerators specially trained for the purpose) as being haemorrhage (29.6%), severe
anaemia (19.0%), sepsis (16.1%), obstructed labour and ruptured uterus (9.5%), abortions (8.9%) and pre-eclampsia (8.3%). The recent National Family Health Survey has estimated that nearly 49.7% of pregnant women surveyed were having some form of anaemia or the other. There were 21.8% who had mild anaemia (Hb of 10 to 11 g %), 25.4% with moderate anaemia (7 to 10 g %) and 2.5% with severe anaemia. (Rawal, 2003).

Anaemia among pregnant women continues to be unabated, as 84.9% of pregnant women were found to be anaemic according to ICMR study undertaken in 16 districts of 13 states. Anaemia amongst adolescents was a universal phenomenon as over 90% of adolescents were reported to be anaemic (ICMR, 2001).

Nutritional anemia is one of the major public health problems in India affecting almost 90% poor children, adolescent girls and women with serious implications. As women of all ages are more susceptible to anemia than men, it is now viewed as “female disease" which is causing Red Alert for Indian women.

In India incidence of anemia in pregnancy ranges from 40% to 90% in various states. In WHO study 88% of pregnant Indian women were found to be anaemic which is the highest among the neighbouring countries (Philippines 48%, Pakistan 52%, Bangladesh 63% and Indonesia 74%). According to the National Family Health Survey II, carried our during 1998-99, more than three quarters of Indian children under the age of three are anaemic. There is no significant difference between urban and rural children. Various estimates from all states of the country indicate that 70-85% infants and young children are anaemic. Lowest estimates were found in the state of Kerala.(44%). In adolescent girls, anaemia ranged from 65% to 90%. The Departement of Family Welfare has completed and published the data on prevalence of
anaemia in preschool children, adolescent girls and pregnant women. The survey showed that prevalence of anemia is very high i.e. is over 90% in all these groups (IMA, 2005).

**Prevalence of anaemia in Kerala**

The annual sentinel surveillance study done by Kerala State AIDS Control Society (KSACS in September 2004) in four centres in the State showed that there has been a gradual increase in the prevalence of HIV infection among pregnant women in the State. Anaemia in pregnancy continues to be a common cause for maternal mortality and morbidity in the country. It has been noted that despite the distribution of free iron and folic acid supplements to pregnant women in the Government sector, anaemia among pregnant women in Kerala is on the high side, at 22 per cent (NFHS II), though this is the lowest in the country.

In Kerala the growing levels of educational and social awareness have implication on nuptiality rates, particularly the age of marriage. Age of marriage in Kerala has always been higher. It would appear that the demographic characteristic of female population in Kerala has been quite high. Unlike the typical situation expected in a developing country is definitely different from that found in India. In certain respects, it is even comparable to the quality of the population found in several developed countries (Tilak, 1992).
Data from the National Family Health Surveys, conducted in 1992-3 and 1997-98, show that child malnutrition and maternal anaemia are also on the decline at the state level. Shows the prevalence of anaemia among women in different states. Kerala has the lowest prevalence of anaemia (22.7). Andhra Pradesh is one of the states showing high prevalence of anaemia among women of reproductive age group.

Chronic moderate maternal under nutrition and anaemia have been shown to be associated with adverse outcomes of pregnancy. Food supplementation coupled with effective treatment of anaemia and adequate antenatal care to detect and promptly treat obstetric problems in the high risk groups would ward off these adverse effects.

The HemoCue system method used by the NFHS-2 might have slightly lower estimated prevalence of anaemia. The HemoCue has been found to give accurate results on venous blood samples, comparable to estimates from more
sophisticated laboratory instruments (Von Schenk, 1986). A recent small-scale study in India (Prakash et al., 1999) however found that the HemoCue provided slightly higher estimates of haemoglobin than the standard blood cell counter (BCC) method. Because the first 2-3 drops of blood are wiped away to be sure that the sample used for analysis consists of fresh capillary blood, it is actually the third or fourth drop of blood that is drawn into the cuvette (NFHS-2, 2000). Hemocue method tends to overestimate the levels of Hb and as a result the prevalence rates of anaemia would be lower (Mohan ram et al., 2002).

IV. Requirement of iron for pregnant women to overcome anaemia.

The normal infant has 250-300mg (65 to 95 mg/kg) of iron at birth 60% is present in the form of haemoglobin and the rest is present in the tissues. Iron deficiencies in the mother have little effect on the iron stores of the newborn infant unless it is very severe. The child should add about 0.5 mg of iron to its body stores every day throughout childhood to reach the normal adult level of about 4 g of total iron mass (Zhou et al., 2005).

This iron requirement is distributed unequally over the 40 weeks of a normal pregnancy. The daily iron requirements during the first 20 weeks of pregnancy are about the same as for a non-pregnant woman, if not lower because of the temporary suspension of menstrual iron losses. At about 20 weeks iron requirements increase markedly. The expansion in maternal red cell mass occurs maximally between weeks 20 and 25 of gestation, after which the daily iron requirements to maintain this mass remain constant at about 3-4 mg. However, the total iron requirements continue to increase after week 25 up to week 36 due to the needs of the placenta and the foetus. The total iron needs
near the end of the second and third trimesters are about 3.5 mg/day and 7 mg/day, respectively (Bothwell, 1995).

The high risk of women of fertile age and pregnant women for incurring negative balance and iron deficiency is due to their increased iron needs because of menstruation and the substantial iron demands of pregnancy. Median requirements of absorbed iron are estimated to be 1.36 and 1.73 mg per day among adult and teen-age menstruating females. However, 15% of adult menstruating women require more than 2.0 mg per day, and 5% require as much as 2.84 mg per day. The superimposition of menstrual losses and growth in menstruating teenage girls increases the demands for absorbed iron; 30% need to absorb more than 2.0 mg of iron per day; 10% as much as 2.65 mg, and 5% 3.21 mg. These requirements are very difficult, if not impossible to satisfy even with good quality, iron-fortified diets (Ekstrom, 1994).

Birth spacing favors iron nutrition among fertile-age women because each pregnancy has a high cost in terms of iron (see below). However, the use of intrauterine devices almost doubles the iron menstrual loss while women using anovulatory contraceptive methods reduce it by almost half. Importantly, multiparous women tend to have greater menstrual losses that increase with parity (Fleming, 1991).

The following table shows the total iron requirements during pregnancy (Hallberg, 1988).
Table 11. Iron Costs of Pregnancy

<table>
<thead>
<tr>
<th>Factor</th>
<th>Milligrams of iron</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal iron</td>
<td>Range 200-450</td>
<td>Median 270</td>
</tr>
<tr>
<td>Placental iron</td>
<td>Range 30-170</td>
<td>Median 80</td>
</tr>
<tr>
<td>Partum and puerperium losses</td>
<td>Range 90-310</td>
<td>Median 250</td>
</tr>
<tr>
<td>Hemoglobin and tissue expansion</td>
<td>Range 130-430</td>
<td>Median 200*</td>
</tr>
<tr>
<td>Maintenance during amenorrhea</td>
<td>Range 160-220</td>
<td>Median 190</td>
</tr>
<tr>
<td>Subtotal 1 (total iron costs)</td>
<td>Range 610-1580</td>
<td>Median 990</td>
</tr>
<tr>
<td>Postpartum involution iron</td>
<td>Range 130-430</td>
<td>Median 200</td>
</tr>
<tr>
<td>Total</td>
<td>Range 480-1150</td>
<td>Median 790</td>
</tr>
</tbody>
</table>

*Iron un-supplemented women. For iron-supplemented women this value is 450mg.

Changes in Iron Absorption during pregnancy

The principal changes in iron absorption during pregnancy relate to increases in the efficiency of iron absorption. Studies using small doses of iron, either as isolated iron salts or non-haem iron in a mixed meal, have demonstrated that iron absorption decreases in early pregnancy, starts to increase from about mid-pregnancy and at term is 3-4 times higher than at the beginning of pregnancy. The mechanisms of both the early decrease and the later increase in iron absorption are not known (Baron et al., 2005).

The iron intake in early humans was probably adequate to supply iron to both the mother and the foetus and, that changes in lifestyle in the past few generations have reduced energy expenditure leading to a lower intake of energy and nutrients that are often below the physiological needs of the human body. The inability to cope with iron needs in pregnancy that we see today is not nature’s poor design but simply that nature has not had the time or the chance to adjust to our present way of living (Hallberg et al., 1993).

Transfer of iron from the mother to the fetus is supported by a substantial increase in maternal iron absorption during pregnancy and is regulated by the
placenta. Serum ferritin usually falls markedly between 12 and 25 wk of gestation, probably as a result of iron utilization for expansion of the maternal red blood cell mass. Most iron transfer to the fetus occurs after week 30 of gestation, which corresponds to the time of peak efficiency of maternal iron absorption (Harrington et al., 2002).

Serum transferrin carries iron from the maternal circulation to transferrin receptors located on the apical surface of the placental syncytiotrophoblast, holotransferrin is endocytosed, iron is released, and apotransferrin is returned to the maternal circulation. The free iron then binds to ferritin in placental cells where it is transferred to apotransferrin, which enters from the fetal side of the placenta and exits as holotransferrin into the fetal circulation. This placental iron transfer system regulates iron transport to the foetus. When maternal iron status is poor, the number of placental transferrin receptors increases so that more iron is taken up by the placenta. Excessive iron transport to the foetus may be prevented by the placental synthesis of ferritin. As discussed later in this review, evidence is accumulating that the capacity of this system may be inadequate to maintain iron transfer to the foetus when the mother is iron deficient (Starreveld et al., 1995) (Allen, 2000).

**Bioavailability and Factors Affecting Bioavailability**

Dietary factors that influence iron bioavailability include the biochemical form (heme or nonheme) and concurrently consumed enhancers (eg, ascorbic acid and an unidentified "meat" factor) or inhibitors (eg, phytic acid, polyphenols, phosphates, calcium, and egg). Although dietary iron bioavailability influences iron absorption from single meals by as much as 10-fold, longitudinal studies lasting weeks or months indicate little or no responsiveness of body iron stores (estimated from serum ferritin) to changes
in dietary iron bioavailability, including changes in intakes of ascorbic acid, calcium, and meat. Despite documented 6- to 8-fold differences in the amount of iron initially absorbed from whole, controlled diets, consumption of such diets for 7–12 wk did not affect the serum ferritin concentrations of premenopausal women or of men (Sokoll et al., 1992)(Minihane et al., 1998)(Hunt et al., 2000).

Only a small and variable proportion (5-20%) of iron in the diet is absorbed (Ross, 1980). Many factors determine the proportion of iron absorbed from the diet (Bothwell et al., 1979). The iron content and composition of a meal and the iron status of the individual person (Beutler, 1980; Cook et al., 1991) are important factors that influence the amount of iron absorbed (Meier et al., 2003).

Iron is present in the diet in two forms, haem iron and non-haem iron. Haem iron is found in muscle and organ meats such as red meat, fish and poultry. The amount of haem iron in the normal Western-style diet is 1-2 g per day. It has a relatively high absorption rate (20-25%) which is mostly unaffected by iron status and the co-presence of enhancing or inhibiting factors. Most dietary iron is non-haem iron. Non-haem iron is found in foods such as rice, corn, wheat, vegetables, fruit, eggs and dairy products. It is less well absorbed than haem iron. Its absorption may vary from 2-20% depending on the iron status of the individual, the total amount of iron in the diet and the co-presence of enhancing and inhibiting factors. Dietary factors that enhance iron absorption include ascorbic acid and muscle protein including fish and poultry. Ascorbic acid is the main factor enhancing iron absorption and its effect is dose related (Hallberg et al., 1992).
The intake of even small amounts of muscle protein together with non-haem foods greatly increases the iron absorption from these foods. Without these enhancing factors, the absorption of non-haem iron is very low. The main dietary factors inhibiting iron absorption are phytates (e.g. cereals, bran), polyphenols (such as tannins in spinach, tea and coffee), and calcium and soy protein. Vegetarian diets may contain large amounts of these inhibiting factors and this may contribute to the poor iron status observed in people who have non-meat diets (Cook et al., 1991).

As both total iron intake and the bioavailability of the iron in the diet remain concerns during pregnancy, women should be advised of the implications of concurrent taking of meals high in iron and calcium. There is a significant negative correlation between SF and dietary calcium intake. In practical terms it has been suggested to keep calcium intake low in meals which provide significant amounts of haem and non-haem iron, and to meet the calcium requirements at breakfast and during mid-meal snacks (Wessling, 2000).

Gleerup et al. (1995) found that over a 10-day period, 30-35% more iron was absorbed if calcium intake was kept low at the main iron-containing meals. They have also calculated that such a redistribution of calcium intake could result in a fall in the prevalence of iron deficiency in a Scandinavian population of premenopausal women from 30% to 14%.

In conclusion, an adaptation occurred to reduce the influence of dietary iron bioavailability in women by altering their general absorptive efficiency, but the magnitude of the adaptation within several weeks was quite low. This tendency for short-term adaptation occurred whether iron absorption was tested with low- or high- bioavailability labeled diets, which suggests altered absorptive efficiency rather than adjustment to specific inhibitors or enhancers.
of absorption. These results, when added to the limited published measurements of iron absorption from whole diets, show that nonanemic women with low iron stores can absorb up to 4.5 mg or 30–35% of the iron from a high-bioavailability diet and that such a diet is necessary for substantially increased iron absorption by women with low body iron stores (Hunt, 2003).

V. Effect of anaemia on the outcome of pregnancy.

In pregnancy, anaemia has a significant impact on health of foetus as well as that of the mother. Anaemia especially if severe may impair the oxygen delivery to placenta and foetus and interfere in normal intrauterine growth. In Maternal anaemia placental weight, volume and surface area were reduced. A striking difference is observed in the mean birth weight between anaemic and non-anaemic mothers. (Badole et al., 1992).

Agarwal (1991) reported that maternal anaemia resulted in 12 to 28% of foetal loss, 30% of prenatal deaths and 7 to 10% neonatal deaths. The remaining births have around fifty percentage chance of resulting in a low birth weight baby. Low birth weight is the most important factor in determining the chance of survival of the new born.

Klebanoff (1991) stated that anaemia during the second trimester was associated with preterm birth. Preterm delivery was increased five fold for iron deficiency anaemia and doubled for other anaemia. Anaemia in pregnancy is also associated with increased maternal morbidity. Maternal deaths to the extent of 15-20% are directly or indirectly due to anaemia (Vijayaraghavan et al., 1990).
Severe anaemia in pregnancy results in relatively poor maternal and foetal outcome. Apparently maternal risks increase prior to foetal risks. In order to improve maternal and foetal outcome, it is recommended that district hospitals in low-income countries make prevention, early diagnosis, and treatment of severe anaemia in pregnancy a priority (Geelhoed et al., 2006).

1. Health consequences in children

The clinical pattern of poor fetal growth depends on the cause of the poor growth, its timing and its duration. Earlier under nutrition tends to cause symmetric growth retardation, whereas later under nutrition causes the proportions of the fetus to be more asymmetric. Many factors have been associated with increased risk of fetal growth retardation, as reviewed elsewhere (Lin and Santolaya-Fargas 1998).

Non nutritional causes of foetal growth retardation include haemorrhage, multiple births, uterine and placental abnormalities, parental size and genetics, and major congenital malformations. These explain up to 50% of the variance in birth weight in both developed and developing countries. In developing countries, more IUGR is due to low maternal weight and height (under nutrition during the mother's development), low pregnancy weight gain (which is influenced by energy intake during pregnancy) and maternal infection. Low maternal weight at conception and low weight gain during pregnancy are independent predictors of poor foetal growth and IUGR. Low maternal height also plays a role independently of low body mass index (Allen, 2000)
a. Premature birth

When maternal anaemia is diagnosed before midpregnancy, it has been associated with an increased risk of preterm delivery. Maternal anaemia detected during the later stages of pregnancy, especially the third trimester, often reflects the expected (and necessary) expansion of maternal plasma volume. Third-trimester anaemia usually is not associated with increased risk of preterm delivery. High haemoglobin concentration, elevated hematocrit and increased levels of serum ferritin late in pregnancy, however, all have been associated with increased preterm delivery. This increased risk may reflect in part the failure to expand maternal plasma volume adequately, thus diminishing appropriate placental perfusion. Although controlled trials of iron supplementation during pregnancy have consistently demonstrated positive effects on maternal iron status at delivery, they have not demonstrated reductions in factors that are associated with maternal anaemia, which is increased risk of preterm delivery and infant low birth weight. One reason for discordant findings may be the exclusion of many gravidas with iron deficiency from these trials or the data concerning gravidas with pregnancy outcomes such as preterm delivery from the analysis (Theresa et al., 2000).

In a follow-up study of this population at 28 wk gestation, Scholl and Hediger (1994) demonstrated that the risk was no longer increased for women who had iron deficiency anaemia (15.6%) at this time or anaemia from other causes. Although risk for preterm delivery was increased when iron deficiency anaemia occurs early investation, iron deficiency later in pregnancy probably reflects mainly normal physiological expansion of maternal plasma volume.
b. Low birth weight,

Nearly a third of full-term babies born in India are reported to be of low birth-weight (less than 2.5 kg). This figure has remained more or less stationary for the last few decades in spite of striking declines in neonatal and infant mortality, giving the impression that India has not made much progress with respect to the improvement of nutritional status of its women (UNDP, 1999) (UNICEF, 1999).

Low birth weight (LBW) is one of the most widely prevalent adverse birth outcomes in India- with a prevalence rate of 33%, the second highest in the world after Bangladesh. LBW is significant, not only because it is an important cause of neonatal mortality and morbidity, but also because LBW attributable to Intra-Uterine Growth Retardation (IUGR) has been identified as a risk factor for cardiovascular disease and diabetes in later life. IUGR infants are also much more likely to exhibit sub-optimal growth, which cannot always be compensated for in later life. Moreover, IUGR babies tend to experience sub-normal neurocognitive development, which increases in severity with decreasing birth weight below 2500 gms (Mahajan et al., 2005).

Factors contributing to low birth weight (LBW) include poverty, ignorance, and inability to use health care services. Early marriage and low family income lead to poor maternal nutrition reserves, which lead to reduced foetal nutrition. Poor maternal nutrition is also the result of ignorance, short birth intervals, multi-parity, and lack of prenatal care. Both heavy manual labor and smoking contribute to placental ischemia, which, along with reduced foetal nutrition, leads to intrauterine growth retardation (IUGR). In developing countries, IUGR accounts for over 66% of all LBW neonates. About 7 million Indian babies annually are LBW (Dhar et al., 1991).
Birth weight is a single most important criteria for determining the neonatal and infant survival. WHO defines LBW as "Birth weight less than 2500 gm". Globally, it is estimated that 25 million LBW infants were born in 1990 constituting 18% of all the live births. Of these 90% belonged to the developing countries. In India, 30-35% babies are LBW and more than half of these LBW infants are full term babies. This study was, therefore, designed to study the effect of various socio-economic and maternal factors on the birth weight of a newborn (Park et al., 1991) (Belsey, 1993) (Anand, 2000).

Amongst the Indian population, a very high incidence of maternal anemia has been noticed and is a known cause of prematurity and growth retardation. Maternal anaemia and previous pre-term delivery were important maternal risk factors (Arvind et al., 2003).

The World Health Organization (WHO) weight defines low birth weight < two processes, however, determine 2500 g. Birth weight: duration of gestation and rate of fetal growth. Thus, infants can have a birth weight <2500 g either because they are born early (preterm birth) or are born small for gestational age (SGA), a proxy for IUGR. WHO defines preterm birth as delivery before 37 completed weeks of gestation and SGA as a birth weight below the 10th percentile for gestational age. Some SGA infants are merely constitutionally small rather than nutritionally growth restricted; conversely, some IUGR infants who would otherwise be constitutionally large do not meet the standard criteria for SGA. Moreover, newborn infants may be growth-restricted or preterm without having LBW. For example, the WHO cut-off for SGA for males at 40 wk is 2944 g whereas the median birth weight for males at 35 wk is 2562 g (Williams et al., 1999) (Kramer et al., 2001).
Strong evidence exists for an association between maternal haemoglobin concentration and birth weight as well as between maternal haemoglobin concentration and preterm birth. It was not possible to determine how much of this association is attributable to iron-deficiency anaemia in particular. Minimal values for both low birth weight and preterm birth occurred at maternal haemoglobin concentrations below the current cut-off value for anaemia during pregnancy (110 g/L) in a number of studies, particularly those in which maternal haemoglobin values were not controlled for the duration of gestation (Rasmussen, 2001).

Several studies have shown that a baby's birth weight correlates with the birth weight and adult size of both its parents, but more strongly with those of its mother, suggesting that both the 'maternal environment' and inherited genes influence size at birth. There are no previous such intergenerational data from India (Sachdev, 1999).

The simple relationship between maternal macro nutrient status and perinatal survival in Fig 12

Fig: 12 Relationships between maternal macro nutrient status and perinatal survival

<table>
<thead>
<tr>
<th>Increased macronutrient intake</th>
<th>→</th>
<th>increased maternal weight</th>
<th>→</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased fetal growth</td>
<td>→</td>
<td>Improved survival</td>
<td></td>
</tr>
</tbody>
</table>

That is usually positioned is no longer defensible. First maternal weight and weight gain are remarkably resistant to either dietary advice or
supplementation. A further increased birth weight attribute to maternal nutrition does not necessarily increase perinatal survival (because pre pregnant weight is positively associated with both birth weight and higher perinatal mortality). Finally, whereas dietary supplements during pregnancy may have a modest effect on birth weight in non-famine condition (by contrast with a large effect in famine or near famine condition) their impact is not mediated by maternal energy deposition. Rather the component of maternal weight associated with accelerated fetal growth is maternal water (presumably plasma) volume(David, 2001).

The baby of an anaemic mother is more likely to be low birth weight and to become sick or die during early childhood. Red blood cells last for only four months, so the body has to replace them continually .the nutrient needed to replace red blood cells include iron, to make haemoglobin, folate for the development of the red blood cells and protein to build the red cells and haemoglobin (WHO, 2000).

The association of low birth weight with malaria is well known the mean birth weight of neonates born to infected mothers in a study being 350 g less than that of their counterparts born to non-infected mothers. This finding must be interpreted with caution, however, because it is malaria infection of the placenta that is associated with low-birth-weight infants. Peripheral parasitaemia does not mean that there is a placental parasite infection similarly, we cannot be sure that clearance of parasites from peripheral blood indicates the elimination of placental infection (Dwigh, 2003).

c. Infections.

Several potential biological mechanisms were identified through which anaemia or iron deficiency could affect pregnancy outcome. Anaemia (by
causing hypoxia) and iron deficiency (by increasing neither serum nor epinephrine concentrations) can induce maternal and fetal stress, which stimulates the synthesis of corticotrophin-releasing hormone (CRH). Elevated CRH concentrations are a major risk factor for preterm labour, pregnancy-induced hypertension and eclampsia, and premature rupture of the membranes. CRH also increases fetal cortisol production, and cortisol may inhibit longitudinal growth of the fetus. An alternative mechanism could be that iron deficiency increases oxidative damage to erythrocytes and the fetoplacental unit. Iron deficiency may also increase the risk of maternal infections, which can stimulate the production of CRH and are a major risk factor for preterm delivery (Allen, 2000).

Sub clinical ascending infections through the lower female genital tract are predominant worldwide. Important micronutrient deficiencies may prevail in low-income countries where these infections are much more common than in high-income countries. Important morbidities related to poor perinatal outcome both for the mother and for the fetus and newborn comprise preterm birth, prelabor rupture of membranes, placental abruption (predelivery detachment of the placenta), postpartum sepsis and maternal anaemia (Stephen, 2004).

There is some evidence that iron deficiency adversely affects immune function. For example, it can alter the proliferation of T and B cells, reduce the killing activity of phagocytes and neutrophils, and lower bactericidal and natural killer cell activity. Infection is one of the main pathological risk factors for preterm labor. The presence of bacteria or inflammatory cytokines in amniotic fluid or chorioamnionitic membranes is strongly associated with preterm labor and premature rupture of the membranes. The bacteria are believed to come from the vagina. Early bacterial vaginosis (before 16 wk) is
associated with a relative risk of preterm delivery of 5–7.5. If this condition occurs after 26 wk, the risk is 1.4–1.9 (Kurki et al., 199†).

There is potential for CRH to regulate inflammatory responses and vice versa. The cytokine interleukin-1 stimulates production of CRH, and CRH in turn regulates cytokine production by immune effector cells. Because maternal stress is associated with preterm birth, abnormalities in the regulation of CRH and the production of inflammatory cytokines may be a mechanism that could form the pathophysiological basis for this association.

Falkenberg et al., (1999) examined the effect of maternal infections on the fetal hypothalamic-pituitary-adrenal axis. Subjects were 361 women with normal pregnancy (including some with preterm delivery) and 110 with infections. Cord blood was analyzed at delivery, which occurred between 24 and 44 wk of gestation. The infants born to women with infections were born 1.5 wk earlier, and cord blood concentrations of cortisol and dehydroepiandrosterone sulfate were significantly higher. The authors suggested that products of the activated immune system of mothers with infections may have crossed the placenta and activated the fetal hypothalamic-pituitary-adrenal axis.

Cortisol has been reported to inhibit the activity of natural killer cells both in vitro and in vivo. In a study of the effect of delivery method on cortisol in cord blood, natural killer cell activity in the cord blood of the group with the low cortisol concentrations (because of caesarean delivery and general anaesthesia) was twice that of the two groups with higher cortisol concentrations (De Amici et al., 1999).
d. Elevated risk of death.

In pregnancy, anaemia has a significant impact on the health of the foetus as well as that of the mother. Anaemia especially if severe may impair the oxygen delivery to placenta and foetus and interfere the normal intra-uterine growth. Agarwal et al., (1991) reported that maternal anaemia resulted in 12 to 28 percent of foetal loss, 30 percent of prenatal death and 7 to 10 percent of neonatal deaths. The remaining births have around 50 percent chances of resulting in a low birth weight baby. So it is important to diagnose and treat anaemia to ensure optimal health of the mother and newborn (WHO, 1994).

Foetal under nutrition affects large numbers of infants in developing countries, with adverse consequences for their immediate survival and lifelong health. It manifests as intrauterine growth retardation (IUGR), defined as birth weight <10th percentile, which probably underestimates the number failing to achieve full growth potential. Birth weight is a crude measure of the dynamic process of foetal growth and does not capture effects of fetal under nutrition on body composition and the development of specific tissues. The link between maternal nutrition and foetal nutrition is indirect. A complex supply line that includes the mother’s diet and absorption, endocrine status and metabolism, cardiovascular adaptations to pregnancy and placental function nourishes the foetus. Micronutrients are essential for growth, and maternal micronutrient deficiency, frequently multiple in developing countries, may be an important cause of IUGR (Kramer, 2003).

Supplementation of undernourished mothers with micronutrients has several benefits but there is little hard evidence of improved fetal growth. However, this has been inadequately tested. Most trials have only used single micronutrients and many were inconclusive because of methodological problems. Several food-based studies (some uncontrolled) suggest benefits
from improving maternal dietary quality with micronutrient-dense foods. One trial of a multivitamin supplement (HIV-positive mothers, Tanzania) showed increased birth weight and fewer fetal deaths. Well-conducted randomized controlled trials of adequate sample size and including measures of effectiveness are needed in populations at high risk of micronutrient deficiency and IUGR and should include food-based interventions and better measurements of fetal growth, maternal metabolism, and long-term outcomes in the offspring (Fall et al., 2003).

In developing countries, more IUGR is due to low maternal weight and height (under nutrition during the mother's development), low pregnancy weight gain (which is influenced by energy intake during pregnancy) and maternal infection. Low maternal weight at conception and low weight gain during pregnancy are independent predictors of poor fetal growth and IUGR. Low maternal height also plays a role independently of low body mass index (Fowles, 2004).

e. Later physical and cognitive developments are impaired, resulting in lowered school performance.

The evidence associating iron deficiency anaemia with poor developmental outcome in children is mounting. A number of studies carried out both in developing countries, and in Britain have shown that varying degrees of anaemia in young children are associated with poor cognitive and non-cognitive outcomes. Although under some circumstances iron supplementation has been shown to partially reverse the damage, a general consensus has yet to be reached on causation, as the relation between anaemia and development is complicated by multiple confounding variables. A number of animal studies have shown physical and functional effects of poor nutrition on the developing brain, particularly affecting arousal and reactivity (Kramer et al., 2001).
Recent studies have indicated that anaemia affects both mental and physical development of children. Severe iron deficiency anaemia (widely prevalent during the first two years of life when the infant’s brain development is maximal) may cause permanent neurological damage. Iron deficiency anaemia (IDA) during the first two years of life has been found to be associated with poor performance in intelligence tests related to specific cognitive processes at or near school age in studies conducted in Israel, Costa Rica and Chile. In one case, delay in mental development was observed in infants and toddlers with IDA that did not reverse even after being supplemented with iron. It is believed that intellectual deficits due to IDA are mediated by either anatomic or neuro-chemical changes in the brain. Intellectual functioning in terms of intelligence quotient (IQ) at school age was studied in boys who had been severely malnourished during their first two years of life. Full scale, verbal and performance IQ’s were found to be significantly low in these children. (Lansdow et al., 1995) (Andraca et al., 1997).

The brain of the iron deficient rat shows impaired myelination, and altered neurotransmitter function, particularly if the iron deficiency exists during the brain growth spurt between 10 and 28 days of life. Results from a recent study suggest that a chronic marginal iron deficiency during the pre- and postnatal development of mice can result in functional changes in motor development, even in the absence of iron deficiency anaemia (Kwik et al., 1999).

Although studies of early diet in humans have shown negative effects of poor nutrition on developmental outcome later in childhood, there is little evidence to implicate iron deficiency in the absence of anaemia with subsequent developmental impairments. Questions as to whether a critical period of vulnerability to iron deficiency exists during the human brain growth spurt,
and what degree of anaemia caused by iron deficiency is needed to impair development, have yet to be satisfactorily answered (Emond et al., 1996).

This study examines the relation between haemoglobin concentrations at 8, 12, and 18 months of age and subsequent developmental outcome at 18 months. Specifically, we explore whether a critical period of vulnerability to anaemia exists in the first 18 months and if so, what degree of anaemia is required to observe impaired development (Lao et al., 2000).

f. Cardiovascular diseases later in life.

Iron supplementation of initially nonanemic pregnant women without iron depletion from the first trimester to 28 wk of gestation may have important benefits by preventing small preterm births. Because small preterm births are a major determinant of perinatal morbidity and mortality (Wilcox, 2001), Iron supplementation could reduce health care costs. Furthermore, accumulating evidence suggests that in adult life, infants with low birth weight may be at greater risk of various chronic disorders, including type 2 diabetes, hypertension, and coronary artery disease (Barker, 1995), (Ravelli et al., 1998). Iron supplementation during pregnancy deserves further examination as a measure to improve birth outcomes and reduce health care costs.

Over the past 5 years, much evidence has accumulated linking sub-optimal fetal growth to increased death rates from coronary heart disease, stroke and higher levels of cardiovascular risk factors including blood pressure, plasma lipids and clotting factors. Specifically we have found that: stroke and atheroma of the carotid artery are associated with brain-sparing adaptations in utero. These adaptations may have persisting effects on arterial structure and liver metabolism that increase the risk of cardiovascular disease; the offspring of mothers who are overweight are at increased risk of coronary heart disease,
while those whose mothers are thin tend to be insulin resistant; and the high rates of coronary heart disease in people of Indian origin may be linked to their low rates of fetal growth (Fall et al., 1995) (Stein et al., 1996) (Barker et al., 1998).

g. Diabetes in later life.

In 1991 the MRC unit published the first evidence that low birth weight is associated with a high risk of developing type 2 diabetes or its precursor, glucose intolerance, in adult life. Over the past decade we have shown that low birth weight is associated with resistance to the metabolic actions of insulin, a fundamental metabolic abnormality that leads to type 2 diabetes. Low birth weight is also associated with a high prevalence of the insulin resistance syndrome (a common condition comprising glucose intolerance, elevated blood pressure and high blood lipid concentrations which is known to predispose to heart disease). Data from animals and recent human observations have suggested a mechanism in that adverse events in early life, which lower birth weight, appear to permanently alter or ‘programme’ the secretion of stress hormones including cortisol. Together with obesity this leads to a high risk of the metabolic syndrome and the predisposition to cardiovascular disease (Phillips 1998).

Adult insulin resistance is widespread in India, due to low birth weight. In women, if they become even mildly obese, this leads to hyperglycaemia in pregnancy. Maternal hyperglycaemia in turn leads to changes in the fetus, impaired fetal pancreatic development, and insulin deficiency and NIDDM in adult life (Fall et al., 1998) (Reynolds, 2001).
2. Health consequences in mother.

Anaemia reduces physical productivity and the capacity to work and learn. It also diminishes the tolerance for haemorrhage during childbirth and abortion and the chances of delivering healthy babies posing serious risks for the 35% of the world’s women who suffer from anaemia during their reproductive years and 50% during pregnancy. The highest rate of anaemia in the world are found among South Asian Women 58% overall and 75% during pregnancy (United Nations, 1994).

The experience of women in India where early pregnancies in adolescents and repeated pregnancies at short intervals play havoc with their lives with very high maternal and perinatal mortality and morbidity. Nutritional anaemia plays a significant role in poor pregnancy outcome in India where anaemia complicates 72-96 percent of all pregnancies. As the women enter their pregnancies with florid anaemia or with poor iron stores they have poor pregnancy outcome. After the childbirth they all breastfeed putting an extra load on their iron stores and then they enter their next pregnancy even before their iron stores are fulfilled putting them at greater risk in their subsequent deliveries. This cycle must be broken if we want their iron stores to get any better. They need to improve their nutritional status and need to practice contraception to increase interpregnancy interval to improve pregnancy outcome which will be of vital importance for countries like India. Most women in India are vegetarian or occasionally meat eaters precluding it to be a factor in their nutrition (Malhotra et al., 2002) (Smith, 2003) (Sharma, 2003) (Sharma et al., 2003).
a. Maternal haemorrhage

Blood loss in childbirth is very dangerous for anaemic women and is the main cause of about 20 percent of maternal deaths. Maternal anaemia also leads to foetal growth retardation, low infant birth weight and increased perinatal mortality (death in the first week of life). Foods such as dark green leafy vegetables, legumes and red meat are rich in iron, as are iron-fortified food products. However, because of the low bioavailability of iron in plant foods and the high cost of red meat, prevention and cure of iron deficiency anaemia is not an easy task, even in developed countries (FAO, 2002).

Maternal mortality in India is estimated to be 407 in 1998 (SRS-RGI). This is significantly higher compared to even the countries like Sri Lanka where it is about 60. The Tenth plan target is to bring it down to less than 200 by the year 2007.

Data on major causes of maternal mortality is available from the SRS of the Registrar General of India. The major causes of maternal mortality are ante and post partum haemorrhage, anaemia, obstructed labour, hypertensive disorders, post partum sepsis and unsafe abortions and quick repeated pregnancies. Deaths due to anaemia obstructed labour, hypertensive disorders and sepsis is preventable with provision of adequate antenatal care, referral and timely treatment of complications of pregnancy. District Household Survey (1998-99) shows that about 33% pregnant women do not avail of even a single ante natal check up (White Ribbon Alliance for safemotherhood, 2005).

The FOGSI (Federation of Obstetric and Gynaecology Societies of India, 1992-94.) study found the common causes to be anaemia, PET/eclampsia, sepsis, haemorrhage and abortion related in that order. These together
contributed to over 80% of the deaths. The SRS has estimated the causes of death (estimated through verbal autopsy conducted by lay enumerators specially trained for the purpose) as being haemorrhage (29.6%), severe anaemia (19.0%), sepsis (16.1%), obstructed labour and ruptured uterus (9.5%), abortions (8.9%) and pre-eclampsia (8.3%). The recent National Family Health Survey has estimated that nearly 49.7% of pregnant women surveyed were having some form of anaemia or the other. There were 21.8% who had mild anaemia (Hb of 10 to 11 g%), 25.4% with moderate anaemia (7 to 10 g%) and 2.5% with severe anaemia. With such high levels of anaemia in the country, it can be said that most of the interventions to prevent maternal deaths have to occur immediately after the onset of the early symptoms such as bleeding during pregnancy, non-progression of labour, fever etc (Rawal, 2003).

Table 12. Causes of maternal death (%)

<table>
<thead>
<tr>
<th>Cause</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemorrhage</td>
<td>30</td>
</tr>
<tr>
<td>Anaemia</td>
<td>19</td>
</tr>
<tr>
<td>Sepsis</td>
<td>16</td>
</tr>
<tr>
<td>Obstructed labor</td>
<td>10</td>
</tr>
<tr>
<td>Abortion</td>
<td>8</td>
</tr>
<tr>
<td>Toxemia</td>
<td>8</td>
</tr>
<tr>
<td>Others</td>
<td>8</td>
</tr>
</tbody>
</table>

Source: (GOI Survey of causes of Death 1998)

The fetoplacental unit is very susceptible to oxidative damage induced by reactive oxygen species. Oxidative stress is one mechanism thought to cause preeclampsia, pregnancy-induced hypertension and pregnancy-induced diabetes (Cester et al. 1994, Poranen et al. 1996). Interest is increasing in the possibility that antioxidant nutrients might improve pregnancy outcome by reducing oxidative stress (Scholl et al., 2000), (West et al., 2000).
b. Maternal Anaemia and Gestational Diabetes.

Measurement of Hb concentration has become a standard investigation in pregnancy. Maternal Hb concentration reflects not only maternal nutritional status but also the degree of hemodilution, both of which would impact pregnancy outcome as reflected by the relationship between high and low Hb concentration with adverse pregnancy outcome (Murphy et al., 1986) (Knottnerus et al., 1986) (Rasmussen et al., 1993) (Steer, 2000).

In our population, the incidence of Gestational Diabetes Mellitus (GDM) was 10.9% in women with a booking Hb of between 10 and 11.5 g/dl, which was similar to that in the overall population. On the other hand, the incidence of GDM in women with anaemia due to iron deficiency was 4.6%, compared with the 9.4% found in women with anaemia due to thalassemia trait (Lao et al., 2002).

Increased maternal ferritin concentration has been found at the time of diagnosis of GDM in the third trimester. It is therefore logical to hypothesize that women with iron deficiency anaemia would have a reduced likelihood of GDM.

In this study, we have focused on women with iron deficiency anaemia, and we demonstrated that iron deficiency anaemia is independently associated with a reduced prevalence of GDM. Furthermore, the prevalence of GDM was related to the duration and timing of anaemia. These women also had significantly decreased gestational increment in weight and BMI, which agreed with the finding that iron deficiency anaemia diagnosed in early pregnancy was associated with low dietary energy and iron and inadequate gestational weight gain. Because our obstetric population is of the same ethnic background and culture, different dietary habits were unlikely to have played
an important role in our findings, especially when vegetarians were excluded. In our anaemic group, the nutritional deficiency had probably antedated pregnancy because although these patients were younger, they were shorter, which suggested poorer nutrition during childhood and adolescence. However, anaemia in the third trimester is associated with less nutritional deficiency and lower impact on pregnancy outcome and this would help explain the increasing prevalence of GDM from group 1 to group 3 in this study (Scholl et al., 1994).

Findings indicate that the likelihood of GDM is significantly reduced with maternal iron deficiency anaemia, which probably acts also as a surrogate for general nutritional deficiency. In the developing world, overall nutritional improvement and correction of anaemia could be contributing factors to the increasing prevalence of diabetes and GDM (King, 1998) (Toure et al., 2004).

C. Maternal iron deficiency anaemia and postpartum emotions and cognition.

Maternal hematologic and iron status, socioeconomic, cognitive, and emotional status, mother-infant interaction, and the development of the infants were assessed at 10 wk and 9 mo postpartum. Behavioral and cognitive variables at baseline did not differ between iron-deficient anaemic mothers and non anaemic mothers. However, iron treatment resulted in a 25% improvement (P < 0.05) in previously iron-deficient mothers' depression and stress scales as well as in the Raven's Progressive Matrices test. Anaemic mothers administered placebo did not improve in behavioral measures. Multivariate analysis showed a strong association between iron status variables (haemoglobin, mean corpuscular volume, and transferrin saturation) and cognitive variables (Digit Symbol) as well as behavioral variables
This study demonstrates that there is a strong relation between iron status and depression, stress, and cognitive functioning in poor African mothers during the postpartum period. There are likely ramifications of this poorer "functioning" on mother-child interactions and infant development, but the constraints around this relation will have to be defined in larger studies (Godfrey et al., 1997) (Beard et al., 2005).

VI. National prophylaxis programme on anaemia.

In spite of all these impressive developments on records, one third of newborns start their life with low birth weight, more than half of young children below five years of age continue to suffer from moderate and severe malnutrition, over 60% of women are anaemic and this figure rises to 85% during pregnancy state, 40-60% of adolescent girls tend to be anaemic. Malnutrition is thus widespread in rural, tribal and urban slum areas and it is a significant public health problem described as silent killer, silent emergency, invisible enemy affecting those who cannot express, their voice and have to depend upon others for their advocacy. (Planning Commission, 2002)(NFI, 2003).

Nutrition Policy in 1993; which identified the National Nutritional Goals in line with the world summit on children in 1990. India has made commitment to achieve the following goals by 2000 AD13-17(National Population Policy, 2000) (National Health Policy, 2002).

- Reduction in moderate and severe malnutrition among preschool children by half.
- Reduction of low birth weight babies below 10%.
- Eliminate blindness due to vitamin A deficiency.
- Reduce anaemia in expectant women to 25%.
• Universal iodization of salt and virtual elimination of iodine deficiency disorders.
• Achieving production of 250 million tonnes of food grains per year.
• Improving household food security through poverty alleviation programme, in urban and rural areas.
• Promoting appropriate diets and healthy life styles.

Anaemia among pregnant women continues to be unabated, as 84.9% of pregnant women were found to be anaemic according to ICMR study undertaken in 16 districts of 13 states. Anaemia amongst adolescents was a universal phenomenon as over 90% of adolescents were reported to be anaemic. Prevalence of goitre among 6-12 years children was 4.78% and night blindness in children (24-71 months of age) was 1.03% and bitot spots and night blindness were reported to be of the level of 0.34% and 0.71% respectively (Indian Council of Medical Research, 2001).

The elimination of iron deficiency anaemia among pregnant women has long been recognised as a public health priority in India. The National Nutritional Anaemia Prophylaxis Programme has been in existence since 1970. The target groups for this programme include pregnant and lactating women, family planning acceptor women and children between 1 and 11 years. Women with a haemoglobin level of 10 gms per dl and above qualify for the prophylaxis programme (pre-school children: 8 gms per dl and above). Women with a haemoglobin level of less than 10 gms per dl are to be put on anti-anaemia treatment immediately (pre-school children: below 8 gms/ dl. (ICMR, 1990).

Many of the problems with the National Nutritional Anaemia Prophylaxis Programme can be traced to programmatic/managerial problems. However, research is increasingly suggesting the need for a qualitative change in the
public health response to iron deficiency anaemia. The suggested change is to build the iron stores of women before (the first and each subsequent) pregnancy in order to prevent anaemia. This suggests the need to include adolescent girls i.e. girls who are in the 10 to 19 years, in the target group. This should be viewed as part of a lifecycle approach, and does not imply that iron supplementation during pregnancy is unnecessary (Meashan et al., 1999).

However the coverage of children and women as beneficiaries under this programme has been identified as being quite poor. Therefore the search for an alternative approach to prevent anaemia lead to the idea of fortifying common salt with iron. Technology- is now available to fortify common salt successfully with iron, and community studies have clearly shown the beneficial effect in improving haemoglobin status on consumption of iron fortified salt (IFS) (ICMR, 1989).

Fortification of common salt with ferrous sulphate and sodium hexametaphosphate is considered to be a satisfactory method for the production of iron fortified salt. There is no discolouration of the fortified salt. Iron stability is satisfactory. Iron absorption from cereal-based meal is around 7% and from wheat-based meal about 4%. It is now felt that both available strategies could be effectively utilized to tackle the problem of widespread anaemia in population groups. While IFS distribution can serve as a preventive measure. folifer tablet distribution can profitably be used as a strategy to control anaemia in particularly vulnerable groups throughout the country(Datta et al., 1982) (Ranganathan, 1992).

The National Nutritional Anaemia Control Program in India, which is in existence since 1970, aims at significantly decreasing the prevalence and incidence of anaemia in women in the reproductive age group, especially pregnant women. Their policy emphasize the following strategies:
• Promotion of regular consumption of foods rich in iron.
• Provision of iron and folate supplements in the form of tablets to the high-risk groups.
• Identification and treatment of severely anaemic cases. (Kanani, 1998).

The national goal and approaches to controlling IDA
The National Tenth Plan has set the goal of reducing the prevalence of anaemia by 25 percent among children and pregnant and lactating women (Government of India, 2002). National programmes and institutional approaches are being undertaken to achieve this goal.

The major approaches to controlling IDA, which are not mutually exclusive, are medicinal supplementation with iron and folic acid and food-based approaches, i.e. dietary diversification and fortification of foods, both complemented by programmes to counter parasitic infestations. While supplementation with iron is considered necessary for groups at high risk as a short-term emergency measure, it fails to address the root causes and cannot provide the overall long-term benefits of economy and sustainability. Evaluation studies of India's nationwide and long-standing supplementation programme showed irregular supplies, non-compliance by the beneficiaries, poor counselling, etc. As such, the supplementation strategy has proved to be inadequate (Vijayaraghvan, 2002).

Comprehensive review of food-based approaches
Food-based approaches to addressing IDA in India are being promoted, but information on which and to what extent food combinations would improve the bioavailability of dietary iron is fragmentary. Long-term controlled consumption and feeding studies are lacking owing to the difficulty and costs of dealing with several variables in large populations. Several experimental
studies on the availability of food iron and related aspects have been reported, which showed the possibility of assessing how to improve the bioavailability of iron in plant foods (Allen and Ahluwalia, 1997), which should reduce the prevalence of IDA in the long run. With this objective, a comprehensive review was carried out that attempted to highlight how food-based approaches could improve the bioavailability of Indian diets. The review included food and nutrient intake (especially haematinic nutrients such as iron, folic acid, vitamin A and protein) by the Indian population, factors influencing the bioavailability of food iron, cooking and processing methods and other factors particularly relevant to the Indian context.

VIII. Nutritional Status.
India’s food and nutrition is still one of the crucial problems in the process of development. Nearly two-third of India’s population is on a nutritionally deficient diet. Nutritional surveys conducted and repeated over a number of years have indicated that a majority of population of every age group, including both the sexes, suffers from malnutrition on both calorie and protein starvation and complete lack of protective food, rich in mineral and vitamins (Mathews et al., 1999).

In developed countries, dietary macronutrient or micronutrient deficiency are rarely thought to be responsible for clinically significant impaired foetal growth. Lower birth weight is associated with lower social class, but although it is often assumed that this is nutritional, there are many confounders such as smoking and genetic factors.

Recent human pregnancy studies do not confirm the dietary hypothesis, but these studies have been criticised. Contemporary studies in Australia, however, indicate that nearly 30% of women who deliver babies with a low
birth weight (<2500 g) suffer from eating disorders. Experimentally increasing maternal nutrition in sheep enhances birth weight (Robinson et al., 2000).

Table 13 Nutrition Statistics of India (UNICEF 2006)

<table>
<thead>
<tr>
<th>% of infants with low birth weight (1998-2004*)</th>
<th>30</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of children (1996-2004*) who are:</td>
<td></td>
</tr>
<tr>
<td>Exclusively breastfed (&lt;6 months)</td>
<td>37</td>
</tr>
<tr>
<td>% of children (1996-2004*) who are:</td>
<td></td>
</tr>
<tr>
<td>breastfed with complementary food (6-9 months)</td>
<td>44</td>
</tr>
<tr>
<td>% of children (1996-2004*) who are:</td>
<td></td>
</tr>
<tr>
<td>Still breastfeeding (20-23 months)</td>
<td>66</td>
</tr>
<tr>
<td>% of under-fives (1996-2004*)</td>
<td></td>
</tr>
<tr>
<td>Suffering from: underweight (moderate)</td>
<td>47</td>
</tr>
<tr>
<td>% of under-fives (1996-2004*)</td>
<td></td>
</tr>
<tr>
<td>Suffering from: underweight (severe)</td>
<td>18</td>
</tr>
<tr>
<td>% of under-fives (1996-2004*)</td>
<td></td>
</tr>
<tr>
<td>Suffering from: wasting (moderate &amp; severe)</td>
<td>16</td>
</tr>
<tr>
<td>% of under-fives (1996-2004*)</td>
<td></td>
</tr>
<tr>
<td>Suffering from: stunting (moderate &amp; severe)</td>
<td>46</td>
</tr>
<tr>
<td>Vitamin A supplementation coverage rate</td>
<td></td>
</tr>
<tr>
<td>(6-59 months) (2003)</td>
<td>45</td>
</tr>
<tr>
<td>% of households consuming iodized salt (1998-2004*)</td>
<td>50</td>
</tr>
</tbody>
</table>

* Data refer to the most recent year available during the period specified in the column heading.
The main reasons for IDA have been determined to be inadequate intake of iron, low bioavailability (1-6 percent) of dietary iron from plant foods (Narasinga Rao et al., 1983) due to inhibitory factors, low levels of absorption enhancers in the diet, repeated pregnancies, increased needs during growth and development among children and adolescents, parasitic infestations and chronic blood loss. Poverty compounds these factors through inadequate access to dietary diversity, safe water, knowledge about safe food handling and proper feeding practices (FAO/ILSI, 1997) (Symonds et al., 2000).

The National Family Health Survey (MOHFW, 1998-1999) asked a sample of married women to specify the frequency (daily, weekly, occasionally or never) of the various types of foods that they consumed. Table 14 shows that there are substantial differentials in food consumption levels of different food groups. Age does not play an important role in women's consumption patterns. Women in urban areas are more likely than those in rural areas to include every type of food in their diet, particularly nutritious foods such as fruits and milk or curd. Illiterate women have poorer and less varied diets than literate women.

**Food and nutrient intake: patterns and levels**

Food consumption in India is varied and influenced by regional, ethnic, cultural, income and agricultural production differences. The amounts of animal foods (meat, fish, and eggs) varied from 0 g (Haryana and Tamil Nadu) to 193 g (Arunachal Pradesh), and show the wide discrepancy among populations with respect to dietary sources of bioavailable iron (FAO, 1998).

Among children, the median intake of all the nutrients was low compared to the recommended dietary allowances (RDAs). The intake of micronutrients such as iron, vitamin A, riboflavin and folic acid was 40-60 percent of RDA
among adolescent girls. However, the mean intake of ascorbic acid among adolescent girls and boys was 32-40 mg compared with the RDA of 40 mg. Among adults, nutrient intakes were close to the RDA levels except for iron, vitamin A and riboflavin (vitamin B2). Intake of energy and all the nutrients was less than the RDA among expectant and nursing mothers (NNMB, 2003).

Table 14: Women's food consumption: percent distribution of married women by frequency of consumption of specific foods, India, 1996-99

<table>
<thead>
<tr>
<th>Type of food</th>
<th>Frequency of distribution</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Daily</td>
<td>Weekly</td>
</tr>
<tr>
<td>Milk and curd</td>
<td>37.5</td>
<td>17.4</td>
</tr>
<tr>
<td>Pulses or beans</td>
<td>46.9</td>
<td>40.8</td>
</tr>
<tr>
<td>Green Leafy vegetables</td>
<td>41.8</td>
<td>43.4</td>
</tr>
<tr>
<td>Other vegetables</td>
<td>65.1</td>
<td>28.0</td>
</tr>
<tr>
<td>Fruits</td>
<td>8.1</td>
<td>24.9</td>
</tr>
<tr>
<td>Eggs</td>
<td>2.8</td>
<td>25.0</td>
</tr>
<tr>
<td>Chicken, meat or fish</td>
<td>5.8</td>
<td>26.1</td>
</tr>
</tbody>
</table>

Cereals form the major staple food and bulk of the diet of individuals in all the states studied. Millets are consumed in some states. Consumption of pulses, green leafy vegetables (GLV), milk, fruits and fats and oils was inadequate. The average consumption by adult females (sedentary) of cereals and millets (389 g) was about 95 percent of the recommended dietary intakes (RDI) of 410 g. Barring roots and tubers and other vegetables, the intake of all the other foods was lower than the suggested intakes. The deficit with respect to GLV was the highest of all the food groups. The intake of cereals and millets among expectant mothers was comparable to the RDI and that of nursing mothers was higher than the RDI. The intake of all other foods was much lower than the RDI. No additional amounts were consumed to meet the increased needs of pregnancy (NFI, 2003).

The low-income population consumes only two meals a day, comprised mainly of wheat or millet chapatti (an unleavened bread prepared on an iron plate) or rice, with tea, pickles, onion, salt and chillies, vegetables or pulses. The middle- and high-income populations generally eat three meals a day. As income rises, the intake of foods such as milk, fruits, vegetables and meat (if accepted culturally) increases. The intake of convenience foods also increases. The pattern is shown in Table 15.
Table 15: General food-consumption pattern of low-middle/high income populations (Gopalan, 2000)

<table>
<thead>
<tr>
<th>Meal</th>
<th>Low – income population</th>
<th>Middle / high income population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning</td>
<td>Tea</td>
<td>Tea or office</td>
</tr>
<tr>
<td>Breakfast/brunch</td>
<td>Wheat and millet chapatti or Rice+ tea; vegetable; pickle; Onion + salt + chilli; jaggery</td>
<td>Wheat parantha (sort of chapatti shallow fried in an iron pan) And/or millet milk or curd (a type of yoghurt) and/or tea; rice + vegetable and or pulse + banana or bread, butter, jam + fruit</td>
</tr>
<tr>
<td>Mid-morning</td>
<td>Tea (sometimes)</td>
<td>Tea or coffee+snack (biscuit, sandwhich, samosa or pakora, or burger)</td>
</tr>
<tr>
<td>Lunch</td>
<td>Wheat and/or millet chappati or rice + vegetable and/or pulse + salad and/or fruit</td>
<td></td>
</tr>
<tr>
<td>Mid-afternoon</td>
<td>Tea-sometimes a smalls bun or biscuit or savoury snack</td>
<td>Tea or coffee +snack (biscuit, sandwich, samosa or pakora or burger)</td>
</tr>
<tr>
<td>Evening?dinner</td>
<td>Same pattern as for brunch generally includes a vegetable or pulse variety</td>
<td>Same as lunch with more</td>
</tr>
</tbody>
</table>
Factors influencing dietary iron absorption

The bioavailability of dietary iron is the proportion of iron that is actually available for absorption and utilization by the body. As seen in table 16, the bioavailability of food and dietary iron is influenced by certain factors, some of which are briefly described below.

Table 16: FACTORS INFLUENCING DIETARY IRON ABSORPTION

<table>
<thead>
<tr>
<th>Haem iron absorption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron status of subject</td>
</tr>
<tr>
<td>Amount of dietary haem iron, especially from meat</td>
</tr>
<tr>
<td>Content of calcium in meal (e.g. milk, cheese)</td>
</tr>
<tr>
<td>Food preparation (time, temperature)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Non-haem iron absorption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron status of subject</td>
</tr>
<tr>
<td>Amount of potentially available non-haem iron (adjustment for fortification iron and contamination iron)</td>
</tr>
</tbody>
</table>

**BALANCE BETWEEN ENHANCING AND INHIBITING FACTORS**

**Enhancing factors**
- Ascorbic acid (e.g. certain fruit juices, fruits, potatoes and certain vegetables)
- Meat or chicken, fish and other seafood
- Fermented vegetables (e.g. sauerkraut), fermented soy sauces, etc.

**Inhibiting factors**
- Phytates and other inositol phosphates (e.g. bran products, bread made from high-extraction flour, breakfast cereals, oats, rice [especially unpolished rice], pasta products, cocoa, nuts, soybeans and peas)
- Iron-binding phenolic compounds (e.g. tea, coffee, cocoa, certain spices, certain vegetables and most red wines)
- Calcium (e.g. milk, cheese)
- Soy proteins

**Haem and non-haem iron.** Food iron is classified as either haem iron (the iron from meat, poultry and fish), or non-haem iron (from cereals, pulses, legumes, fruits and vegetables). In humans, haem iron is well absorbed and its absorption varies little with the composition of the meal. Absorption is inversely related to the quantity of iron stores in the body, i.e. absorption ranges from 15 to 25 percent in normal subjects and 25 to 35 percent in iron-deficient subjects (Monsen, 1988). Baking and prolonged frying have been shown to reduce haem iron absorption by about 40 percent (Bothwell *et al.*, 1989). The absorption of non-haem iron ranges from 2 to 20 percent. The specific rate of absorption of non-haem iron from plant foods is highly dependent on the effect of concomitantly ingested dietary components (reducing substances such as ascorbic acid keep iron in the reduced ferrous form) and the amount of body iron stores. Severely iron-deficient individuals absorb non-haem iron at higher rates than those with normal iron levels. Absorption was shown to be the highest (5-13 percent) in pregnant anaemic women (Dubey, 1994). In Indian studies, cooking of cereals and pulses was shown to cause a loss of 22-24 percent of their iron (Chiplonkar *et al.*, 1993). However, baking chapatti on an iron plate raised the iron content by 19 percent (Maingi and Sharma, 1972).

**Phytates and polyphenols.** The iron in Indian diets is mainly non-haem, the absorption of which is inhibited by food components, primarily phytates in grains, legumes, nuts, vegetables, roots and fruits, and polyphenols (tannates) in tea, coffee, vegetables, herbs and spices. Phytates can decrease non-haem iron absorption by 51-82 percent, and are found in higher concentrations in unrefined, non- or under-milled cereals than in refined, milled cereals. Fermentation can degrade the phytate and increase the bio availability of iron in bread made from whole-wheat flour. Polyphenols in tea are strong inhibitors of iron absorption. For example, one large cup (250 ml) of black tea
can inhibit non-haem iron absorption by approximately 50 percent even when drunk one hour after consuming the meal; it has no effect, however, when consumed between meals. This inhibition is strongly dose-related. The inhibiting effects can be reduced to some extent by serving tea with lemon or adding sufficient milk (100 ml) to the cup of tea. Some research from other countries indicates that black tea consumption does not cause IDA in people with diets containing a sufficient quantity of iron-rich foods. Iron absorption is affected less by coffee than tea. To overcome the inhibitory effects, therefore, tea or coffee should not be consumed with the main iron-containing meals (Brune et al., 1991).

**Calcium.** Calcium from dairy products interferes significantly with iron absorption of both haem and non-haem iron. Studies showed that about 30-50 percent more iron was absorbed when no milk or cheese was served with the main meal, which provided most of the dietary iron. The first 40 mg of calcium in a meal showed no inhibiting effect, whereas 300-600 mg of calcium inhibited iron absorption by 60 percent, which is the maximum inhibition of iron (Hallberg, 1998). However, in an Indian study, the absorption of iron from cereal-based milk diets was shown to be better than that of meat or fish diets (Narasinga Rao et al., 1983). The high iron availability of breast milk, which averages 50 percent (compared to 10-20 percent in cow's milk), is reduced when breast milk is taken together with cow's milk or weaning foods. Weaning foods should therefore be given separately from the breast milk (Chaudhary and Vir, 1994). Because calcium is also an important nutrient, it should be included in the diet for optimum health. Practical solutions for the competition of calcium with iron is to increase iron intake, increase its bioavailability or avoid taking calcium- and iron-rich foods at the same time.
Soyabean. Soy protein in a meal reduces the amount of iron absorbed. It has been found that the iron availability of an Indian meal is lowered more by adding soymilk than soy meal (Christian and Seshadri, 1989), but the effect of soybean on non-haem absorption has been controversial. Some fermented soy sauces have, however, been found to enhance iron absorption (Hallberg and Rossander, 1982) (Baynes et al., 1990).

Ascorbic acid. Ascorbic acid (vitamin C) is the most potent enhancer of non-haem iron absorption even in the presence of inhibitors such as phytates, tannates and calcium. It can reduce food ferric iron to the better-absorbed ferrous iron by 75-98 percent. In Indian studies, the addition of ascorbic acid to cereals and pulses enhanced the available iron (NIN, 1992). In cereal-based diets, absorption was the best for rice and vegetable combinations, which may result from ascorbic acid present in the vegetables (Rao et al., 1991). Children who consumed GLV once a week or more frequently had higher iron levels than non-consumers (Seshadri 1997). Daily intake of guava fruit with the two major meals by young anaemic women resulted in a significant increase in iron. In a community-level study, anaemic preschool children were given supplements of 100 mg synthetic ascorbic acid at each of their two daily meals for a period of two months; this improved their iron levels significantly and the prevalence of anaemia was reduced from 96 to 26 percent (Seshadri, 1993).

In regional meals, the addition of citrus fruit juices or a portion of potato, cauliflower or cabbage increased iron availability markedly (Chaudhary and Vir, 1994). The addition of 25 mg of ascorbic acid as lemonade consumed at two meals a day doubled the absorption of iron from a meal and improved the iron status of the participating women (García et al., 1998). The comprehensive review has shown that a food source containing 50 mg of ascorbic acid consumed with the main meal (Cook and Monsen, 1977) providing most of the daily intake of iron enhances iron bioavailability...
significantly. Ascorbic acid also improves the availability of iron from fortified foods.

The enhancing effect of ascorbic acid is dose-dependent, but little extra benefit is derived by increasing the intake of ascorbic acid beyond 100 mg in a meal. The influence of ascorbic acid is greatest on meals with low iron bioavailability, such as vegetarian meals.

**Meat, fish, poultry.** Meat and fish taken even in small amounts markedly improve the bioavailability of non-haem iron. The addition of 90-100 g of meat, fish or poultry to the daily diet improves the bioavailability of iron significantly (John and Walker, 1992), but because these foods are costly and culturally unacceptable, their use is uncertain. Moreover, a non-vegetarian diet containing 3 oz (approximately 85 g) of meat provided the same increase in non-haem iron absorption as 75 mg of ascorbic acid (Baynes and Bothwell, 1990).

Eggs are rich in iron content, but its bioavailability is poor. Studies showed that when two eggs were consumed per day there was a significant reduction in iron absorption from Indian meals (Kaur, 1981). Eggs are an important supplement in the diets of vulnerable mothers and children as they are a particularly good source of quality protein and are rich in vitamins and minerals (and even among vegetarians, they are accepted with less reluctance than meat or fish); thus the consumption of eggs may not be avoided. However, as a source of iron, eggs should be eaten along with a fruit or any other source containing 100 mg of ascorbic acid, or between meals.
Increasing intake and enhancing bioavailability of iron

A number of experimental studies on improving the bioavailability of iron have been conducted in different countries. However, very little research has been undertaken on methods to improve or optimize the bioavailability of iron from Indian diets. Furthermore, hardly any community or impact evaluation studies have been conducted on large Indian populations using food-based approaches. The following are some practical suggestions to provide a basis for such studies and community programmes. The overall intake of iron from iron-rich foods needs to be increased to obtain the optimum level of RDA of iron in Indian population groups. This increase should be coupled with efforts to combine appropriate foods in the diet to enhance the bioavailability of iron and reduce inhibitory factors (Gopalan et al., 1993).

Cereals and millets, pulses and legumes, Green leafy vegetables, nuts and oilseed are good sources of iron. Even without the haem iron found in fish or poultry, vegetarians are not at greater risk from iron deficiency than non-vegetarians (Miller, 1999). Plant foods can supply all the haematinic nutrients in adequate amounts with the exception of vitamin $B_{12}$ (cobalamin). The latter comes mostly from animal products and bacteria on plant foods.

Vitamin C-rich foods must be consumed at the same meal that contributes the major part of daily dietary iron (Cook and Monsen, 1977). Furthermore, household processes such as germination, malting of grains/pulses and fermentation should be used to overcome phytates (Chaudhary and Vir, 1994) and enhance the ascorbic acid and B-vitamins. The presence of carotene in rice-, wheat- and corn-based diets improved iron absorption from one to more than threefold suggesting that both ascorbic acid and carotene (Garcia-Casal et al., 1998) prevented the inhibitory effect of phytates on iron absorption.
The values of iron, mg/100 g contained in raw edible portion in the Figures and Table 17 have been calculated using the *Nutritive Value of Indian Foods* by Gopalan *et al.* (1989). The raw edible quantity of vegetables shown in Figure 2 would, however, need to be doubled to allow for about 50-75 percent loss of ascorbic acid in cooking (of all the methods of cooking, pressure-cooking retains the maximum amount). Cabbage, radish leaves and capsicum, after food-safety aspects have been observed, should preferably be eaten raw as salads to avoid loss of their vitamin C content.

Encouraging the production, processing, marketing and consumption of foods rich in these nutrients could increase dietary consumption of iron and ascorbic acid. Nutrition education could be a means to further this promotion process.

**TABLE 17: Plant foods rich in iron**

<table>
<thead>
<tr>
<th>Food group</th>
<th>Food</th>
<th>Iron, mg/100 g contained in raw edible portion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cereals and millets</td>
<td>Bajra (Indian millet, <em>Pennisetum typhoidenum</em>)</td>
<td>8.0</td>
</tr>
<tr>
<td></td>
<td>Samai (little millet, <em>Panicum miliare</em>)</td>
<td>9.3</td>
</tr>
<tr>
<td></td>
<td>Rice bran</td>
<td>35.0</td>
</tr>
<tr>
<td></td>
<td>Wheat germ</td>
<td>6.0</td>
</tr>
<tr>
<td>Pulses and legumes</td>
<td>Soybean</td>
<td>10.4</td>
</tr>
<tr>
<td></td>
<td>Chickpea, roasted</td>
<td>9.5</td>
</tr>
<tr>
<td></td>
<td>Cowpea</td>
<td>8.6</td>
</tr>
<tr>
<td></td>
<td>Lentil</td>
<td>7.6</td>
</tr>
<tr>
<td></td>
<td>Peas, dry</td>
<td>7.1</td>
</tr>
<tr>
<td></td>
<td>Horse-gram (<em>Dolichos biflorus</em>), whole</td>
<td>6.8</td>
</tr>
<tr>
<td>Green leafy vegetables</td>
<td>Amaranth, beet, cauliflower, chekkur manis, chickpea, cowpea, manathakkali, mint, mukarrate keerai, mustard, parsley, radish, shepu, turnip</td>
<td>15.6-40</td>
</tr>
<tr>
<td>Other vegetables</td>
<td>Lotus stem, dry</td>
<td>60.6</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>-----------------------</td>
<td>------</td>
</tr>
<tr>
<td></td>
<td>Karonda, dry</td>
<td>39.1</td>
</tr>
<tr>
<td></td>
<td>Sundakai, dry</td>
<td>22.2</td>
</tr>
<tr>
<td></td>
<td>Onion stalks</td>
<td>7.4</td>
</tr>
<tr>
<td></td>
<td>Plaintain greens</td>
<td>6.3</td>
</tr>
<tr>
<td>Nuts and oil-seed</td>
<td>Garden cress seeds</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td>Coconut meal, deoiled</td>
<td>69.4</td>
</tr>
<tr>
<td></td>
<td>Niger seeds</td>
<td>56.7</td>
</tr>
<tr>
<td></td>
<td>Gingelly seeds</td>
<td>9.3</td>
</tr>
<tr>
<td></td>
<td>Mustard seeds</td>
<td>7.9</td>
</tr>
<tr>
<td>Dry fruits</td>
<td>Pistachio nuts</td>
<td>7.7</td>
</tr>
<tr>
<td></td>
<td>Blackcurrants</td>
<td>8.5</td>
</tr>
<tr>
<td></td>
<td>Dates</td>
<td>7.3</td>
</tr>
<tr>
<td>Condiments and spices</td>
<td>Turmeric</td>
<td>67.8</td>
</tr>
<tr>
<td></td>
<td>Mango powder</td>
<td>45.2</td>
</tr>
<tr>
<td></td>
<td>Tamarind pulp</td>
<td>17.0</td>
</tr>
<tr>
<td></td>
<td>Poppy seeds</td>
<td>15.9</td>
</tr>
<tr>
<td></td>
<td>Black pepper, cloves, cumin</td>
<td>12.0</td>
</tr>
</tbody>
</table>

Source: *Nutritive Value of Indian Foods* by Gopalan et al. (1989).

The bioavailability of iron is low in predominantly cereal-based diets because of their high phytate content. It has been suggested that the bioavailability of iron may be significantly improved by ascorbic acid supplementation. As little as 50 mg of ascorbic acid can double iron absorption when taken with a meal. The comparative efficacy of iron/folate supplementation with and without the addition of vitamin C to the supplement would seem to need further investigation (Rao, 1996).
Table 12 shows the iron content of plant foods that are consumed in India. Figures 13.

(a) and (b) shows the fruits and Green leafy vegetables (GLV) that can provide 50 mg equivalent portions of ascorbic acid, which is essential as a bioavailability enhancer in Indian diets.

Fig 13(a)

Ascorbic acid in one 50 mg portion of fruit

Fig 13(b)

Ascorbic acid in one 50 mg portion of green leafy vegetables

Source: Nutritive Value of Indian Foods by Gopalan et al. (1989)
Combinations and proportions of foods

On the basis of the factors influencing dietary iron absorption, a balanced vegetarian diet has been calculated for a woman of reproductive age. Table 4 shows the food groups and suggested daily intakes required to enhance its iron availability.

TABLE 18: Balanced diet (vegetarian) for sedentary and moderately active women of reproductive age, suggested daily intake

<table>
<thead>
<tr>
<th>Food group</th>
<th>Sedentary</th>
<th>Moderate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Quantity, raw edible part (g)</td>
<td>Quantity, raw edible part (g)</td>
</tr>
<tr>
<td>Cereals and millets</td>
<td>300</td>
<td>360</td>
</tr>
<tr>
<td>Pulses and legumes</td>
<td>60</td>
<td>75</td>
</tr>
<tr>
<td>Green leafy vegetables</td>
<td>75-100</td>
<td>75-100</td>
</tr>
<tr>
<td>Roots and tubers</td>
<td>75-100</td>
<td>100</td>
</tr>
<tr>
<td>Other vegetables</td>
<td>75-100</td>
<td>100</td>
</tr>
<tr>
<td>Fruits</td>
<td>75-100</td>
<td>75-100</td>
</tr>
<tr>
<td>Milk and dairy products</td>
<td>200</td>
<td>200</td>
</tr>
<tr>
<td>Sugar and jaggery</td>
<td>20</td>
<td>30</td>
</tr>
<tr>
<td>Fats and oils, visible</td>
<td>25</td>
<td>35</td>
</tr>
<tr>
<td>Condiments and spices</td>
<td>7-10</td>
<td>7-10</td>
</tr>
</tbody>
</table>

The suggested food combinations were formulated on the basis of using foods that are normally consumed, familiar, locally available and low-cost; containing enhancing factors and limiting inhibitors to the extent possible and providing an overall balanced diet to provide all the major nutrients required by the body (NIN, 1992-93). Tea with milk, lemon tea or herbal tea has been included between meals (and not with them) for better iron absorption from the meals. Milk is taken at breakfast, in the evening or at bedtime and not with the main meals that contribute most of the daily iron intake. Milk intake may be increased to 400 ml per day provided it is distributed as suggested. Jaggery instead of sugar is included, as it contains iron whereas sugar
contains only a trace. Lunch and dinner can be interchanged depending upon the convenience of cooking. Early morning tea may be deleted and replaced with mid-morning or mid-afternoon tea. Meals may be cooked as one dish, e.g. missi roti (chapatti) comprising wheat or millet flour + pulse flour (chickpea) + Green Leafy Vegetables or gingelly seeds; or rice khichdi consisting of rice + green gram or chickpea split pulse + greens to improve nutritive value by supplementary action and to reduce cooking time. An example of a daily menu is given in Table 19.

Table 19: Combinations and proportions of foods for daily consumption to enhance iron bio availability (Gopalan et al., 1989)

<table>
<thead>
<tr>
<th>Meal</th>
<th>Menu</th>
<th>Food, raw edible part (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early morning</td>
<td>Tea with milk/lime or herbal tea + biscuits (two) or rusk (one) Sugar</td>
<td>150 + 50/10 or 150</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Breakfast</td>
<td>Stuffed chapatti or parantha Wheat + potato (boiled) Curd (like yoghurt) or milk</td>
<td>100 + 75</td>
</tr>
<tr>
<td>Lunch</td>
<td>Wheat + millet flours + cauliflower chapatti Lentil dal Cabbage, raw + tomato + lime juice salad Jaggery + gingelly seeds gazak</td>
<td>50 + 50 +50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25 + 30 + 15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 + 10</td>
</tr>
<tr>
<td>Mid-afternoon</td>
<td>Tea with milk/lime or herbal tea Sugar Snack (sweet or savoury), 1 or 2 pieces or equivalent</td>
<td>150 + 50/10 or 150</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Dinner</td>
<td>Rice khichdi: Rice parboiled + Green gram split + Amaranth leafy vegetables Onion stalks Guava, orange or papaya</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>75</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50</td>
</tr>
</tbody>
</table>
PREVIOUS STUDIES

1. **Fetal growth in maternal anaemia** (Singla et al., 1997).

The effect of maternal iron deficiency anaemia on foetal growth was studied in 54 anaemic (haemoglobin <11.0 g/dl) mothers. Twenty-two mothers served as controls (haemoglobin ≥11.0 g/dl). All the women had singleton live births at term gestation. The maternal iron status was assessed by serum ferritin estimation. The birth weight, head circumference, chest circumference, mid-arm circumference, and crown-heel length were significantly low in infants born to women with moderate (haemoglobin 6.1±8.5 g/dl) and severe anaemia (haemoglobin ≤6.0 g/dl), in comparison to infants born to non-anaemic women. Similarly, birth weight, mid-arm circumference, and crown-heel length were significantly low in infants of women with depleted iron stores (serum ferritin <10 µg/l) than in infants of women with serum ferritin levels of 20 µg/l or more. All indices of foetal growth showed linear relationships with maternal haemoglobin, as well as with serum ferritin. The growth retarding effect of maternal anaemia was more on foetal birth weight and mid-arm circumference than on other anthropometric indices of the newborn.

2. **Maternal haemoglobin concentration and birth weight** (Steer, 2000).

Pregnancy requires additional maternal absorption of iron. Maternal iron status cannot be assessed simply from haemoglobin concentration because pregnancy produces increases in plasma volume and the haemoglobin concentration decreases accordingly. This decrease is greatest in women with large babies or multiple gestations. However, mean corpuscular volume does not change substantially during pregnancy and a haemoglobin concentration <95 g/L in association with a mean corpuscular volume <84 fl probably indicates iron deficiency. Severe anaemia (haemoglobin <80 g/L) is associated with the birth of small babies (from both preterm labour and growth
restriction), but so is failure of the plasma volume to expand. Haemoglobin concentrations >120 g/L at the end of the second trimester are associated with a 3-fold increased risk of preeclampsia and intrauterine growth restriction. The minimum incidence of low birth weight (<2.5 kg) and of preterm labour (<37 completed weeks) occurs in association with a haemoglobin concentration of 95–105 g/L. This is widely regarded as indicating anaemia in the pregnant woman but, if associated with a mean corpuscular volume >84 fL, should be considered optimal.


To determine the relationship between maternal anaemia haemoglobin and various birth outcomes, a meta-analysis was conducted based on published literature identified by Medline and manual search from 1966 through 1999. It was conclude that early pregnancy anaemia is associated with slightly increased risk of preterm birth. The trend toward an inverse association of anaemia determined during late pregnancy with preterm birth and low birth weight may reflect the benefit of plasma volume expansion.


The study was to find the associations among haemoglobin concentration at first measurement during antenatal care, change in haemoglobin concentration during pregnancy, and risk of stillbirth. And the results conclude that high haemoglobin concentration at first measurement during antenatal care appears to be associated with increased risk of stillbirth, especially preterm and SGA ante partum stillbirths.
5. **Anaemia in the first but not in the second or third trimester is a risk factor for low birth weight** (Henna et al., 2002).

The study design involved a retrospective chart review of all women registering for prenatal care in the area of Kuopio University Hospital between 1990 and 2000. The frequency of anaemia was 2.6%, with 0.3% occurring in the first trimester. After controlling for confounding factors, anaemia detected in the first trimester was associated with low-birth-weight infants whereas the mid- and third-trimester anaemia groups showed no significantly different outcomes when compared with the non-anaemic women. Results showed first trimester anaemia was not significantly associated with small birth weight for gestational age or with premature delivery <37 weeks.

6. **Maternal and perinatal outcome in varying degrees of anaemia** (Malhotra et al., 2002).

The study was done to analyze the maternal and perinatal outcome in varying degrees of anaemia. The results showed that mild anaemia fared best in maternal and perinatal outcome. Severe anaemia was associated with increased low birth weight babies, induction rates, operative deliveries and prolonged labour.

7. **Severe maternal anaemia and pregnancy outcome** (El Guindi et al., 2004).

The aim of this study was to determine the effects of severe antenatal maternal anaemia on pregnancy outcome. The literature is not conclusive on the influence of anaemia in pregnant women. More frequent preterm birth and low birth weight have been reported in the majority of studies considering mild to moderate maternal anaemia (in contrast to this study where the mothers had severe anaemia). Many studies indicated that routine iron supplementation during pregnancy may have beneficial effects on pregnancy outcome. Severe
anaemia in pregnancy may have adverse effects for the newborn and should be treated or prevented early in pregnancy.

8. A prospective, partially randomized study of pregnancy outcomes and hematologic responses to oral and intramuscular iron treatment in moderately anaemic pregnant women (Sharma et. al., 2004).

The study was done to compare the safety and efficacy in treating pregnancy anaemia of 3 intramuscular doses of iron given at monthly intervals with those of daily oral iron supplementation. Haemoglobin and iron indicators improved significantly with both treatments. The increase in serum ferritin concentration after parenteral iron treatment was significantly higher than that after oral iron treatment. No significant differences between the 2 groups in pregnancy outcomes and birth weight were observed. Systemic side effects were more common in the parenteral iron group, whereas gastrointestinal side effects were more common in the oral iron group. The intramuscular administration of 3 doses of 250 mg Fe at monthly intervals appeared to have good compliance and efficacy and may be used in women who cannot tolerate oral administration of iron. However, intramuscular administration of iron is appropriate only in hospital settings well equipped to treat anaphylactic crises.

9. Impact of maternal anaemia on birth outcomes of teen twin pregnancies: a comparative analysis with mature young mothers. (Shumpert et. al., 2004)

The study investigated the impact of maternal anaemia on birth outcomes among adolescent twin pregnancies in the United States using the vital statistics records for matched multiple births covering the years 1995-1997 inclusive. The study group consisted of mothers aged 19 years or younger who had a twin pregnancy. A cohort of women aged 20-29 years with twin
pregnancies served as the comparison group. The main birth outcomes of interest were: low and very low birth weight, preterm and very preterm delivery, small-for-gestational age, and stillbirth, neonatal and perinatal mortality. Crude and adjusted odds ratios for the above outcomes were calculated using the generalised estimating equation framework (GEE) that captured both intra- and intercluster sources of heterogeneity. Although not statistically significant, we detected an elevated risk for stillbirth among anaemic women (20-30%) in either age cohort, a magnitude that is substantial at the population level as well as warranting further aetiological investigations.

10. Maternal anaemia: effect on the newborn (Fall et al., 2003).

The purpose of this study was to measure the effect of maternal anaemia on the foetus and the effect of iron supplementation on the maternal and foetal reserves. The study was conducted in a three-month cross-sectional study at the gynaecological and obstetrics clinics of Aristide Le Dantec Hospital. Ninety-five women aged 16 to 43 years old and having an haemoglobin rate < 11 g/dl were recruited. Most of them were primipares. Among them 69 had a low ferritinemia (< 50 ng/ml), 36, a ferritinemia collapsed (< 30 ng/ml) and 13 virtually non-existent reserves (< 12 ng/ml). All newborns were born in terms with an apgar score >/= in 93 of them. Among them 24 had anaemia (rate of haemoglobin < 14 g/dl) and 54.7% a low ferritinemia. There is no relationship between the maternal and foetal rates of haemoglobin; 74% of newborn had a normal rate of haemoglobin. Among 36 women with low ferritinemia only two gave birth to a newborn without iron reserves. In this study, among 68 women who received iron regularly, 41 had normal reserves and 43 gave birth to a newborn with high ferritinemia. There was significant difference between the women having received iron during their pregnancy and those not supplemented as regards the effect on newborn. The prevention of iron
deficiency and anaemia can be done by the iron systematic and premat supplementation.

11. Maternal anaemia and its impact on perinatal outcome in a tertiary care hospital in Pakistan (Lone et. al., 2004).

The study investigated the relationship between maternal anaemia and perinatal outcome in a cohort of 629 pregnant women from October 2001 to 2002. Of these, 313 were anaemic (haemoglobin < 11 g/L). Perinatal outcomes included preterm delivery, low birth weight, intrauterine growth retardation, perinatal death, low Apgar scores and intrauterine fetal death. Univariate and multivariate analyses were performed. The risk of preterm delivery and low birth weight among the anaemic women was 4 and 1.9 times more respectively than the non-anaemic women. The neonates of anaemic women also had 1.8 times increased risk having low Apgar scores at 1 minute and there was a 3.7 greater risk of intrauterine fetal death among the anaemic women than the non-anaemic women.

12. Maternal anemia during pregnancy is an independent risk factor for low birthweight and preterm delivery (Levy et. al., 2005).

The study was designed to investigate the outcome of pregnancy and delivery in patients with anemia. A retrospective population-based study comparing all singleton pregnancies of patients with and without anemia was performed. Deliveries occurred during the years 1988-2002 in the Soroka University Medical Center. Maternal anemia was defined as hemoglobin concentration lower than 10 g/dl during pregnancy. Patients with hemoglobinopathies such as thalassemia were excluded from the analysis. During the study period there were 153,396 deliveries, of which 13,204 (8.6%) occurred in patients with anemia. In a multivariable analysis, the following conditions were significantly associated with maternal anemia: placental abruption, placenta
previa, labor induction, previous cesarean section (CS), non-vertex presentation and Bedouin ethnicity. Higher rates of preterm deliveries (<37 weeks gestation) and low birth weight (<2500 g) were found among patients with anemia as compared to the non-anemic women (10.7% versus 9.0%, p < 0.001 and 10.5% versus 9.4%, p < 0.001; respectively). Higher rates of CS were found among anemic women (20.4% versus 10.3%; p < 0.001). On the whole study concluded that maternal anemia influences birth weight and preterm delivery, but in the population studied, it was not associated with adverse perinatal outcome.


Supplementation with iron is generally recommended during pregnancy to meet the iron needs of both mother and fetus. When detected early in pregnancy, iron deficiency anemia (IDA) is associated with a > 2-fold increase in the risk of preterm delivery. Maternal anaemia when diagnosed before midpregnancy is also associated with an increased risk of preterm birth. Results of recent randomized clinical trials in the United States and in Nepal that involved early supplementation with iron showed some reduction in risk of low birth weight or preterm low birth weight, but not preterm delivery. During the 3rd trimester, maternal anaemia usually is not associated with increased risk of adverse pregnancy outcomes and may be an indicator of an expanded maternal plasma volume. High levels of hemoglobin, hematocrit, and ferritin are associated with an increased risk of fetal growth restriction, preterm delivery, and preeclampsia. While iron supplementation increases maternal iron status and stores, factors that underlie adverse pregnancy outcome are considered to result in this association, not iron supplements. On the other hand, iron supplements and increased iron stores have recently been linked to maternal complications (eg, gestational diabetes) and increased
oxidative stress during pregnancy. Consequently, while iron supplementation may improve pregnancy outcome when the mother is iron deficient it is also possible that prophylactic supplementation may increase risk when the mother does not have iron deficiency or IDA. Anaemia and IDA are not synonymous, even among low-income minority women in their reproductive years.

14. Maternal and foetal outcome after severe anaemia in pregnancy in rural Ghana (Geelhoed et al., 2006).
This study analyzes adverse maternal and foetal outcome after severe anaemia in pregnancy in rural Ghana. Results showed that compared to nonexposed women, exposed women had an increased risk of maternal death (5/157 versus 0/152). Foetal outcome did not significantly differ between the study groups, although perinatal mortality was increased with exposure to Hb < 7.0 g/dl (OR 3.1; 95% CI 1.0-9.4), and low birth-weight was increased with exposure to Hb < 6.0 g/dl (OR 2.5; 95% CI 1.2-5.4). Overall foetal outcome was significantly better when haemoglobin prior to childbirth was at least 8.0 g/dl (OR 3.9; 95% CI 1.6-9.6), body mass index at least 20 kg/m2 (OR 2.8; 95% CI 1.5-5.3), and number of antenatal visits at least 4 (OR 2.0; 95% CI 1.1-3.7). Hence it was concluded severe anaemia in pregnancy results in relatively poor maternal and foetal outcome. Apparently maternal risks increase prior to foetal risks. In order to improve maternal and foetal outcome, it was recommended that district hospitals in low-income countries make prevention, early diagnosis, and treatment of severe anaemia in pregnancy a priority.

15. Determinants of anaemia among pregnant women in Mali
(Ayoya et al., 2006)
The study was done to examine the prevalence and likely etiologies of anaemia in pregnancy in a poor urban population in Bamako, Mali. Pregnant women (n = 190) were selected randomly. Haemoglobin, serum iron, and total
iron-binding capacity were measured; blood smears were examined for Plasmodium falciparum malaria; and single stool and urine samples were examined for Schistosoma haematobium and hookworm. Gynaecologic examinations were performed and interviews conducted to qualitatively assess food consumption and other socioeconomic characteristics. Associations among mild, moderate, and severe anaemia; iron and parasite status; erythrocyte sedimentation rates; and the presence of abnormal vaginal discharge were evaluated. Differences in haemoglobin and serum iron concentrations, total iron-binding capacity, and anaemia were compared according to trimester of pregnancy and between infected and non infected women. The data suggest that infections and food accessibility contribute to the high rates of anaemia during pregnancy in Mali.

VII. Anaemia screening tests.

(a) Blood test for haemoglobin concentration.

Haemoglobin was estimated by Sahli’s and Drabkin’s cyanmethemoglobin methods. Standardised haemoglobin pipettes were used in both methods. Drabkin's solution containing potassium ferricyanide, potassium cyanide and sodium bicarbonate was prepared. 20 microliter of blood was added to 5ml of Drabkin's solution. Readings were taken at 530 nm in a spectrophotometer. Haemoglobin values were calculated from haemoglobin curve prepared using haemoglobin standard (Chemkit) (Wintrobe, 1975) (Cook, 1985).

A number of workers have compared haemoglobin estimated by different methods in order to establish the efficacy and reliability of the methods. Some of the methods of haemoglobin estimation may have an error of + / -20% or more which when compounded with poor technique makes the method highly unreliable.
The principle in Sahli's method involves the conversion of haemoglobin to acid hematin and comparing visually the colour developed with that of standard tinted glass. Haemoglobin value is directly read from the graduated haemoglobin tube. The methodology has following inbuilt disadvantages viz: i) subjective visual colour comparison, ii) need for accurate pipetting of 20 microliter of blood, iii) estimation of only acid hematin formed, iv) fading of comparator on prolonged use and v) poor sensitivity and reliability (Gammon & Baker, 1977) (Stone et al., 1984) (Lewis, 1988).

In the Drabkin’s method of haemoglobin estimation haemoglobin is oxidised to methemoglobin by potassium ferricyanide, which reacts with cyanide ions of potassium cyanide to form cyanmethemoglobin. The haemoglobin is estimated with the help of cyanmethemoglobin curve. The advantages of this method are i) error due to subjective visual matching is avoided as spectrophotometer is used and hence reading is precise and reliable, ii) measures all forms of haemoglobin except sulphaemoglobin. iii) single step procedure using single reagent. iv) Cyanmethemoglobin formed produces broad absorbent band at 530 rim v) good stable haemoglobin standards are available. (NIN, 1992-1993).

Analysis of the results of haemoglobin estimated by Sahli's and Drabkin's methods in samples of blood collected by fingerprick and venepuncture showed statistically significant difference. This could be due to the inbuilt errors of Sahli's method of haemoglobin estimation. The subjective error in colour comparison in Sahli's method is proved by the fact that readings repeated in the same samples but by two different groups of workers were significantly different. On the other hand comparisons of haemoglobin estimated by Drabkin’s method in the same samples by the two groups of
workers were not statistically significant stressing thereby the reliability of Drabkin's method.

Thus the Drabkin's method of haemoglobin estimation can be used in undergraduate teaching schedule as well as in anaemia detection and management in hospitals replacing Sahli's method. Since the cut off point decides the requirement of therapy, the Drabkin's method being more sensitive is the method of choice. Also, for research purposes where small variations in haemoglobin values are to be detected, the Drabkin's method would be ideal (Baul et al., 2004)

**Nutrition foundation of India (2003) has validity of Various Methods for Estimation of Haemoglobin**

Various methods have been recommended for the assessment of haemoglobin (Hb) for the identification of anaemia. All methods have their merits and limitations. A study was carried out to assess the validity of Cyanmethaemoglobin method (with and without filter paper) and Haemoglobin Colour Scale method. Detailed methodology of each of these methods is given below.

**Cyanmethaemoglobin method (with filter paper):** This method uses the Filter Paper Technique. In this, an accurate volume (20ul) of blood was sucked from the pricked finger into the Hb pipette and immediately delivered on to Whatman No. 1 filter paper (cut into 1.5 X1.5 cm squares). It was allowed to dry and the squares of paper were labelled. These squares were then dropped into accurately measured amount (5ml) of diluent (Drapkin's solution), and the blood was allowed to diffuse out of the filter paper and into the diluent. The solution was then centrifuged. The supernatent was separated and its absorbance read at 540 nm in a photoelectric colorimeter. Since a
major part of the study had to be carried out in distant villages, this technique was found feasible.

**Cyanmethaemoglobin method (without filter paper):** The method is the same as above, the only exception being that the blood is directly put in the Drapkin's solution.

**Hb colour scale:** This is the standard method also recommended by the World Health Organization (WHO) since 1995. The procedure for the same is as follows.

- Take up a drop of blood at one end of the test paper so that it forms a stain of 8-9mm in diameter. Wait 30 seconds.
- Then compare the stain in daylight (but not bright sunlight) or artificial light - with the booklet open in the left hand, avoiding shadow, and at an angle that allows you to distinguish the different shades easily.
- Slide the blood scale up and down behind the colour scale apertures.
- If the blood scales closely matches one of the shades on the scale, record its Hb value. If the colour of the stain lies between the two shades, record the lower value.
- Wipe the surfaces that have been in contact with the test paper with a damp tissue.

**Hemocue method:** The procedure for estimation of Hb by this method is as follows:

- The person should be relaxed and only the middle finger should be used for sampling.
- Press the finger lightly to stimulate the blood flow.
- Use gentle pressure and prick the side of the fingertip.
- Wipe away the first two or three drops.
• Make sure the drop of blood is big enough to fill the curette completely.

• Wipe off the excess blood. Inspect the curette for air bubbles.

• Place it in the holder immediately and push it into measuring position.

• Analyse it after 10 minutes. Take the reading.

• The curette should be disposed off after the measurement.

Haemoglobin levels were estimated for 38 females using all the three methods. The average for the direct method was 10.80gm% and that of the filter paper was 10.69gm%; whereas the average Hb value for the colour-scale method was observed to be 9.09gm%.

It is clear from the study that the Hb values from the colour scale method were significantly lower than those estimated from cyanmethaemoglobin method (with and without paper). Also, the direct method gave a higher value of Hb than that got from the filter paper technique, though the difference was not significant. Thus, the colour scale method underestimated the Hb value significantly.

Another set of estimations to find out the validity of the methods for Hb estimation was carried out on random subjects in order to compare the results by using two different techniques (cyanmethaemoglobin - both direct and filter paper methods) and hemocue method. It was observed that Hb values using direct and filter paper techniques were similar with an average difference of 0.25gm%. The results of the estimations using Hemocue were varied and did not compare with the results of the cyanmethaemoglobin method. They gave a significantly higher reading of the Hb levels in the same subjects as against the cyanmethaemoglobin method (with and without filter paper technique). And the difference between the filter paper and direct method was not at all significant concluding that cyanmethaemoglobin
method, (with filter paper) is the best for the field-related studies (Sari et al., 2001) (Mohanram et al., 2002).

(b) Stool test for hookworm infestation.

Early morning specimens were collected from the children in provided containers. Stool specimens were examined under direct light microscopy of smear in normal saline. The laboratory diagnosis of smear was based upon demonstration of ova, cysts or trophozoïdes. The negative cases were tested on the following two days and were taken as negative if no ova, cysts or trophozoïdes were seen in 3 consecutive specimens. (Walker et al., 1996). Ascaris infestation has become an important consideration in hepatopancreato-biliary diseases in endemic areas and requires prompt recognition and treatment to prevent complications (Sharma, 1998). Worm infestation is not only confined to certain geographical areas of the world but is an emerging problem world wide with increasing number of cases being reported from Europe and the USA (Scriver, 2001). In stark contrast to earlier studies, Ascaris related clinical disease is not just restricted to patients with a heavy worm load. (Knutson et al., 1997) but may be seen with a single worm lodged in the biliary tract and negative parasitic tests in the stools. This thus is not an uncommon disease and should be considered in patients presenting with hepato-pancreato-biliary symptoms even from non-endemic areas. In view of the above findings, it is highly recommended that measures to reduce worm infestation including mass chemotherapy; should deserve high priority because of the known harmful effects of these worms. (Singh, 2001).