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# Evaluation of Serum Iron And Copper Status In Pregnant Women With Iron Deficiency Anemia

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**ABSTRACT**

*Iron deficiency is thought to be the most common cause of anemia globally. Pregnancy is associated with increased demand for all the nutrients like iron, copper, zinc, vitamin-B12, folic acid and ascorbic acid. Deficiency of any of these substances might affect pregnancy, delivery and outcome of the pregnancy. Minerals have important influence on the health of pregnant women and of the growing fetus. All body functions are affected by iron deficiency in general and not only by anemia, which appears late in the process of tissue iron deficits. The study included 40 pregnant women suffering from IDA (Iron deficiency anemia) with haemoglobin level less than 11.0 g/dl as cases and 20 non-anemic pregnant women with normal blood hemoglobin 12 g/dl were taken as controls. In pregnant women; intestinal iron absorption is significantly affected by competing high serum copper. Adequate and balanced iron diet and supplements are required during pregnancy. More research in copper iron interaction is recommended in pregnant women with IDA.*

**KEYWORDS : Iron-deficiency, pregnancy, Anaemia, Ferritin, Iron and TIBC.**

**Introduction:**

Iron is a universal co-factor for mitochondrial energy generation and supports the growth and differentiation of all cell types. During pregnancy there is a significant increase in the amount of iron required to increase the red cell mass, expand the plasma volume and to allow for the growth of the fetal-placental unit and this impose such a demand on maternal iron stores that iron supplementation at daily doses between 18 and 100 mg from 16 weeks gestation onwards could not completely prevent the depletion of maternal iron stores at term[1]. The development of iron deficiency anaemia is associated with increased risk of preterm births and low birth-weight infants[2]. The physiologic importance of storage iron is that it provides a rapidly available supply in the event of blood loss[3]. To achieve iron balance, towards the end of pregnancy, the absorption of 4-5 mg/day is necessary. Requirements are higher during periods of rapid growth in early childhood and adolescence[4].

Iron deficiency is thought to be the most common cause of anemia globally[5]. Pregnancy is associated with increased demand for all the nutrients like iron, copper, zinc, vitamin-B12, folic acid and ascorbic acid. Deficiency of any of these substances might affect pregnancy, delivery and outcome of the pregnancy[6]. Minerals have important influence on the health of pregnant women and of the growing fetus. All body functions are affected by iron deficiency in general and not only by anemia, which appears late in the process of tissue iron deficits[7].

Iron is distributed in the body in a number of different compartments; hemoglobin, myoglobin and tissues mainly liver spleen and bone marrow. Only 0.1% of total body iron is spread in plasma. Iron deficiency results in anemia, which may increases the risk of death from hemorrhage during delivery[8]. Iron-deficiency anemia in pregnancy may have a serious effect on the health of both the mother and the baby; anemia can increase maternal and infant morbidity and mortality[9,10]. The mechanisms leading to increased morbidity include a decreased oxygen delivery capacity and the dysfunction of enzymes[9].

The cause of iron-deficiency anemia in pregnancy is a complex combination of increased iron demand, low iron intake, and chronic blood loss[11,12]. Many factors have been associated with the risk of iron-deficiency in pregnancy, such as nutritional status, socioeconomic variables, culture, age, parity, spacing of pregnancies[9,13,14]]. Iron is stored in the body as ferritin[15]. Serum ferritin concentration declines very early in the development of iron deficiency and it serves as a very sensitive indicator of iron deficiency [15,16].

Iron binding capacity is a measure of an iron that serum protein can combine. Nearly all the binding capacity is due to transferrin. Normally; only about one third of the iron binding sites of transferring are occupied by iron, so that serum transferrin is considered as reserve iron binding capacity. A decrease in iron binding capacity may be due to heamochromatosis, acute iron poisoning. Increased IBC appears in iron deficiency anemia[16,17].

Copper is an essential trace element, it is widely distributed in foodstuff. Its daily requirement is a round 1.5-3 µg for adult. Only 5 to 10% of dietary copper is absorbed, after absorption it is first loosely bound to plasma albumin and then transferred to circulating ceruloplasmin in firm combination[18-20]. During pregnancy, the metabolism of copper and iron is tightly interlinked. Deficiency of one has marked effects on the metabolism of the other metal. In the mother, iron deficiency results in the increase of liver copper levels. This is associated with an increase of serum copper levels in the mother and in the activity of maternal serum ceruloplasmin[21].

Copper is required for the formation of many enzymes, with important role in the human body. It has an important role in pregnancy for the formation of a wide variety of enzymatic and other processes within the developing fetus. During pregnancy, many changes occur in copper levels and transport in both mother and fetus. The serum copper increases in early pregnancy and continues to rise to reaching levels at full term approximately twice those found in non-pregnant women. Maternal age does not influence copper serum levels[22]. The placental transport system changes during the latter stages of the development resulting in the transport of higher copper values towards the end of gestation than that of earlier pregnancy. The third trimester copper is higher than in the first trimester[21]. Serum ferritin levels are measured in medical laboratories as part of the iron studies workup for anemia. The ferritin levels measured usually have a direct correlation with the total amount of iron stored in the body. If the ferritin level is low, there is a risk for lack of iron, which could lead to anemia. In the setting of anemia, low serum ferritin is the most specific laboratory test for iron deficiency anemia[23]. Total iron binding capacity (TIBC) is a blood test to see if a body has too much or too little iron in the blood. Iron moves through the blood attached to a protein called transferring. This test indicates how well that protein can carry iron in the blood[24].

The ratio of serum iron to TIBC (called iron saturation or transferring saturation index or percent) is the most specific indicator of iron deficiency[25].

Iron supplements are commonly recommended during pregnancy. Worldwide, poor pregnancy outcome has been most commonly associated with anemia caused by low plasma levels of iron[26]. The alteration of iron status during pregnancy alters copper levels that can be explained by changing levels of gene expression. In the mother, iron deficiency results in an increase in copper levels in the liver. This is associated with an increase in serum copper levels in the mother and in activity of ceruloplasmin in the maternal serum [27].

**Material and methods:**
The present study was conducted in Department of Pathology, Pacific Institute of Medical Sciences, Umarada, Udaipur, Rajasthan, India. The study was carried out among Rajasthani pregnant women with IDA as patients and non anemic pregnant women as control. All of them were in the third trimester, attending antenatal clinic in the department of obstetrics and gynecology of the Pacific Institute of Medical Sciences, Umarada, Udaipur, Rajasthan, India during the period from June 2015 to November 2015. The study included 40 pregnant women suffering from IDA with haemoglobin level less than 90g/l (<11.0 g/dl) aged 20 to 45 years (mean 30.5) and 20 non-anemic pregnant women with normal blood hemoglobin according to WHO hemoglobin cut-off of 110 g/l(12 g/dl) for pregnant women, with mean age (28.2), were taken as control (previous studies bases). All the subjects were in normal diet (three meals per day), and not taking any drug except Fefol one capsule per day (150mg ferrous sulphate and 0.5mg folic acid), which is a part of antenatal care, with no religion restrictions concerning any type of meat. Ethical clearance was obtained from the ethical committee in the Pacific Institute of Medical Sciences. Informed consents were taken before blood collection.

Patients with any obstetrical abnormalities or diseases complicating pregnancy were excluded. 5ml of venous blood were collected from all subjects in the ethyl diamine tetra acetic acid (EDTA) anticoagulant and a plain container using vacutainer. EDTA samples were used for performing full blood counts by computerized heamoanalyzer, from the same specimen, peripheral blood films (PBF) were prepared and stained with Leishmann's stain, for confirming anemia (microcytic hypochromic red blood cells). Serum was separated using electric centrifuge at 2500 RPM for five minutes. Full automated chemical analyzer was used for the measurement of serum iron, ferritin and total iron binding capacity, while iron saturation was calculated using the formula (iron /TIBCx100). Flameless atomic absorption was used for the measurement of serum copper. Statistical analysis was done using SPSS-16. The differences between means of more than two groups were tested by performing ANOVA.

**Results and Discussion:**
A total of 60 women were selected in the study, 40 pregnant women suffering from IDA as test group and 20 non-anemic pregnant women as controls. Overall, the subjects were in the age range 20–45 years. The mean age of control group was 28.2±0.9 year, and the mean of hemoglobin (Hb) was found (10.37±0.78 g/dl) for the patients versus (12.50±1.17g/dl) for control. The mean cell volume (MCV) was (61.9 ± 0.8fl) for the patients versus (78.5 ± 0.6 fl) for non anemic pregnant women. The mean age for the IDA women was (30.5±0.3 year) versus (28.2±0.9 years) for the control women.

**Table 1: Evaluation of haemoglobin, MCV, serum iron, serum ferritin, total iron binding capacity, iron saturation and serum copper in Rajasthani pregnant women with iron deficiency anemia and non anemic pregnant women:**

| Variables | Anemic pregnant women (n=40) (Mean ± Std) | Non anemic pregnant women (n=20) (Mean ± Std) | P value |
|---|---|---|---|
| Age (years) | 30.5±0.3 | 28.2±0.9 | - |
| Hb(g/dl) | 10.37±0.78 | 12.50±1.17 | 0.001 |
| MCV (fl) | 61.9 ± 0.8 | 78.5 ± 0.6 | 0.001 |
| Ferritin (µg/l) | 11.81±4.11 | 54.39±20.05 | 0.001 |
| Iron (µg/dl) | 52.82± 19.3 | 70.65± 16.12 | 0.001 |
| TIBC (µg/dl) | 438.66± 46.4 | 304.76± 28.76 | 0.001 |
| Saturation (%) | 14.3 ± 0.7 | 26.5 ± 0.7 | 0.001 |
| Copper (µg/l) | 242.7 ± 2.1 | 201.7 ± 2.2 | 0.001 |

**(Statistically Significant (P<0.05)**

Iron deficiency and iron deficiency anaemia in pregnancy is an important preventable cause of maternal and perinatal morbidity and mortality. Iron deficiency is the most prevalent specific single micro-nutrient deficiency affecting approximately 50% of the world population. Among the most affected by this malady are pregnant women due to added iron requirements during pregnancy. This is primarily because the amount of dietary iron absorbed is often too small to meet the increased demand during pregnancy.28

In pregnancy hemoglobin concentrations change to accommodate the increasing maternal blood volume and the iron needs for the fetus. It is also associated with adjusted amount of all other trace elements like iron and copper. Micronutrients interactions are particularly important during pregnancy[29].

Data from the present study show significant decrease in the levels of serum iron, serum ferritin and iron saturation in the Rajasthani pregnant women with IDA when compared with non anemic pregnant women in Table-1 (p value=0.001). These findings are consistent with that previously reported by Emmanuel and co-researcher in Nigeria, Chitra and colleagues from India and Bushra and coworkers from Sudan[30,31,32]. Decreasing of serum iron, ferritin and iron saturation in the mechanism of erythropoiesis in the fetus and mother. These marked iron metabolism disturbance in the patient's group, may be due to reduction intake or simultaneous intake of food inhibiting iron absorption or increased metabolic demands. As there is no religion restriction for diet in Rajasthan, it is common that the pregnant women suffer from vomiting and nausea that reduce the food available for absorption. Others eat river mud (River Nile mud) that may interrupt the intestinal absorption of microelements especially the iron. In this study the data also show significant increase in the serum copper (p<0.001) in the pregnant anemic women. This finding is consistent with the an Indian study reported by Chitra et al. and Sengupta et al. and while in disagreement with that reported by Bushra et al. from Central Rajasthan who reported a lower level of copper in anemic pregnant women[29,33].

The significant increase in serum copper in this study is due to the alteration of iron status during pregnancy that alters copper levels due to changing levels of gene expression, leading to increase copper levels in the serum of the pregnant women, which associated with reduced serum iron, as reported by McArdle et al.[31]. Women with iron deficiency anemia show significantly lowered serum iron, serum ferritin and iron saturation. The study revealed a significant increase in serum copper. Iron deficiency results in an increase in copper levels in the liver. This is associated with an increase in serum copper levels in the mother and in activity of ceruloplasmin in the maternal serum[21,27].

**Conclusion:**
A single best marker of iron deficiency does not exist, however, the different tests efficiently compliment each other by detecting different stages, and individually show the clinical extent of iron deficiency. In pregnant women; intestinal iron absorption is significantly affected by competing high serum copper. Adequate and balanced iron diet and supplements are required during pregnancy. More research in copper iron interaction is recommended in pregnant women with IDA.

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