ORIGINAL ARTICLE

EFFECT OF IRON WITH MINERAL AND MULTIVITAMIN SUPPLEMENTATION ON TRANSFERRIN SATURATION INDEX IN IRON DEFICIENCY ANEMIA DURING PREGNANCY

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Background: Anaemia during pregnancy is associated with labour/delivery complications like, preterm delivery, low birth weight, reduced infant iron stores, impaired mother-child interactions, and increased infant and maternal mortality. The objective of current study was to find out whether supplementation of oral iron (three times a day) would affect Transferrin Saturation Index as effectively as supplementation with combination therapy (iron with multiple vitamin and minerals) in pregnant women with iron deficiency anaemia. **Methods**: Two hundred primigravidae visiting the obstetric outpatient department of Services Hospital Lahore, between 14th and 18th week of gestation were included in the study. Among 200 pregnant women, 100 women receiving once daily tablet of supplementation including 2 supplements in tablet form containing 60 mg Iron with multivitamin and minerals were considered as group A. Group B consisted of 100 women receiving ferrous sulfate tablet three times a day (60 mg elemental iron). Level of serum iron and Total Iron Binding Capacity (TIBC) were estimated by standard kit methods. After informed consent, blood samples were taken between 14th to 18th week of gestation and follow-up samples were taken at 36th week of gestation. **Results:** Levels of hematological parameters were compared before and after therapy at 14th to 18th week and 36th weeks respectively. The level of TIBC was increased significantly (p<0.001) after the combination therapy. Ratio of iron to TIBC or transferrin saturation index was markedly decreased after the combination therapy in this group. The level of TIBC was significantly decreased (p<0.001) after the therapy. Ratio of iron to TIBC or transferrin saturation index was markedly increased after the iron therapy in this group.
Conclusion: Supplementation of iron with multivitamins and minerals has a role in increasing TIBC in pregnant females with iron deficiency anaemia.

Keywords: Iron deficiency anaemia, iron supplement, multiple micronutrients, Pregnancy

INTRODUCTION

Iron deficiency anaemia (IDA) is the most frequent form of anaemia in pregnant women especially common in the 3rd trimester. Less than 50% women do not have adequate iron stores for pregnancy.[1, 2] According to estimates from WHO, an average of 56% of pregnant women in developing countries while 18% of women from industrialized countries are anemic.[3] Nearly half of the pregnant women in Pakistan are anemic.[4]

The reason for high prevalence of anaemia during pregnancy is nutritional deficiency of iron and folate.[5] Insufficient dietary intake and absorption of iron and/or iron loss from intestinal bleeding, parasitic infestation, menstruation, etc. are the main causes.[6] In pregnant women a significant increase in the amount of iron is required to increase the red cell mass and to expand the plasma volume to allow for the growth of foetal-placental unit.[1,2]

Anaemia during pregnancy is associated with complications like preterm delivery, low birth weight, reduced infant iron status, impaired mother-child interactions, and increased infant and maternal mortality.[6–8] At time of entry in the trial, women with IDA had a significantly lower energy intake (500 Kcal/d less) and iron intake from diet.[9,10] This difference of energy may be associated with increased risks of inadequate weight gain for gestation.[5]

Adverse pregnancy outcomes include intrauterine growth retardation, premature delivery, and infant haematologic compromise.[11,12] Anaemia is defined as haemoglobin (Hb) of <110 g/L in the first and third trimester and <105 g/L in the second trimester. The diagnosis relies on haemoglobin, a full blood count and plasma ferritin and it can be supported by plasma transferrin saturation. Minor causes of anaemia are folate and vitamin B_{12} deficiency, haemoglobinopathy and haemolytic anemia.[13] Mean corpuscular volume (MCV) declines throughout the 1st and 2nd trimesters reaching the lowest point late in 2nd to early in the 3rd trimester. A low MCV and Mean corpuscular haemoglobin concentration (MCHC) often appears next during the course of body iron depletion. It corresponds to a high number of abnormally small red blood cells in peripheral smear.[14]

Body-store iron deficiency is diagnosed by low serum ferritin and iron level, an elevated serum transferrin and a high TIBC. However, serum ferritin can be elevated by any type of chronic inflammation and so is not always a reliable test of iron status. The ratio of serum iron to TIBC (called iron saturation or transferrin saturation index) is the most specific indicator of iron deficiency. The iron saturation of <5% almost always indicates iron deficiency, while levels from 5% to 10% make the diagnosis of iron deficiency possible but not definitive.[11,13]

Treatment of IDA should aim at replenishing body iron deficits by oral and/or intravenous administration of iron. Requirements for absorbed iron increase during pregnancy from 0.8 mg/day in the first trimester to 7.5 mg/day in the third trimester to reduce the frequency of prepartum IDA. However, IDA is efficiently prevented by oral iron supplements in doses of 30–40 mg ferrous iron from early pregnancy to delivery.[11,14] During the past few years, the relation between anaemia early in pregnancy and an increased risk of preterm delivery has been suggested.

The aim of this study was to find out whether three times a day supplementation of oral iron would improve saturation index for iron as effectively as supplementation with combination therapy (iron with multiple vitamin and minerals) in pregnant women with iron deficiency anaemia.

MATERIAL AND METHODS

A total of 200 primigravidae between 14th and 18th week of gestation presenting to the obstetric OPD of Services Hospital Lahore were included. This study was designed for 12 weeks. Women included in the study had Hb <11.0 gm/dl irrespective of their age, social status and education. Patients were divided into two groups on the basis of supplementation they received. Among 200 pregnant women, 100 women receiving once daily tablet of supplementation containing 60 mg iron with multivitamin and minerals were considered as group A. while Group B was consisting of 100 women receiving ferrous sulfate tablet thrice daily (60 mg elemental iron). Inclusion criteria were singleton pregnancy, more than 12 weeks of gestation with no prior intake of iron in current pregnancy.

Women with chronic blood loss, UTI and any chronic diseases like tuberculosis and rheumatoid arthritis were excluded from the study. No placebo group was included in the study. Level of serum iron and TIBC were estimated by standard kits (supplied by Wiener Laboratories SAIC Riobamba 29442000-Rosario-Argentina). After informed consent blood samples were taken between 14th to 18th week of gestation and second blood samples were taken at 36th week of gestation.

Statistical analysis was carried out by using SPSS-12. The values are presented as Mean±SEM. Student's *t*-test was used to compare between the two groups and $p<0.05$ was considered as significant.

RESULTS

Comparison of level of blood haemoglobin, serum Iron, TIBC and its ratio in different groups before and after iron alone and combination therapy are shown in Figure-1 and Figure-2. Levels of all parameters were estimated before (at 14-18 weeks) and after therapy (36th week). It was observed that in group A the level of haemoglobin and serum iron were decreased after the combination therapy but the level of TIBC was significantly increased. Ratio of iron to TIBC or transferrin saturation index was markedly decreased after the combination therapy ($p<0.001$). In Group B the level of TIBC was significantly decreased after the therapy and this showed a highly significant difference ($p<0.001$). Ratio of iron to TIBC or transferrin saturation index was markedly increased after the iron therapy. Comparison of haematological parameters in group A and B are shown in Table-1.

DISCUSSION

The observation that maternal anaemia increases risk of poor pregnancy outcome may depend on the stage of pregnancy, when the anaemia is measured. In mid-pregnancy and late in the 3rd trimester, the influence of maternal anaemia on pregnancy outcome is markedly attenuated but not reversed. However several studies have reported reduced risks of preterm delivery or low birth weight or no association between anaemia and preterm birth when the relation was studied during the 3rd trimester.[15,16]

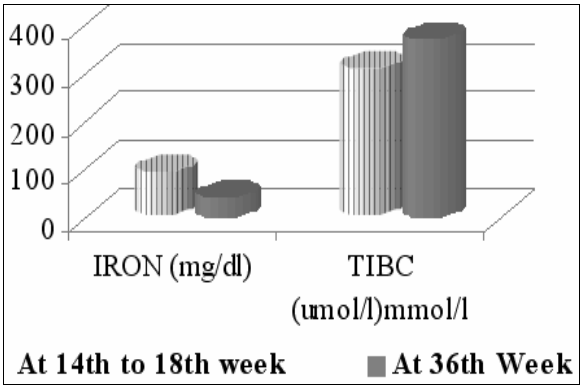

Figure-1: Comparison of pre- and post-treatment iron and TIBC in Group A

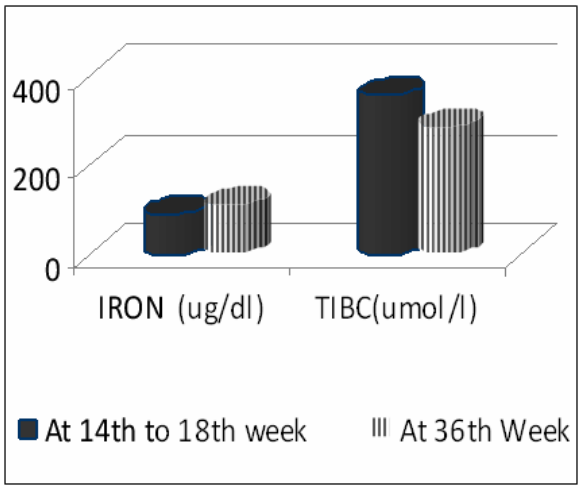

Figure-2: Comparison of pre- and post-treatment iron and TIBC in Group B

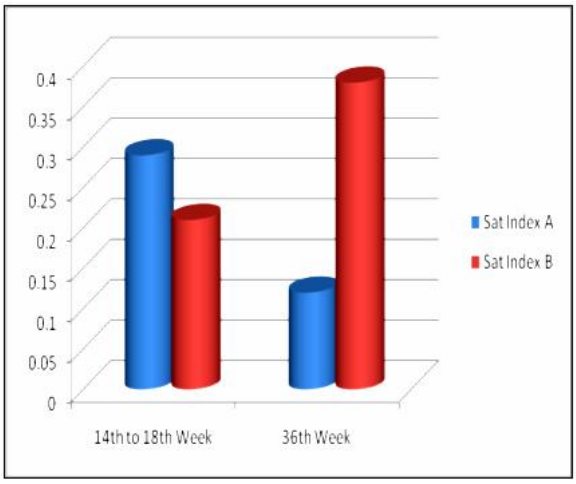

Figure-3: Comparison of Saturation Index between Group A and Group B

Table-1: Iron and Total Iron Binding Capacity (TIBC) before and after treatment in group A and B

Group	Iron (Mean±SD)		*p*	TIBC (Mean±SD)		*p*	Transferrin Saturation Index
	14 to 18 Week	36th Week		14 to 18 Week	36th Week		*p*
A	90.89±40.27	47.26±23.94	<0.001	309.02±40.17	475.83±35.31	<0.001	Decreased <0.001
B	49.60±24.27	108.43±31.38	<0.001	357.08±49.19	281.08±14.20	<0.001	Increased <0.001

Present study measured anaemia according to standard set by Food and Nutrition Board which define that TIBC>400 µg/dl, transferring saturation<16%, serum ferritin<12 µg/l indicate iron deficiency anemia.[17] Number of studies reported that risk of preterm delivery and low birth weight were increased >2-fold in moderately anaemic women and >3-fold in those who were severely anemic.[16,18]

Current study supports that with decreased haemoglobin and serum iron, the values of MCV and MCHC were significantly decreased (p<0.05) after the combination therapy. A study observed that haemoglobin showed a significant correlation with MCH, MCHC, serum iron, and percent transferrin saturation, suggesting that the anaemia was likely to be due to iron deficiency.[17]

A study suggested three potential mechanisms whereby maternal IDA might give rise to preterm delivery: hypoxia, oxidative stress and infection (reduced immune function, increased production of prostaglandin, increasing risk of a preterm birth).[19] Our study is in accord with a study that indicates that multiple micronutrients including multi-vitamins and minerals show no reduction in the risk of low birth weight.[6]

In many studies it has been found that gravidas receiving iron and folate increased birth weight by 37 g and showed a reduction of 14% in risk of low birth weight.[5] Randomised trials of iron prophylaxis during pregnancy have demonstrated positive effects on reducing low haemoglobin and increasing serum iron and other measures.[20,21] Another study reported that a comparative small increase in Hb and other RBCs indices might favour an iron over load in daily iron therapy. Observations of a study favour intermittent iron (once a week) as an effective mode of treatment for IDA in pregnancy.[22]

A study reported that iron supplementation during pregnancy increases maternal iron status including haemoglobin, serum iron, MCV, MCHC and transferrin saturation. Transferrin saturation and MCHC displayed the highest true positive rates of iron status markers.[23] However another study showed that iron react with reactive oxygen species is capable of changing valence of iron, ($Fe^{2+} \rightarrow Fe^{3+}$) into a very reactive free radical. These free radicals have the potential to damage cells, organs, and tissues in the body.[24] Prenatal supplement uses, appears to reduce the risk of low folate and B_{12} blood values but not biochemical iron status.[25] A research suggests that women who develop iron deficiency anaemia in mid-pregnancy can be effectively treated with low doses of iron (20–40 mg per day) as body adapts to oral iron supplementation. The lower dose produces fewer gastrointestinal complaints.[26]

In view of this it is suggested that iron supplements along with multivitamins and minerals in low doses preferably (60 mg) should be taken on a regular basis, starting from first trimester of pregnancy.

CONCLUSION

Supplementation of iron with multivitamins and minerals may play a role in increasing TIBC in pregnant women.

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