

Study of serum transferrin and serum ferritin during pregnancy and their correlation with pregnancy outcome

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Abstract

Background: Iron deficiency is more prevalent in young children and women of reproductive age group. Iron deficiency is generally slow to develop and often remain undetected until clinical picture arises due to its deficiency. Thus, early detection of iron deficiency is beneficial before the anemia sets in. The maternal iron level is important for the growth of growing fetus and is always required to have markers which can detect iron deficiency in early stage. The timely implementation of intervention to correct maternal iron status will improve the maternal outcome.

Objectives: To study levels of serum transferrin and serum ferritin during pregnancy and their correlation with outcome of pregnancy.

Materials and Methods: Longitudinal study was conducted on pregnant women reporting antenatal clinic in first trimester. Data in each trimester of 57 women was collected. Birth weight of new born delivered was recorded and statistical analysis was done by paired *t*-test.

Result: 57 pregnant women were divided into two groups according to weight of delivered babies. 46 delivered low birth and 11 delivered normal birth weight babies. Serum transferrin was significantly higher ($p < 0.05$) in third trimester in group I subjects as compared to first and second trimester. Also it was significantly higher ($p < 0.001$) in third trimester in group I subjects as compared to third trimester level of group II subjects. The same comparison does not hold true when serum ferritin levels were compared.

Conclusion: The finding of the present study suggests that serum transferrin levels measurement could be a better parameter for predicting pregnancy outcome and can be advised along with other routine hematological investigations.

KEY WORDS: Pregnancy, serum transferrin, serum ferritin, birth weight

Introduction

According to Global Prevalence of Anemia 2011 report by WHO the global prevalence of anemia in pregnant women is approximately 38.2%.^[1] In India, the estimated percentage of pregnant women with blood hemoglobin concentration

less than 11 mg/dl is 54%, posing a significance of severe health problem.^[1] A survey conducted by the national nutrition monitoring bureau (NNMB) and national family health survey (NFHS-3)^[2] also showed high prevalence of anemia in all segments of Indian population. NFHS-3 has reported prevalence of anemia in 56.2% women of age group 15–49 years and 58.7% in pregnant women.^[2] Iron deficiency is common in women of reproductive age group and during pregnancy. During pregnancy there is significant increase in the amount of iron required due to increased red cell mass and for growth of fetal placental unit. Consequently, this situation worsens when there is an inadequate iron supply from the diet of the mother.^[3] Maternal iron deficiency has been proved as a risk factor for poor maternal outcome like low birth weight and pre-term delivery. Iron deficiency anemia during pregnancy may

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result in low birth-weight and increased preterm birth rate and perinatal mortality.^[4-6] Maternal iron deficiency subsequently may lead to iron deficiency in the fetus also which may lead to sometimes irreversible damage to the central nervous system, with impairment of psychomotor development.^[7]

No single parameter specifically indicates iron status, and several tests are used to determine iron status and anemia such as hemoglobin, hematocrit or packed cell volume, mean cell volume and mean cell hemoglobin, red cell distribution width, reticulocyte hemoglobin concentration, percentage of hypochromic red cells, serum ferritin, and serum transferrin.^[8] Although, most of these parameters are good indicators of iron status but an indicator is required which can mark the change in iron status as early as possible to prevent the worst outcome. Transferrin is a plasma protein for iron ion delivery. It is a glycoprotein that binds iron very tightly but reversibly. The ferritin is the storage form of intracellular iron. Both prokaryotes and eukaryotes produce ferritin molecules for iron storage.^[9,10] Our hospital is a 1000 bed tertiary care center catering health services in Mahakaushal region of central India. The hospital has 24 h functioning centralized laboratory equipped with various automated analyzers. The antenatal clinic of Obstetrics and Gynecology Department is attending all the pregnant women reporting at the institute. Regardless of clinical presentation and blood indices status at the time first antenatal visit the complete blood count is advised for the expecting mothers. The serum levels of transferrin and ferritin are not investigated as routine during pregnancy in this institution. As it has been already established that maternal iron deficiency is a risk factor for poor maternal outcome, a marker which can predict early changes in iron status and possible outcome of pregnancy is needed. The present study was conducted to study the changes in levels of serum transferrin and serum ferritin in all trimesters. Changes in the serum level of transferrin and ferritin were also correlated with the outcome of pregnancy.

Materials and Methods

The study was done after obtaining ethical clearance from ethical committee of the institute in the department of Physiology in collaboration with department of Obstetrics and Gynecology of NSCB Medical College, Jabalpur. The duration of study was 2 years. The subjects were selected from the antenatal clinic of Obstetrics and Gynecology department. The subject's inclusion was voluntary after informed consent. Expecting mothers included in the study were of the age group 20–30 years and were healthy and primigravida. Subjects with high risk pregnancy were excluded from the study. Subject who have missed regular follow up or discontinued their supplementation were also excluded.

Study subjects chosen were residing within the city and in vicinity area of the city so as to avoid drop out during follow up visits. During the tenure of study the subjects included were followed on their antenatal visits in each trimester. The relevant history and examination of the subjects and prescription

of iron supplementation was done in association with the attending doctors of Obstetrics and Gynecology department. Taking all aseptic precautions from each subjects, 5 ml venous blood sample has been collected in each trimester. From each sample serum values of ferritin and transferrin was obtained in the analyzer model A25 manufactured by Biosystems Reagents and Instruments. The subjects included delivered their babies within the institution. The birth weight of new born was recorded.

Control values of serum ferritin and transferrin were obtained from non-pregnant, non-anemic, healthy females of the same age group. Statistical analysis of the data obtained was done on software SPSS 15.

Result

The study group comprising of pregnant women were followed in antenatal clinic visit from first trimester till delivery. The study extended for a period of 2 years. Out of the all enrolled subjects 57 subjects delivered the babies in our institution. For statistical analysis according to the birth weight of babies the study subjects were divided into two groups - group I and group II. Group I comprised of 46 subjects who delivered low birth weight babies and 11 subjects delivered normal birth weight babies were included in group II. Serum levels of transferrin and ferritin in subjects were obtained in each trimester.

The mean serum transferrin and ferritin in control group was 293 ± 32.55 mg/dl and 87.6 ± 16.65 μ g/l, respectively. In group I the observed mean values of transferrin in first, second, and third trimester was 342.11 ± 52.57 , 346.83 ± 57.18 , 374.72 ± 54.31 mg/dl, respectively. In group II mean values of transferrin in first second and third trimester was 321.18 ± 42.62 , 317.36 ± 60.15 , 301.73 ± 86.63 mg/dl, respectively. In group I the observed mean values of ferritin in each trimester was 49.95 ± 23.85 , 60.42 ± 20.24 , 58.49 ± 34.25 μ g/l, respectively. In group II mean values of ferritin in each trimester was 66.25 ± 22.40 , 47.33 ± 13.49 , 59.84 ± 24.21 μ g/l. The levels of serum ferritin in all trimesters were significantly lower in all subjects as compared to control group. While the serum transferrin level was significantly higher only in group I subjects as compared to control subjects (Table 1).

Trimester wise changes in levels of transferrin and ferritin in group I and II were also analyzed. In each group values obtained in first trimester were compared with second and third trimester. Second trimester value was compared with third trimester in each group (Table 2). Similarly, changes in serum transferrin and ferritin in each trimester of group II subjects were compared with respective trimester values of group I subjects (Table 3).

Discussion

Iron deficiency is a global health problem including developing countries like India. It remains undetected in a person until clinical features sets in. Various factors like unavailability

Table 1: Level of serum transferrin and ferritin in control group, in each trimester of group I and II. Each trimester value of transferrin and ferritin are compared with that of control group

Parameter (Group)	First trimester	Second trimester	Third trimester	Control group	p value		
Serum Transferrin (mg/dl)					Control and first	Control and second	Control and third
Group I	342.11 ± 52.57	346.83 ± 57.18	374.72 ± 54.31	293 ± 32.55	< 0.001*	< 0.001*	< 0.001*
Group II	321.18 ± 42.62	317.36 ± 60.15	301.73 ± 86.63		> 0.05	> 0.05	> 0.05
Serum ferritin (µg/l)							
Group I	49.95 ± 23.85	60.42 ± 20.24	58.49 ± 34.25	87.6 ± 16.65	< 0.001*	< 0.001*	< 0.001*
Group II	66.25 ± 22.40	47.33 ± 13.49	59.84 ± 24.21		< 0.05*	< 0.05*	< 0.05*

(* =Significant)

Table 2: Changes in serum transferrin and ferritin levels of group I and II subjects and comparison from first trimester to third trimester and statistical significance

Parameter	First trimester	Second trimester	Third trimester	p value		
Serum Transferrin (mg/dl)				First and second	First and third	Second and third
Group I	342.11 ± 52.57	346.83 ± 57.18	374.72 ± 54.31	> 0.05	< 0.05*	< 0.05*
Group II	321.18 ± 42.62	317.36 ± 60.15	301.73 ± 86.63	> 0.05	> 0.05	> 0.05
Serum ferritin (µg/l)						
Group I	49.95 ± 23.85	60.42 ± 20.24	58.49 ± 34.25	< 0.05*	> 0.05	> 0.05
Group II	66.25 ± 22.40	47.33 ± 13.49	59.84 ± 24.21	< 0.05*	> 0.05	> 0.05

(* =Significant)

Table 3: Comparison of serum transferrin and ferritin levels of respective trimesters of group II subjects with subjects of group I and statistical significance

Parameter (Unit)	First trimester	Second trimester	Third trimester	p value		
Serum Transferrin (mg/dl)				First of group II and first of group I	Second of group II and second of group I	Third group II and third of group I
Group II	321.18 ± 42.62	317.36 ± 60.15	301.73 ± 86.63	> 0.05	> 0.05	< 0.001*
Group I	342.11 ± 52.57	346.83 ± 57.18	374.72 ± 54.31			
Serum ferritin (µg/l)						
Group II	66.25 ± 22.40	47.33 ± 13.49	59.84 ± 24.21	< 0.05*	< 0.05*	> 0.05
Group I	49.95 ± 23.85	60.42 ± 20.24	58.49 ± 34.25			

(* =Significant)

of food, unawareness, illiteracy, poverty, deficiency in diet, dietary inhibitors are responsible due to which it remain a major health problem in the society.^[11,12] Our hospital is tertiary care institute serving health care facility to a large population of Mahakaushal region of Central India. Being a Government run institute it is easily accessed by those who cannot afford the expenses of private run facilities. At the antenatal clinic

of Obstetrics and Gynecology department routine hematological tests including complete blood indices are advised. Estimation of serum ferritin and transferrin are not advised to the pregnant women during their antenatal visits on routine basis. The study was conducted with the aim to assess the levels of serum ferritin and transferrin during pregnancy and their correlation with outcome of pregnancy.

There are various investigations available nowadays which can diagnose and describe anemia accurately. Various researches from past have described about different parameter for evaluating iron status and are currently being used in clinical practice.^[8,13,14] Still researchers are trying to describe such parameter which can be helpful in predicting possible pregnancy outcome accurately despite physiological changes such nutrition of mother, psychological status of mother, genetic factors, and gravid status.^[15-18]

The changes in serum ferritin and transferrin during three trimesters of pregnancy were studied. In this study, continuous rise in serum transferrin levels in subjects of group I in all three trimesters were found. The rise in third trimester was significant as compared to first and second trimester in group I ($p < 0.05$). The third trimester serum transferrin level in group I was also significantly higher than group II ($p < 0.001$) (Table 3). The rise in serum transferrin level in third trimester as obtained in this study was also reported by Chang *et al.*^[19] The result of their study showed that the serum transferrin level rises significantly ($p < 0.001$) from the non-pregnant stage till third trimester. Chaudhari *et al.*^[20] also studied serum level of iron and transferrin in normal and anemic pregnant women. Irrespective of the anemia status they also recorded rise in serum transferrin. This study is different from the study conducted by Chang *et al.*^[19] and Chaudhari *et al.*^[20] The blood samples collected in both the studies for estimating first, second, and third trimester serum transferrin level were from pregnant females at different periods of gestation. While, in this study the pregnant women were inducted in first trimester and followed through all trimesters till delivery. Their studies lack the comparison of the transferrin levels with outcome of pregnancy. The serially obtained serum transferrin and serum ferritin levels were utilized in comparing with outcome of pregnancy.

The other parameter investigated was serum ferritin. Serum ferritin is an acute phase reactant.^[21] According to a report by WHO on serum ferritin concentrations for assessment of iron status in populations, interpretation of normal or high level of serum ferritin cannot be used conclusively for anemia as conditions like infection and inflammation leads to increase in serum ferritin level also.^[9] During pregnancy serum ferritin level remain at higher level during first trimester and tends to decrease as pregnancy progresses.^[22,23] Serum ferritin level in all trimesters of pregnancy were serially recorded and compared it with outcome of pregnancy. Drop in serum ferritin level as reported by previous studies were not observed.^[22,23] In group II, drop in serum ferritin level were observed from first trimester to second trimester which again rises in third trimester. Decrease in serum ferritin level in second trimester is in accordance with finding of earlier studies like Asif *et al.*^[24] and Bhale *et al.*^[25] They reported changes in ferritin at different stages of pregnancy in different pregnant subjects. In this study, changing trends in ferritin level as pregnancy progresses were recorded and correlated it with birth weight of new born babies. In this study, the rise in serum ferritin level were observed in group I in second and third trimester as compared to first trimester.

Total iron binding capacity values are strongly correlated with serum transferrin concentrations.^[26] Total iron binding capacity of the serum rise significantly during pregnancy which suggest that serum transferrin level rises accordingly.^[27,28] In this study, the change in serum transferrin in group II subjects were insignificant while the rise in serum transferrin level in group I correlated well with the low birth weight. The subjects of group I were having adequate iron stores reflected by serum ferritin level. On the other hand, there was increase in serum transferrin in group I subjects. Body's mechanism to meet the sufficient supply of iron could be the reason for this rise in transferrin in these subjects. The new born delivered by these subjects were low birth weight. Possible underlying cause for low birth weight could be inadequate mobilization of stored iron to the fetus. The serum ferritin levels obtained remain inconclusive. In this study, it was considered that all the pregnant women were taking adequate supplementation of iron as well as on adequate diet. But it cannot be ignored that they might lack regular diet as well iron supplementation which is not strictly followed in this study. So, it is further recommended that studies carrying larger cohort, considering all the confounding factors as well as strict follow up on diet and iron supplementation are required which is the further aspect of this study. There are various investigations available nowadays which can diagnose and describe anemia accurately. Although, there could not be a single parameter for solving this problem. The finding of the present study suggests that serum transferrin level measurements could be a better parameter which can be advised along with other routine hematological investigations. At tertiary level health institution there is still more possibilities available for research to be done in this field. The drop out of subjects during follow up antenatal visits and at the time of delivery limits the number of subjects included in the study. Considering the cost for serum ferritin and transferrin estimation during entire duration of pregnancy effort should be undertaken to reduce cost of tests so that benefits of medical advancement can be afforded by individuals of all income groups.

Conclusion

The finding of the present study suggests that serum transferrin levels measurement could be a better parameter for predicting pregnancy outcome and can be advised along with other routine hematological investigations.

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