

Original Article

Serum Ferritin in Preeclampsia and Eclampsia: A Case Control Study

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Abstract :

Preeclampsia is a pregnancy specific, multi-system disorder of unknown etiology characterized by new onset of elevated blood pressure & proteinuria after 20 weeks of gestation. Globally preeclampsia and other hypertensive disorders of pregnancy are a leading cause of maternal and infant illness and death. But the exact pathophysiology is yet to be explored. It was a case control study and was conducted during the period of January 2010 - December 2010 in the department of Obs & Gynae DMCH and dept. of Biochemistry of BSMMU. The main objective of the study was to evaluate the association of serum ferritin and iron in preeclampsia & eclampsia. A total 100 pregnant women were included in this study. Of them 50 preeclamptic or eclamptic, nonanaemic patients not in labour (26-40weeks) were taken as case and 50 normotensive pregnant women were taken as control. Mean Serum ferritin level in case and control group was 100.03 ± 123.52 $\mu\text{gm/L}$ and 31.53 ± 20.86 $\mu\text{gm/L}$ respectively which is highly significant ($P < 0.001$). Out of 50 cases ferritin level was raised in 10 cases (20%). In 80% cases ferritin level was below the cut-off value that is normal or below normal but in 100% of controls had ferritin level below the cut off value.

Key words: Preeclampsia, Eclampsia, Serum ferritin, TIBC.

Introduction :

Preeclampsia-eclampsia is a grave disease peculiar to pregnant and puerperal women, worrisome concern both for pregnant women and physicians¹. Preeclampsia-eclampsia is a multisystem disorder of unknown etiology, unique to pregnant women². The condition usually resolves soon after delivery, but early delivery increases the risk of complications to the baby.

This has to be balanced against delay, which increases the risk that eclampsia and organ damage threatening the lives of both³.

Serum ferritin is a reliable indicator of total body iron status in non-diseased individuals, with low concentrations diagnostic of iron deficiency. However, high ferritin not always signify iron excess. Ferritin is a major iron storage protein found in spleen, liver, bone marrow, mucosa of small intestine, placenta, kidney, testes, skeletal muscle and in plasma⁴. Its concentration is highly correlated with bone marrow iron stores, and decreased⁵ before changes in transferrin saturation, serum iron or haemoglobin concentration. In pregnancy, serum ferritin concentration is maximum at 12-16 weeks, then falls with advancing gestation to reach nadir at third trimester⁵. The lowest quartile of ferritin concentrations at 28-30 weeks associated with decreased risk of preeclampsia, PROM, infant admission in NICU⁶. Various studies show ferritin & iron increases in preeclampsia & eclampsia which act as a pro-oxidant promoting lipid per oxidase activity and induces endothelial cell damage. There is evidence that increased serum ferritin level plays pathogenic role in development of preeclampsia⁷ performing as an

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acute phase reactant⁸. Lower ferritin level during 28-30 weeks would be associated with lower incidence of preeclampsia⁹. When tissue become ischemic, reactive oxygen species such as superoxide, hydrogen peroxide are produced but not reactive enough to initiate cellular damage directly. But presence of catalytic amounts of transition metal, particularly iron arising from ischemic placenta by destruction of RBC from thrombotic, necrotic and hemorrhagic area¹⁰ can generate highly reactive hydroxyl radical by Fenton reaction which initiate the process of lipid per oxidation causing endothelial injury.

It would seem inadvisable, in the absence of evidence of iron deficiency, to give iron supplements to pregnant women at high risk for preeclampsia¹¹. Therefore, routine iron supplementation in preeclampsia is questionable.

Materials and Methods:

It was a case-control study done from January, 2010 to December, 2010 at Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital (DMCH) and Department of Biochemistry, Bangabandhu Sheikh Mujib Medical University (BSMMU) with a sample size of 100. Out of them 50 were case and 50 were control. The case group (50 pre-eclamptic or eclamptic women) and the control group (50 healthy parturient) was selected from the pregnant women who attended indoor and outdoor of DMCH, who fulfilled the exclusion and inclusion criteria. In order to eliminate the confounding effect of anemia on increasing the ferritin and Total Iron Binding Capacity (TIBC) level, patients who were clinically anaemic or had haemoglobin <11 mg/dl was excluded.

Moreover, multiple pregnancies, pregnancy with chronic kidney disease, diabetes, liver disease, autoimmune disease, heart disease were not included in the study. Both groups were matched by age, gestational age, educational, social and economical situation. After taking informed written consent, 2 cc blood samples were taken to analyze the serum ferritin level in Biochemistry Department of BSMMU by Microparticle Enzyme Immunoassay (MEIA) technology. Data were processed and analyzed using SPSS version 16.0. The test statistics used to analyze the data were descriptive statistics, Chi-square (χ^2) test, Student's t-Test. For all analytical tests, the level of significance was set at 0.05 and $p < 0.05$ was considered significant. The summarized data were presented in the form tables and diagram.

Results:

Age and gestational age distribution of study subjects show that mean age of case & control was 24.76 ± 6.12 Years & 24.30 ± 4.950 Years respectively. The mean gestational age was 32.80 ± 3.18 weeks & 31.82 ± 3.57 weeks respectively in case & control group. No statistically significant ($p > 0.05$) difference was found in both groups in unpaired t-Test in respect of age and gestational age. Primipara was prominent in both study groups. Data were analyzed using Chi-square (χ^2) test which was not statistically significant ($p > 0.05$). Educational status in both groups showed mostly did not complete the primary school. Chi-square (χ^2) test was not statistically significant ($p > 0.05$).

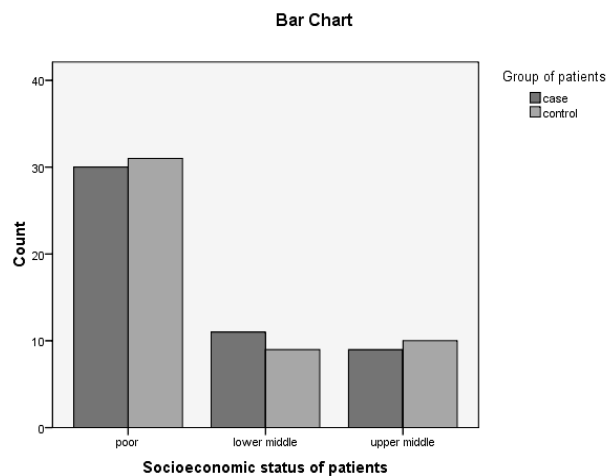


Figure-I: Distribution of the study subjects according to socioeconomic status

Figure I demonstrate that maximum were from poor socioeconomic group and all classes were almost uniformly distributed in both groups.

Mean Serum ferritin level in case and control group was 100.03 ± 123.52 $\mu\text{gm/L}$ and 31.53 ± 20.86 $\mu\text{gm/L}$ respectively which is highly significant (< 0.001) by unpaired t-Test (Table-I)

Table-I: Comparison of serum ferritin levels between case and control*

| Parameter | Group | | P value |
|---|---------------------|-------------------|-----------|
| | Case (n=50) | Control (n=50) | |
| Serum ferritin ($\mu\text{gm/L}$) Mean \pm SD | 100.03 ± 123.52 | 31.53 ± 20.86 | < 0.001 |

*Data were analyzed using unpaired t-Test and were presented as mean \pm SD.

The normal value of serum ferritin is 22-120 µgm/L. So, the cut-off value is taken 120 µgm/L. Out of 50 cases, ferritin level was raised in 10 cases (20%). In 40 cases (80%) level was below the cut-off value that is normal or below normal. But 100% of controls had iron level below the cut off value. Data were analyzed using Chi-square (χ^2) test between case and control and it was found statistically significant (P value <0.001) (Table II).

Table-II: Distribution of the serum ferritin level in pre eclampsia eclampsia and control*

| Serum ferritin level | Group | | P value |
|-------------------------------|-------------|----------------|---------|
| | Case (n=50) | Control (n=50) | |
| Ferritin level raised | 10(20) | 00(00) | < 0.001 |
| Ferritin bellow cut-off value | 40(80) | 50(100) | |

*Data were analyzed using Chi-square (χ^2) test; Figure in the parentheses denoted corresponding percentage.

Discussion:

Preeclampsia is still one of the leading causes of maternal and fetal morbidity and mortality. Despite active research for many decades, the etiology of this disorder remains an enigma. The metabolism of the serum iron and iron-binding proteins, ferritin and transferrin, is abnormal in women with preeclampsia. The reasons for the increased serum ferritin with preeclampsia remain unclear.

In spite of numerous studies, the aetiology of preeclampsia has not been fully elucidated. Preeclampsia has been dubbed the 'disease of theories' because of the multiple hypotheses has been proposed to explain its occurrence¹². Exact patho-physiology of this disorder is not clearly known. The various biochemical changes in this disease is yet to be explored.

This case control study was carried out to evaluate the association of serum ferritin and iron with preeclampsia & eclampsia and its possible contributory role in pathophysiology in pre eclampsia.

There was no statistically significant ($p > 0.05$) difference in maternal age between case and normal pregnant women in the current study. Mean age of case & control was 24.76± 6.12 Years & 24.30 ± 4.95 Years respectively. Hubel¹³ (1989) also shows no difference in age distribution between case and control. In the study by Taheripanth¹⁴, the mean age of patients was 27.7±6.3 years in preeclamptic and 24.5±5.5 in control group.

No significant difference was observed between case and control in terms of gestational age, parity, educational status and socio-economic condition which represent that the study subjects had the similar characteristic. In this study mean gestational age was 32.80 ± 3.18 weeks & 31.82 ± 3.57 weeks respectively in case & control group. Mostly were primi, not completed their primary education and from poor socio-economic condition which reflects the actual status of our country.

In this study mean serum ferritin level in case and control group was 100.03 ± 123.52 µgm/L and 31.53 ± 20.86 µgm/L respectively which is highly significant ($p < 0.001$). Study done by Husein¹⁵ shows mean serum ferritin level in case and control group is 167.11 ± 10.43 ng/ml and 17 ± 3.03 ng/ml. The levels of ferritin in cases are higher than the present study. But the difference is statistically significant which matches with the result of this study.

Correlation of ferritin with pre eclampsia- eclampsia was evaluated in some researchers abroad. These studies suggest that serum iron, ferritin and transferrin saturation rate are remarkably higher and TIBC level is lower than normal subjects¹⁰. In the study done by Taheripanth¹⁴ mean Serum ferritin level in case and control group is 123.8 ± 46.1 ng/dl and 33.4 ± 16.2 ng/dl respectively which is highly significant (< 0.001) like our study. That study reveals that ferritin level in pre eclampsia and HELLP syndrome is 3.6 and 10 times to the normal, respectively. Study by Zafar¹⁶ shows serum ferritin level is significantly higher in pre eclampsia than the normal pregnancy like ours. Siddiqui¹⁷ shows in his study, mean serum ferritin concentration in preeclamptic and normal pregnant women are 32.56 ± 11.72 and 19.89 ± 8.86, respectively ($p < 0.05$). The levels are much lower than the current study but statistically significant.

Ferritin level was raised in 10 cases (20%). In 40 cases (80%) ferritin level was below the cut-off value that is normal or below normal. 100% of controls had ferritin level below the cut off value which was statistically significant (P value <0.001). This result is supported by Husein¹⁵ who took the cut-off value >210 ng/ ml for ferritin. Study reveals 32.5% of cases & none of controls were above the cut-off value of ferritin. Taheripanth¹⁴ shows that none of the normal woman had abnormal ferritin level but 45.5% of preeclamptic patients had abnormal ferritin level, the value is higher than ours.

In spite of different works throughout the world, the exact pathophysiology is still unknown. So, different studies are going on and on. This study revealed that serum ferritin levels were increased to a statistically significant level in preeclampsia and eclampsia in contrast to the normal. The excess iron and ferritin may cause endothelial injury by producing free radicals initiating the process of lipid peroxidation. As different studies show that high levels of serum iron parameters may predict in the earlier weeks of pregnancy about occurrence of preeclampsia and high level associated with poor pregnancy outcome. On the other hand iron supplements and increased iron stores have recently been linked to maternal complications e.g. gestational diabetes and increased oxidative stress during pregnancy.

So, routine investigation of serum iron status of pregnant women with high risk for preeclampsia & eclampsia as part of antenatal checkup may help to establish diagnosis of pre eclampsia before appearance of its clinical manifestations and unnecessary use of iron in a non anaemic pregnant woman can be avoided.

Conclusion:

In this study it was observed that serum ferritin level were significantly higher in preeclampsia and eclampsia patients than the normal pregnancy. So, it may be concluded that increased level of serum ferritin may play a role in pathogenesis of preeclampsia and eclampsia.

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