ORIGINAL ARTICLE

ASSESSMENT OF IRON DEFICIENCY IN PREGNANT WOMEN BY DETERMINING IRON STATUS

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Background: Pregnant women constitute a high risk group for iron deficiency. Maternal iron deficiency and particularly iron deficiency anaemia may be associated with detrimental effects on maternal and infant function and particularly with a higher risk of preterm delivery and delivery of low birth weight neonates. Objective of this study was to assess and compare the iron status of normal healthy non-pregnant women with that of pregnant women of Hazara Division. **Methods:** This study was conducted at Faculty of Health Sciences, Hazara University, and Ayub Medical College, Abbottabad from 1st March to 31st August 2006. Altogether 120 women, 90 pregnant at various stages of pregnancy and 30 non-pregnant women as control group were included in this study by convenience sampling. Their iron status was assessed by determination of haemoglobin (Hb), Serum ferritin, Serum-iron, Total Iron Binding Capacity (TIBC), Unsaturated Iron Binding Capacity (UIBC), and Percentage saturation of transferrin. Data generated on these variables were subjected to ANOVA and correlation analysis. **Results:** The salient finding of this study is a significant decrease in Hb, Serum ferritin, Serum iron, percentage saturation of transferrin and a significant increase in values of TIBC and a pronounced increase in UIBC in 2nd and 3rd trimester compared to 1st trimester in iron deficient pregnant women. The mean values of Hb, SF, and Fe/TIBC% were significantly lower in the cases than in the control and significantly higher values of TIBC and UIBC were observed in the cases compared to controls. Significant correlations were observed for TIBC, UIBC and Fe/TIBC% against serum iron in different trimesters of pregnancy. **Conclusion:** A high percentage of the pregnant women are iron deficient due to factors such as high parity, poor dietary habits and socioeconomic status.

Keywords: Iron-deficiency, pregnancy, Anaemia, Ferritin, TIBC, UIBC, Transferrin

INTRODUCTION

Pregnancy is a physiological condition and usually has no effect on general health of a pregnant woman. However pregnancy results in hormonal, haemodynamic and haematological changes. These physiological changes need to be viewed as normal adaptations determined by nature. Increased total blood volume and haemostatic changes help to combat the hazards of haemorrhage at delivery.[1] The increase is less in iron deficient women than in those with iron reserves. In some iron deficient women this inability to expand plasma volume may mask a decrease in haemoglobin concentration.[2]

The lowest normal haemoglobin in the healthy non-pregnant woman is defined as 12 g/dl. The World Health Organization (WHO) recommends that haemoglobin ideally should be maintained at or above 11.0 g/dl, and should not be allowed to fall below 10.5 g/dl in the second trimester.[3] Pregnancy usually induces a slight increase (2–3 fl) in mean red cell volume (MCV), independent of folate status. This is sometimes enough to mask the microcytosis normally found in iron deficiency. Other causes of microcytic anaemia, such as thalassemia trait, the anaemia of chronic disease and inflammatory anaemia of infection are rarely confused with Iron deficiency anaemia (IDA) in pregnancy and are excluded by standard haematological investigations.[4]

Iron absorption during pregnancy is determined by the amount of iron in diet, its bioavailability (meal composition) and the changes in iron absorption that occur during pregnancy. Iron requirements are greater in pregnancy than in non-pregnant state. Although iron requirements are reduced in the 1st trimester because of absence of menstruation these raise steadily thereafter as high as ≥10 mg/day.[5] The amounts that can be absorbed from even an optimal diet, however are less than the iron requirement in later pregnancy and a women must enter pregnancy with iron stores of >300 mg if she is to meet her requirement fully. This is more than most women possess especially in developing countries.[6]

Iron requirements are increased in pregnancy, especially in the 3rd trimester when they may be several times higher than at other stages of the life cycle, the net iron requirements for pregnancy are 840 mg approximately.[7] Iron deficiency can be defined as that moment when body iron stores become depleted and a restricted supply of iron to various tissues becomes apparent. Iron deficiency is one of the most common nutritional deficiencies worldwide. A high proportion of women in both industrialised and developing countries become anaemic during pregnancy. Estimates from the

WHO report that 35–75% (average 56%) of pregnant women in developing countries and 18% of women from industrialised countries are anemic.[8] The prevalence rates in south Asian countries have been estimated as follows: Bangladesh 77%, Bhutan 59%, Nepal 65% and Sri Lanka 60%. Maternal mortality in selected developing countries ranges from 407 in (India) to 500 (Pakistan) deaths per 100,000 live births.[9]

Deficiency of iron in pregnant women limits oxygen delivery to cell resulting in fatigue, poor work performance and decreased immunity. Iron deficiency anaemia early in a pregnancy can double or even triple the risk of having a premature delivery or a low birth weight baby.[10]

When maternal iron stores are depleted, the foetus cannot accumulate much iron and there is a decrease in foetal iron stores. Studies suggest that behavioural abnormalities occur in children with iron deficiency. These abnormalities are related to changes in the concentration of chemical mediators in the brain[11]. Iron deficiency in the absence of anaemia is associated with poor performance on Bayley Mental development Index. Development delay in iron deficient infants can be reversed by treatment with iron.[12]

The objectives of this study were to determine the iron status of the subjects and controls, to compare the iron status of pregnant women of Hazara Division with that of normal healthy non-pregnant women and to determine correlations of TIBC, UIBC and Fe/TIBC% ratio, against serum iron levels.

MATERIAL AND METHODS

This study was conducted at Faculty of Health Sciences, Hazara University, Mansehra, and Ayub Medical College and Hospital Complex, Abbottabad. It was a descriptive study, conducted for six months from 1st March to 31st August 2006. A total of 120 women were included in the study divided to two groups. The test group comprised of 90 pregnant women at various stages of pregnancy and control group of 30 non-pregnant healthy women. The test group were also classified into three subgroups according to stage of pregnancy, i.e., first, second and third trimester. The control group included women of the same age group as of the test subjects. Sampling was done by convenience (non-probability) sampling. Particulars of each subject were recorded on a standard Performa designed for the study including detailed history and examination. Among the subjects, those having any acute or chronic generalised infection (respiratory or renal diseases), women using any Intra-Uterine Contraceptive Device or oral contraceptives, diagnosed cases of haemoglobinopathies, taking Anti-thyroid drugs, Cortisol, NSAIDs, cases of dysfunctional uterine bleeding and taking iron supplements were excluded. Women with any risk factor or diagnosed complication of pregnancy, any other diagnosed disease especially Haemoglobinopathes, renal and thyroid diseases, history of Intra-uterine contraceptive devices, worm-infection and multiple pregnancies were also exclude from the study.

Laboratory investigations of the cases and controls were done to determine haemoglobin, Serum Ferritin, Serum iron level, Total iron-binding capacity (TIBC), Unsaturated iron-binding capacity, and Percentage saturation of transferrin (Fe/TIBC%). Mean and standard deviation were calculated for Hb%, Serum Ferritin, Serum Iron, TIBC, UIBC, and Fe/TIBC%.

Statistical analysis was done using SPSS-16. The differences between means of more than two groups were tested by performing ANOVA. Pearson correlation coefficients were calculated to determine correlation of serum ferritin, TIBC, UIBC, Fe/TIBC ratio against serum-iron.

RESULTS

A total of 120 women were selected in the study, 90 pregnant women as test group and 30 non-pregnant women as controls. Overall, the subjects were in the age range 18–43 years. The mean age of control group was 28.53±5.98 year, and that of the pregnant group irrespective of the trimester of pregnancy was comparable to that of the control group (p>0.05). The age of subjects in 1st trimester was 32.60±6.69 year, of those in 2nd trimester was 31.71±6.94 year, and of those in 3rd trimester was 28.79±7.70 year.

Table-1: Comparison of pregnant women classified by trimester of pregnancy and control subjects with respect to Hb, Serum ferritin, Serum iron, TIBC, UIBC, and Fe/TIBC%

	Pregnant subjects								
	1st trimester (n=15)		2nd trimester (n=32)		3rd trimester (n=43)		Control (n=30)		Comparison
Variables	**MEAN**	**SD**	**MEAN**	**SD**	**MEAN**	**SD**	**MEAN**	**SD**	**ANOVA**
Haemoglobin (g/dl)	11.01^{b}	0.77	10.48^{c}	0.91	10.37^{c}	0.78	12.50^{a}	1.17	**
Serum ferritin (ηg/ml)	16.20^{b}	5.6	13.70^{c}	6.5	11.81^{c}	4.11	54.39^{a}	20.05	**
Serum iron (g/dl)	61.73^{b}	16.43	53.57^{b}	12.4	52.82^{b}	19.3	70.65^{a}	16.12	**
TIBC (g/dl)	325.81^{b}	44.33	341.93^{b}	50.53	438.66^{c}	46.4	304.76^{a}	28.76	**
UIBC (g/dl)	264.08^{b}	58.96	284.35^{b}	61.99	388.98^{c}	61.66	235.00^{a}	23.27	**
Fe/TIBC%	19.98^{b}	8.66	16.34^{c}	5.64	12.25^{d}	5.31	23.05^{a}	4.25	**

** Difference highly significant (p<0.001). Different letter superscripts to mean values in a line indicate significant differences

Table-2: Coefficients of correlation between Serum Iron and TIBC, UIBC and Fe/TIBC% during the 1st, 2nd and 3rd trimesters of pregnancy and in non-pregnant(control) subjects

GROUP	TIBC	UIBC	Fe/TIBC%
Control	0.64**	0.10	0.92**
1st trimester	-0.85**	-0.91**	0.94**
2nd trimester	-0.89**	-0.89**	0.99**
3rd trimester	-0.70**	-0.90**	0.96**
**Difference highly significant (p<0.001)			

Table-3: Distribution of pregnant women with respect to iron deficiency in all the three trimesters of Pregnancy on basis of Hb, Serum ferritin, serum iron, TIBC, UIBC and Fe/TIBC%

	Trimester		
Parameter	1st (n=15)	2nd (n=32)	3rd (n=43)
Hb <11 gm/dl	6 (40%)	18 (56%)	30 (70%)
Serum ferritin <12 ηg/ml	4 (26%)	17 (53%)	26 (65%)
Serum iron <50 g/dl	3 (20%)	13 (41%)	20 (46%)
TIBC >400 g/dl	4 (26%)	12 (37%)	35 (81%)
UIBC >300 g/dl	4 (26%)	14 (43%)	29 (67%)
Fe/TIBC <16%	5 (33%)	15 (46%)	33 (76%)

Table-4: Distribution of iron deficiency in pregnant women cases and non-pregnant control on the basis of Hb, Serum ferritin, serum iron, TIBC, UIBC and Fe/TIBC%

		Cases		Control	
Parameters		Number	%	Number	%
Hb gm/dl	>11	19	21.5	27	90.0
	9.01–11.00	61	67.7	3	10.0
	<9.00	10	11.1	–	–
Serum ferritin ηg/ml	>30	5	5.5	27	90.0
	12.0–30.00	45	50.0	3	10.0
	<12	44	44.4	–	–
serum iron g/dl	>50	40	4	25	83.4
	40–50	36	40.0	5	16.6
	<40	14	15.5	–	–
TIBC g/dl	<400	38	42.2	30	100
	400–500	42	46.6	–	–
	>500	10	11.1	–	–
UIBC g/dl	<300	30	33.3	29	96.7
	300–400	42	46.6	1	3.3
	>400	18	20.0	–	–
Fe/TIBC%	>28	5	5.5	4	13.4
	15–28	32	35.5	26	86.6
	<15	53	58.88		–

DISCUSSION

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.[13]

The prevalence of iron deficiency anaemia remains high in many parts of the world despite significant effort to alleviate this problem. The national health survey of Pakistan reported that 43–47% of rural and 35–40% of urban women aged 15–44 years are anaemic. The incidence of iron–deficiency anaemia among expectant mothers is alarmingly high. It is a serious problem in pregnancy which affects 50–60% of these women.[14]

Iron deficiency is normally the result of inadequate bio available dietary iron and increased iron requirements during a period of rapid growth in pregnancy and infancy. Anaemia of pregnancy has a significant impact on the health of foetus as well as mother, especially if severe, may impair the oxygen delivery to placenta and foetus interfering with intrauterine growth. Placental weight, volume and surface area are reduced if expecting mother is moderately anaemic. It results in 12–28% of foetal loss, 30% prenatal deaths and 7–10% of neonatal deaths.[15]

During the second trimester anaemia is associated with preterm birth, incidence of which is increased five-fold for iron deficiency anaemia and double for other anaemia. The risk of iron deficiency is particularly high in women with high parity and short intervals between pregnancies.[16]

During pregnancy Hb level in woman is naturally lower than when she is not pregnant. This is because the fluid (plasma) increases by about 50% during pregnancy (peaking at about 32 weeks).[17] The increased plasma dilute the red cells, making their level drop. Serum ferritin usually falls markedly between 12 and 25 weeks of gestation, probably as a result of iron utilisation for expansion of the maternal red blood cell mass.[1,2]

Iron transfer from mother to foetus occurs against the concentration gradient. Most iron transfer to the foetus occurs after 30 weeks of gestation which correspond to the time of peak efficiency of maternal iron absorption.[18]

Results of this study did not differ from those of other studies carried out in different parts of the country and abroad and have been found in conformity with previous works carried out by various workers. Several factors were observed to be responsible for a high rate of iron deficiency in a community like ours. Multi parity, poor socio economic and educational status are the principal reasons for a high prevalence of iron deficiency anaemia in our population.[19]

The salient feature of our study is a statistically significant decrease in Hb, serum ferritin level, serum-iron level and Fe/TIBC% and a significant increase in total iron binding capacity (TIBC) and pronounced increase in un-saturated iron binding capacity (UIBC) in pregnant women compared to non-pregnant controls.

The proportion of iron deficient pregnant women was 50–60% of cases, and iron deficient anaemic was about 26%, while 20% of controls were also iron deficient but none of them was iron deficient anaemic.

These findings are not unexpected since the diet of the population in the region (especially rural areas) is heavily reliant on grains such as maize, which contains large amounts of phytates which are known to interfere with the intestinal uptake of iron and other trace minerals, such as Zinc and Calcium.

The data indicates significant differences in haemoglobin, serum ferritin, serum iron levels TIBC, UIBC, and Fe/TIBC%. Significantly lower haemoglobin and serum ferritin and higher TIBC and UIBC were observed in 2nd and 3rd trimester of pregnancy than in the 1st trimester.

Haemoglobin level in all the three trimesters of pregnancy were significantly lower than in the control subjects ($p<0.001$) and the decrease was especially pronounced in the 2nd and 3rd trimesters, which is in agreement with the study conducted by Mah-e-Munir *et al*[20]. Their study revealed that iron deficiency was the most frequent cause of anaemia. In another study conducted by Bondevik *et al*[21] in Nepal, about 76.6% of pregnant women were found anaemic. Approximately 81.3% of anaemia was due to iron deficiency. Low birth weight was especially associated with low haemoglobin level in pregnancy.

Serum ferritin levels in our subjects decreased significantly in all the three trimesters as compared to controls. This is in agreement with the results reported by other studies.[22–25]

Van den Broek and Letsky[26] opined that a ferritin value of 30 ηg/ml or less was the best indicator of iron deficiency in pregnant women. Applying a cutoff value of 30 ηg/ml for iron-deficiency in that study 23% of anaemic pregnant women were deficient in iron, one third of anaemic subjects in that study were also deficient in Vitamin B_{12}, while another one third were deficient in folate.

While determining the iron status of pregnant women in our study it was observed that iron level decreased in all the three trimesters as compared to the controls and fall was markedly significant ($p<0.001$) in the 2nd and 3rd trimesters. We observed the values of serum TIBC and UIBC (un-saturated iron binding capacity) rising throughout the pregnancy, with more pronounced increase in UIBC as the pregnancy advanced to term. Our results are thus in agreement with those of Lee *et al*.[27]

In a study by Monawarul-Islam *et al*[28] biochemical investigations on iron deficiency and nutritional status were carried out in a group of 130 women in the 2nd or 3rd trimester of pregnancy and 42 control non-pregnant women. Anaemia was present in 46.1% of pregnant women. Iron deficiency with and without anaemia as judged from serum transferrin saturation was evident in 59.2% of pregnant women with an incidence of 70.3% in 3rd trimester.

Haemoglobin concentration and haematocrit, because of their low cost and quick assessment, are most commonly used to screen for iron deficiency; these measures reflect the amount of functional iron in the body. But limitation is that changes in haemoglobin concentration and haematocrit occur only at the late stages of iron deficiency, so both the tests are late indicators of iron deficiency; nevertheless these tests are essential for determining iron deficiency anaemia.

Serum ferritin concentration is an early indicator of the status of iron stores and is the most specific indicator available of depleted iron stores especially when used in conjunction with other tests to asses iron status. In the light of above facts it becomes clear that estimation of haemoglobin, serum ferritin, serum iron, TIBC, UIBC and Fe/TIBC% are valuable parameters in assessing iron deficiency in pregnancy. A more effective method is to use various combinations of measurements to enhance the specificity of prevalence estimates or to define varying stages of iron lack.

CONCLUSION AND RECOMMENDATIONS

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. A high percentage of the pregnant women are iron deficient due to factors such as high parity, poor dietary habits and socioeconomic status. Interventions to enhance the intake of several micronutrients should be considered to prevent anaemia in pregnant women.

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