Chapter II  Review of literature
Nutritional Anemia – Historical perspective:

- Father of modern medical science and the great Greek philosopher Hippocrates (460-377 BC) had said nearly 2500 years ago “Let thy food be thy medicine and thy medicine be thy food”. Our body has the inbuilt ability to heal itself if provided proper nutrition (cited by Agarwal R K ⁴⁰).

- The word “anemia” is composed of two Greek roots that together mean “without blood” an (without) + Haima (blood).

- Anemia was first recognized as chlorosis (a Greek term meaning green) “the green sickness”. Historians are not sure when this identification first appeared but in the 16th century it was associated with a series of symptoms i.e. pallor, fatigue, poor appetite, gastrointestinal, neurological and menstrual abnormalities common in adolescent girls. The pale hues of fatigued and fainting women were commonly portrayed in art—particularly by Dutch school of painters and are referred to in several Shakespeare’s plays as love sick women. Ancient Greeks were knowing the benefits of iron. The injured sufferers of war were drinking water in which the swords had rusted to assume some strength.

- Swammerdam in 1658 discovered red cells by looking the blood under microscope and called them “ruddy globules” and French Physician Gabriel
Andral introduced the term anemia around 1829 for chlorosis (cited by Uthman ED\textsuperscript{41}).

Rain\textsuperscript{42} in his historical review of iron deficiency anemia cited that (1) Sydenham a 17\textsuperscript{th} century physician prescribed iron salts for treatment of chlorosis, (2) French physician P. Blaud (1832) introduced pills containing ferrous sulfate and potassium carbonate for the treatment of chlorosis and (3) Stockman in 1895 proposed that chlorosis was the result of a nutritional iron deficiency. But the view of Stockman was largely ignored for decades before nutritional cause of anemia was established in twentieth century.

\begin{quote}
\textbf{Gold is for the mistress, Silver for the maid}
\textbf{Copper for the Craftsman cunning at his trade}
"Good" said the Baron, sitting in the hall,
"But, Iron - Cold Iron, is master of them all".
\end{quote}

- Rudyard Kipling
Nutritional Anemia – Prevalence : India

➢ Rusia U et al\(^4\)\(^3\) (1995) from their study on pregnant women in Delhi observed that 34.3% of the pregnant women were anemic and iron deficiency was the most common cause of anemia.

➢ Vasanthi G et al\(^4\)\(^4\) (1994) studied the nutritional status of adolescent girls and found 25% incidence irrespective of their urban or rural residence. The incidence of anemia increased after menarche was attained.

➢ Rajaratnam J et al\(^4\)\(^5\) (2000) reported 44.8% prevalence of anemia among adolescent girls of rural Tamilnadu. There was decrease in prevalence as the age increased however difference was not statistically significant. The prevalence of anemia was 40.7% in pre-menarchal girls as compared to 45.2% in postmenarchal girls.

➢ Rawat CM et al\(^4\)\(^6\) (2001) reported 34.5% prevalence of anemia among adolescent girls of rural Uttar Pradesh. Anemia was found to be significantly associated with educational status, birth order and awareness regarding anemia but no association with age or menarchal age was found.

➢ Bentley ME\(^2\)\(^2\) (2003) did the survey of 4032 ever married women of 15-49 years of age in India and reported that prevalence was high among all women. Overall 48.8% had anemia with 2.2% having severe anemia. Protective factors include Muslim community and high socio-economic status. Anemia was also found in 41% of over weight women.

➢ Sharma JB et al\(^1\)\(^3\) (2003) from their study on pregnant women of Delhi reported that prevalence of anemia was very high i.e. 96% with 5.3% having
severe anemia. They did not find any effects of dietary habits on prevalence of anemia.

- Malhotra P et al\textsuperscript{47} (2004) reported 50\% incidence of anemia in rural population of North India. Low socioeconomic class, illiteracy and lower Body mass index (BMI) was associated with higher prevalence of anemia.

- National Family Health Survey III (NFHS III)\textsuperscript{21} carried out in 2005-06 by Ministry of Health and Family Welfare, Government of India showed the prevalence of anemia in pregnant women as 57.9\%. As compared to NFHS-II\textsuperscript{48} carried out in 1998-99 prevalence had increased. But Agarwal KN et al\textsuperscript{20} reported that in NFHS-II Hemocue method was used for Hb estimation which over estimates Hb as compared to standard Cyanmethhemoglobin method used in NFHS-III and low prevalence reported in NFHS-II might be due to this reason.

- Toteja GS et al\textsuperscript{19} (2006) conducted Indian Council of Medical research (ICMR) study to assess the status of anemia in pregnant women in 16 districts of 11 states of India. Their data showed that 84.9\% pregnant women were anemic with 13.1\% having severe anemia. In adolescent girls prevalence was 90\% with 7.1\% having severe anemia. They confirmed that nutritional anemia is one of India’s major public health problem.

- Kaur S et al\textsuperscript{18} (2006) did the epidemiological survey in adolescent girls of rural Wardha, Maharashtra and showed the prevalence to be 59.8\%. Low socio-economic, low iron intake, vegetarian diet, history of worm infestation and history of excessive menstrual bleeding showed significant association
with anemia. However age, education and BMI did not contribute significantly.

- Chaudhary SM et al\(^{17}\) (2008) showed the prevalence of 35.1% in adolescent girls of urban area of Nagpur. They found significant association with socio-economic status and literacy status of the parents.

- Patil SM et al\(^{49}\) (2009) reported 41% prevalence in adolescent girls of Rathnagiri district of Maharashtra. There was a significant association of anemia with educational status of adolescent girls. They stressed the need to introduce a comprehensive adolescent health initiative at rural level.

**Prevalence: Global**

- WHO\(^{50}\) (1992) report showed prevalence in pregnant women across the world as 50% with 55-60% in developing countries. For non-pregnant women overall prevalence was 1/3rd population of the world with 44% in developing countries and 13% in developed countries.

- Li et al\(^{51}\) (1993) reported prevalence of iron deficiency anemia to be 34% in Chinese female cotton mill workers.

- Even in USA iron deficiency in adolescent girls was reported to be 9 to 11% (Anne Looker 1997)\(^{52}\) and 8.7% (Halterman 2001)\(^{25}\).

- Singh K et al\(^{53}\) (1998) from their cross sectional study in Singapore reported that iron deficiency is the most common cause of anemia in pregnancy responsible for 81.3% cases.
Faruk Ahmed\textsuperscript{54} (2000) reported that among the rural population of Bangladesh prevalence of anemia was 43\% in adolescent girls, 45\% in non-pregnant women and 49\% in pregnant women. The rates in urban population were slightly lower compared with rural areas. A large proportion was due to iron deficiency.

WHO\textsuperscript{5} in 2001 estimated prevalence of 52\% in pregnant females and 42.3\% incidence in nonpregnant females.

Shah BK et al\textsuperscript{55} (2002) reported 68.8\% prevalence in Nepalese adolescent girls. There was no relation to girls' age, body mass index, menarchal status and occupation.

Kisioglu AN et al\textsuperscript{56} (2004) reported 42.71 incidence in pregnant women of Turkey. Anemia was found more in low education group and housewives.

Innanoti LL et al\textsuperscript{57} (2005) reported that 61\% of African American adolescents pregnant had depleted iron stores. However serum folate and serum vitamin B-12 were found normal in them.

Jayatiss R et al\textsuperscript{58} (2006) reported that prevalence of nutritional anemia among adolescent girls was 11.1\% in Sri Lanka, while Hettiarachchi et al\textsuperscript{59} (2006) reported a high incidence of 58.1\% in adolescent girls of Gale district of Sri Lanka. Of these 58.1\% anemic girls majority (47.8\%) had serum ferritin < 30 \(\mu\)g/l.

Killip S et al\textsuperscript{60} (2007) reported that the prevalence of iron deficiency anemia was 9 to 12\% in white women and 20\% in black and Mexican-American women.
De Benoist et al\textsuperscript{4} (2008) reported for world wide prevalence of anemia 1993-2005 WHO Global Database that globally 41.8% pregnant females and 30.2% of nonpregnant females are anemic.

**Nutritional anemia – General Health and Immunity:**

- Srikanthia et al\textsuperscript{61} (1976) from their study on young children indicated that both the cell mediated immune response and the bactericidal activity of leucocytes are impaired when levels of Hb fall to 10 g/dl or less.
- Strauss RG\textsuperscript{62} (1978) analysed the literature available till 1977 to define possible relationship between infections, immune function and state of iron imbalance and stated that inflammatory response is clearly diminished in iron deficiency. The precise molecular defect remains undefined but the abnormality is detected by several assays measuring cell mediated immunity. Normal function is usually restored following iron repletion.
- Bagchi K et al\textsuperscript{63} (1980) studied humoral immune response in children with iron deficiency anemia and observed that humoral immunity is not affected by iron deficiency.
- Swarup Mitra S et al\textsuperscript{64} (1984) confirmed that cell mediated immunity is significantly impaired in nutritional anemia.
- Dallman PR\textsuperscript{65} (1987) however mentioned in his review article on Iron deficiency and the immune response that abnormalities in cell mediated immunity and ability to kill several types of bacteria are well established in
iron deficient patients. But it remains uncertain whether these abnormalities result in an increased incidence and duration of infection.

- Kandoi A et al\(^6\) (1991) studied the cellular immunity status in anemic pregnant women and found that it was decreased as compared to nonanemic pregnant women and it was significantly decreased in severely anemic women.

- Rangan AM\(^7\) (1998) et al from their cross sectional study of 225 female students aged 15 to 30 years regarding iron status and non specific symptoms found that the association between iron status and non specific symptoms was weak.

- Patterson AJ et al\(^8\) (2000) studied 14762 young and 14072 mid-age women in Australia and reported that iron deficiency is associated with decreased general health and well being and increased fatigue. In 2001 they confirmed that treatment with either iron supplementation or high iron diet, both results in improved mental health and decreased fatigue.\(^9\)

- Verdon F et al\(^7\) (2004) from their double blind randomised placebo controlled study of 144 females of Switzerland concluded that oral iron therapy reduced unexplained fatigue in females whose serum ferritin concentrations were \(\leq 50 \mu g/l\).

- Jarrah SS et al\(^7\) (2007) from their study of 206 adolescent girls and 65 pregnancy women mentioned that 50% of anemic females reported daily symptoms or dizziness, fatigue, headache and depression.
Grondin M et al. (2008) concluded that iron deficiency impairs the perceived general health in female students and suggested that further research should be conducted on this subject.

**Nutritional Anemia – Physical Performance:**

- Gardner GW et al. (1977) studied physical work capacity in female tea estate workers in Sri Lanka with iron deficiency anemia and concluded that working capacity is significantly reduced with a concomitant reduction in productivity.
- Edgerton VR et al. (1981) measured selected parameters related to work tolerance in anemic subjects in Sri Lanka and concluded that decrement in work performance capacity in iron deficient and anemic subjects is related to the level of anemia rather than other non-Hb related biochemical changes that could accompany prolonged iron deficiency anemia.
- Koziol BJ et al. (1982) did a study on rats regarding changes in work tolerance in moderate and severe iron deficiency anemia. Their results indicated that there are physiological and metabolic adjustments in anemia, even though lowered level of work tolerance is reached in these cases.
- Rowland TW (1988) confirmed from their study on adolescent runners that even non-anemic iron deficiency states (serum ferritin level < 20 μg/l) impairs exercise performance and can be improved by iron supplement. However, Klingshrin LA et al. (1992) from their study on female distance
runners concluded that though iron supplement improves iron status in iron depleted female runners it does not enhance endurance capacity.

- Li R (1993) from his study on Chinese female workers showed that physical performance both on the job and in the laboratory tests is impaired in iron deficiency anemia, which can be improved by improving iron status. In 1994 he confirmed that anemic females when supplemented with iron resulted in 17% increase in production efficiency.

- Nelson M et al (1994) from their study of 11-14 years old school girls reported that physical performance may be compromised at mild levels of anaemia.

- Zhu Y et al (1997) did physical performance tests in young women with iron depletion without anemia and found that maximum oxygen consumption was significantly associated with serum ferritin concentration.

- Scholz BD et al (1997) from their study concluded that anemia is associated with reduced productivity of women workers even in less physically strenuous works. Anemic workers produced an average of 5.3% less in the factory and performed an average of 6.5 hours less house work per week.

- Untoro G et al (1998) investigated the relationship between body mass index (BMI) and hemoglobin concentration on work productivity in Indonesian female industrial worker and found that anemic subjects produced 4.9% less than the non anemic subjects. No linear relationship existed between BMI and productivity.
Haas JD et al\textsuperscript{26} (2001) evaluated the causal relationship between iron deficiency and physical work capacity through a systematic review of the research literature. They examined 29 research papers and found that there is strong causal effect of moderate to severe iron deficiency anemia on aerobic capacity in animals and humans. The presumed mechanism for this effect is the reduced oxygen transport associated with anemia. Tissue iron deficiency play a role through reduced cellular oxidative capacity which leads to impaire endurance and enegetic efficiency. Endurance is defined as the maximum length of time an individual can sustain a given load. It was also pointed out that strong causal relationship exists between all levels of iron deficiency and voluntary physical activity. They suggested that biological mechanisms for the effect of iron deficiency anemia on work capacity are sufficiently strong to justify interventions to improve iron status as a means of enhancing human capital.

\textbf{Nutritional Anemia – IQ and Cognitive Performance:}

Soemantri AG et al\textsuperscript{83} (1985) studied the effects of iron supplementation on measures of school performance in iron deficient anemic school children and found that iron supplementation in anemic children benefits learning processes as measured by the school achievement test scores.

Lozoff B et al\textsuperscript{84} (1987) found lower mental and motor test scores in infants with iron deficiency anemia even after factors relating to birth, family background, parental IQ and other nutrition were considered.
Sheshadri S et al. (1989) investigated the impacts of iron supplementation on 163 anemic girls aged 8-15 years and found significantly improved scores in cognitive function after the eighth month.

Pollitt E et al. (1989) conducted a double blind clinical trial to assess the impact of iron treatment on the IQ and educational attainment of 1358 subjects of 9-11 years age and found that there is a positive association between iron status and IQ and a school achievement test. However, they mentioned that there is no support for the internal validity of the hypothesis that this association is causal.

Bruner AB et al. (1996) proved that iron supplementation given to 716 iron deficient adolescent girls for 8 weeks improved verbal learning and memory as compared to controls.

Halterman JS et al. (2001) studied 5398 children from 6 to 16 years old in the United States for iron deficiency anemia and cognitive function and found that lower standardized maths scores were obtained in anemic subjects. The risk of scoring below average was greater than twice in anemic children as compared to children with normal iron stores.

Stungthong R et al. (2004) studied the changes in IQ score in iron supplemented adolescents and concluded that at the end of 16 weeks increase in Hb and IQ score was found in iron supplemented group as compared to placebo.

Beard JL et al. (2005) studied the effects of iron deficiency anemia in postpartum females regarding their cognitive and behavioral performance.
and mother-infant interaction. They found strong relation between iron status and depression, stress and cognitive functioning in mothers during postpartum period.

- Murray Kolb LE et al (2007) did a blinded placebo controlled study in women aged 18-35 years for cognitive performance after giving iron and concluded that iron status is a significant factor in cognitive performance in women of reproductive age. Severity of anemia primarily affects processing speed and severity of iron deficiency affects accuracy of cognitive function over a broad range of tasks.

- McCann JC et al (2007) reviewed the evidence for a causal relation between iron deficiency during development and deficits in cognitive or behavioral function. They concluded that in children > 2 years of age and in adolescents with iron deficiency anemia evidence suggests cognitive or behavioral deficits; however the surprisingly small number of studies conducted in either humans or animal prevents a thorough assessment.

**Nutritional Anemia – Obstetric Outcome: Maternal**

- Williams MD et al (1992) reported that because of increased requirements, nutritional anemia are common during pregnancy particularly in women who have inadequate diet. Severe anemia adversely affects the maternal health and even less severe anemia is associated with poor pregnancy outcome.
Koblinsky MA et al\textsuperscript{93} (1995) of thoroughly reviewing maternal mortality mentioned that maternal mortality is only the tip of the iceberg – for every one maternal death nearly 100 women suffered acute obstetrical complications and 1000 women suffer from anemia.

Lindsay AH\textsuperscript{94} (1997) reported that maternal iron deficiency is associated with higher maternal mortality. In the year 2000 she further confirmed that maternal anemia adversely affects the maternal health and weight of evidence supports the routine iron supplementation during pregnancy\textsuperscript{95}.

Rush D\textsuperscript{92} (2000) reported that the risk of death is greatly increased with severe anemia (Hb $<$ 7.0 g%); but there is little evidence of increased risk associated with mild or moderate anemia.

Bernard JB et al\textsuperscript{96} (2001) analysed the cross-sectional, longitudinal and case control studies to find the relationship of anemia as a risk factor for maternal mortality and reported that the relative risk of mortality associated with moderate anemia was 1.35 and for severe anemia it was 3.51.

Bedi N et al\textsuperscript{97} (2001) studied maternal deaths in an ICMR Task Force Study and found that anemia was responsible for 11.5\% maternal deaths.

Corwin EJ et al\textsuperscript{98} (2003) reported that women suffering from early postpartum anemia is at increased risk of developing postpartum depression.

Verma A et al\textsuperscript{99} (2008) from their 7 years study of maternal mortality in Himachal Pradesh, North India showed that anemia was an important cause of death responsible for 15.4\% cases. It was also associated in other
causes of maternal mortality like hemorrhage (20%) and infection (10.8%). He mentioned that pre-existing anemia workers as pregnancy advances and it increases the likelihood of her dying in childbirth by a factor of four.

**Obstetric Outcome: Perinatal**

- Liberman E et al\(^{34}\) (1988) studied the relation of maternal hematocrit level and preterm labour and reported that with five point decrease in hematocrit the risk of preterm labour was tripled.

- Klebanoff MA et al\(^{100}\) (1989) from prospective study of 35423 pregnancies reported that anemia is not a strong factor in the pathogenesis of preterm birth. Early in the third trimester there was a weak association between anemia and preterm delivery. Anemia after 30 weeks gestation was not associated with preterm birth. Subsequently in 1991 however they reported that anemia during second trimester was associated with preterm labour.\(^{101}\)

- Colomer J et al\(^{35}\) (1990) from their study of 154 newborns for 1 year reported that their results show a relationship between iron deficiency anemia in the mother at delivery and the development of iron deficiency in the infants.

- Lu ZM et al\(^{102}\) (1991) from Birmingham reported that early pregnancy hematocrit below 37% is associated with preterm labour while hematocrit above 34% is associated with both preterm labour as well as IUGR.

- Agarwal KN et al\(^{103}\) (1991) from their study of anemia prophylaxis in pregnant women in Varanasi district in India reported that incidence of low
birth weight decreases with iron supplementation. It is more effective if started by 16-19 weeks gestation.

➢ In the same year Heminski E et al\textsuperscript{104} (1991) from Finland studied 2912 pregnant women confirmed that routine iron supplementation has no deleterious effect on birth weight. Couple of previous reports had shown deleterious effects of high hematocrit on fetal growth and weight.

➢ Scholl TO et al\textsuperscript{105} (1992) from their prospective study reported that risk of low birth weight tripled and preterm delivery doubled with iron deficiency. The risks were associated with iron deficiency anemia but not with anemia from other causes. In 1994 they compiled the data on anemia and pregnancy outcome and reported that in the third trimester maternal anemia was no longer a risk factor for poor pregnancy outcomes. However, the relationship between poor diet and increased likelihood of preterm delivery persisted during the third trimester\textsuperscript{106}.

➢ Hokama T et al\textsuperscript{36} (1996) reported that iron stores measured by serum ferritin are significantly lower in newborns of mothers with iron deficiency anaemia.

➢ Preziosi et al\textsuperscript{107} (1997) from Paris reported from their study of 197 pregnant women that Apgar Scores of newborns at birth was higher in babies whose mothers received iron supplementations as compared to those who received placebo.
Singla PN et al\textsuperscript{108} (1997) from their study of 54 anemic women reported that all indices of fetal growth showed linear relationship with maternal Hb.

Kilbride J et al\textsuperscript{109} (1999) from a case control study in Jordan reported that anemia during pregnancy is a risk factor for iron deficiency anemia in infancy.

Steer PJ\textsuperscript{110} (2000) that hemoglobin below 8 gm\% is associated with preterm labour and IUGR while Hb > 12 gm\% at the end of the second trimester is also associated with IUGR.

Rao S et al\textsuperscript{111} (2001) reported from Pune maternal nutrition study in rural Indian women that one third of Indian babies are low birth weight and this is attributed to maternal undernutrition. Intake of micronutrients rich food improves fetal growth.

Rasmussen KM\textsuperscript{112} (2001) conducted extensive literature review and reported that although there are other reasons to offer women supplemented iron during pregnancy the available evidence at that time was insufficient to support or reject the practice of routine iron supplementation to raise the birth weight or decrease the rate of preterm birth.

Lindsay AH\textsuperscript{113} (2001) in Journal of Nutrition explained the biological mechanisms that might underlie Iron's effects on fetal growth and preterm birth. Anemia (by causing hypoxia) and iron deficiency (by increasing serum norepinephrine concentration) 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 labor, pregnancy induced hypertension and eclampsia and premature rupture of 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 fetoplacental unit. Iron deficiency may also increase the risk of maternal infection which can stimulate the production of CRH and are a major risk factor for preterm delivery.

➢ Tamura T et al\textsuperscript{114} (2002) from their study of cord serum ferritin concentration at birth reported that poor iron status (low ferritin) was associated with diminished performance in mental and psychomotor tests in their study of 278 children.

➢ Lozoff B et al\textsuperscript{115} (2003) from their study of 1123 infants and 534 controls showed that infants whose mothers have received iron supplementation had developmental and behavioral benefits.

➢ Cogswell ME\textsuperscript{116} et al (2003) from their randomized placebo control trial on 513 low income pregnant patients showed that iron supplementation significantly reduced the incidence of low birth weight infants (4\% as against 17\% in placebo group).

➢ Gambling L et al\textsuperscript{117} (2004) by their animal study on rats proved that neonatal size correlates with maternal Fe stores and Fe supplementation is more effective when given early in gestation.
Ronnenberg AG et al (2004) from their study on Chinese women reported that even preconception anemia is related to reduced growth and adverse pregnancy outcome.

Scholl TO et al (2005) however reported that while iron supplementation may improve pregnancy outcome when the mother is iron deficient, it is also possible that prophylactic supplementation may increase risk for preterm labour, IUGR and preeclampsia when the mother does not have iron deficiency or IDA.

Zhou SJ et al (2006) reported that prenatal iron supplementation reduces, the incidence of iron deficiency anemia from 11% to 1% but has no effect on the IQ of the baby at 4 years of age.

Palma S et al (2008) reported that iron but not folic acid supplement reduce the risk of low birth weight in pregnant women.

Zhang Q et al (2009) reported that anemia in pregnancy is associated with increased risk of preterm premature rupture of membranes.

**Nutritional Anemia - Prevention and Treatment**

Sood SK et al (1975) carried out WHO sponsored collaborative study on nutritional anemia in Delhi and Vellore to see the effects of oral iron supplementation to pregnant women. Different doses of iron ranging from 30 to 240 mg were studied. They concluded that 120 mg elemental iron is needed to provide adequate daily supplementation. In 1979 They compared...
parenteral iron with oral iron and concluded that intravenous administration of iron dextran was not superior to oral iron in terms of response however intramuscular iron dextran produced a greater rise in Hb as compared to oral iron.\textsuperscript{124}

\begin{itemize}
  \item Ballin A et al\textsuperscript{125} (1992) studied subjective response to iron therapy in female adolescents and found that there is statistically significant improvement in three parameters i.e. lassitude, the ability to concentrate in school and mood.
  \item Al-Momen AK et al\textsuperscript{126} (1996) compared IV iron sucrose with oral ferrous sulphate and confirmed that iron sucrose is safe and effective in the treatment of iron deficiency anemia.
  \item Halak M et al\textsuperscript{127} (1997) reported that intravenous iron is an effective method of regeration of Hb and iron stores during pregnancy. It should be considered for patients with severe iron deficiency anemia and who can not use oral preparations.
  \item Viteri FE et al\textsuperscript{128} (1999) from their double blind study on non pregnant female of weekly iron supplementation for seven months reported that weekly iron supplementation improves and sustains iron status as well or better than short term daily supplementation.
  \item Beard JL\textsuperscript{129} (2000) pointed out that iron supplementation during pregnancy suffers from real problems of compliance. Large doses of iron are associated with side effects and increased oxidative damage. Alternatively
\end{itemize}
delayed release preparations and intermittent oral supplementation leads to better overall compliance.

➢ Lynch SR\textsuperscript{130} (2000) reported that iron supplements during adolescence is one of the new strategies advocated to improve iron balance in pregnancy. However, the positive effect on iron status will be temporary if their diets do not contain adequate bioavailable iron.

➢ Zavaleta N et al\textsuperscript{131} (2000) studied the efficacy and acceptability of two iron supplementation schedules in adolescent school girls in Lima, Peru and reported that both daily and intermittent supplementation schedules were efficacious in preventing iron deficiency, the daily schedule was better in increasing Hb values and reducing anemic.

➢ Patterson AJ et al\textsuperscript{69} (2001) reported that treatment of iron deficiency in Australian women of child bearing age with either supplementation or a high iron diet results in improved mental health and decreased fatigue.

➢ Breyman C\textsuperscript{132} (2001) from Switzerland also reported that iron sucrose is the treatment of choice in gestational iron deficiency anemia resistant to orally administered iron.

➢ Perewusnyk G et al\textsuperscript{133} (2002) reported their 8 years experience with iron sucrose IV and mentioned that rate of blood transfusion can be decreased to 1% even in severe anemia.
Bayoumen F et al\textsuperscript{134} (2002) from their randomised prospective study confirmed that iron sucrose is without serious side effects and indicated in correction of pregnancy anemia.

Ekstrom EC et al\textsuperscript{135} (2002) from their study of 50 antenatal centres suggested that current international recommendations for daily iron supplementation in pregnancy is higher than necessary. Tablet Ferrous sulfate 60 mg given orally twice a week and repeated weekly may be sufficient.

Makrides M et al\textsuperscript{136} (2003) did a randomized controlled study and reported that even low dose iron supplements during pregnancy of 20 mg iron/day from 20 weeks onwards is also an effective strategy.

Meier PR et al\textsuperscript{137} (2003) reported that world wide attention over iron deficiency anemia in pregnancy has shifted recently from providing supplements during pregnancy to attempting to ensure that women especially adolescents have adequate iron stores prior to conception. The incidence of anemia in pregnancy is substantially reduced with 60 mg elemental iron / day given to adolescents.

Cogswell ME\textsuperscript{138} (2003) reported that in US women group, at highest risk of iron deficiency (e.g. low income and minority women) are often least likely to consume supplements containing iron suggesting that supplement use is unrelated to actual need.
Ragip A et al\textsuperscript{139} (2005) from Ankara Turkey from their study of anemia in pregnancy again confirmed that IV iron restores iron stores faster than oral iron.

Bhandal N et al\textsuperscript{140} (2006) from their study on postpartum patients reported that IV iron sucrose increases the Hb level and replenishes iron stores more rapidly than oral iron.

Haider BA et al\textsuperscript{141} studied nine trials involving 15,378 women for Cochrane Systematic Review (2006) and concluded that there is no added benefit of multiple micronutrient supplementation compared with iron + folic acid supplementation.

Pena Rosas JP et al\textsuperscript{142} studied 49 trials involving 23,200 women and concluded in Cochran Database of Systematic Reviews (2009), that universal prenatal supplementation with iron or iron + folic acid provided either daily or weekly is effective to prevent anemia and iron deficiency at term. However, there is no significant reduction in maternal and neonatal adverse clinical outcomes. There is need for revising iron doses and adjust preventive iron supplementation recommendations.

McClung JP et al\textsuperscript{143} (2009) recently reported that iron supplementation is beneficial for mood and physical performance in female military personnel in USA during training period.

Murraykolb LE et al\textsuperscript{144} (2009) from their study on postpartum women showed that maternal iron deficiency anemia negatively affects mother child
interactions like sensitivity, structuring, responsiveness and involvement. Iron supplementation protects against these negative effects.

- Bencaiova G et al\textsuperscript{145} (2009) compared I/V versus oral route for iron prophylaxis in pregnancy and found no significant difference in hematological, maternal and fetal outcomes with either route of treatment.

**Nutritional Anemia – Food Fortication**

- Vijayaraghavan K et al\textsuperscript{146} (1990) evaluated the National Nutrition Anemia Prophylaxis Program and reported that the reasons for poor coverage were inadequate and irregular supplies. The health functionaries were not properly oriented towards the program and many were unaware of all the beneficiaries under the program. Chemical analysis of tablets indicated that about 30 percent of the tablet samples had iron content less than the expected levels.

- Bothwell TH\textsuperscript{12} (2000) in his article on "Iron requirements in pregnancy and strategies to meet them" stated that preventive supplementation strategy has the drawback of depending on delivery systems and good compliance on a long term basis so iron fortification offers the most cost effective option.

- Baltussen R et al\textsuperscript{147} (2004) also concluded that fortification is economically more cost effective than iron supplementation regardless of the geographic coverage of fortification.
Mannar MG et al\textsuperscript{148} (2004) stated food fortification remains an underutilized opportunity in many developing countries where micronutrient malnutrition remains a public health problem. Fortification of foods can provide meaningful amounts of the nutrient at normal consumption of food vehicle. Proper choice of fortification and processing methods could ensure the stability and bioavailability of the nutrient.

Horton S\textsuperscript{149} (2006) discussed the economics of food fortification and mentioned that it has played an important role in its implementation in public policy. Cost effectiveness (as measured by cost per death averted or cost per disability adjusted life year – DALY saved) has helped to give fortification high priority as a preventive health care intervention.

The focus is primarily on commercial fortification, although home fortification and bifortification are also considered. Home fortification involves adding a micronutrient preparation to home prepared food, biofortification involves selective breeding or genetic modification to produce higher micronutrient varieties. Biofortification of rice is of particular interest because it is more difficult and costly to fortify rice by conventional means than the other grains.

Moretti D\textsuperscript{150} (2006) did double blind study in school children in Bangalore and reported that extruded rice fortified with Micronized Ground Ferric Pyrophosphate (MGFP) reduces the prevalence of iron deficiency.
Anderson M\textsuperscript{151} (2008) from her study on school children in southern India reported that Dual fortification of salt with iodine and iron is efficacious in reducing the prevalence of both anemia and iodine deficiency.

Baqui AH et al\textsuperscript{152} (2008) from their survey in rural Uttar Pradesh reported that NGO facilitation of government programmes is a feasible strategy to improve implementation of maternal and neonatal health programs.

Tako E\textsuperscript{153} (2009) from their study on piglets concluded that the biofortified beans is a promising vehicle for increasing intakes of bioavailable Fe in human populations that consume beans as a dietary staple.