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Original Research Article

The association of serum ferritin with preeclampsia and its severity

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ABSTRACT

Background: Preeclampsia, a pregnancy-related condition with heightened blood pressure and organ damage after 20 weeks, prompts concern. Serum ferritin, an iron-storing protein, gauged by blood tests, mirrors iron levels. Investigating link before conception between serum ferritin and preeclampsia could impact how we identify, manage, and treat this condition during pregnancy. Study aimed to assess the association of serum ferritin with preeclampsia and its severity.

Methods: This case-control study was conducted in Bangabandhu Sheikh Mujib medical university hospital and Dhaka medical college hospital, Dhaka, Bangladesh from July 2011 to June 2012. A total of 100 pregnant women, comprising 50 cases (Preeclamptic) and 50 controls (Normal pregnant women), were purposively included as study subjects. Data analysis was performed using SPSS version 23.0.

Results: In the case group, 64% were with mild and 36% with severe preeclampsia. Mean serum ferritin was significantly higher in cases than in controls ($p < 0.001$); 76% of cases had elevated serum ferritin, compared to 44% in controls ($p = 0.001$). Severe preeclampsia group had a mean serum ferritin of 192.8, mild preeclampsia group had 86.1, and normal pregnant women had 21.7 ng/ml, indicating higher serum ferritin with preeclampsia severity ($p < 0.001$).

Conclusions: Preeclamptic cases exhibit significantly elevated serum ferritin levels, with a fourfold increased likelihood compared to normal pregnancies. Furthermore, the severity of preeclampsia is associated with higher serum ferritin concentrations in comparison to uncomplicated pregnancies.

Keywords: Serum ferritin, Preeclampsia, Proteinuria, Gravidity, Pregnant, Hypertension

INTRODUCTION

Preeclampsia, a serious pregnancy complication, is characterized by high blood pressure, protein in the urine, and fluid retention, affecting 3% to 5% of pregnancies on average. It is a progressive condition with varying manifestations and rates of advancement.¹ Preeclampsia is a significant pregnancy concern, and although it often resolves quickly after delivery, early delivery increases the risk of complications for the baby.² This multisystem illness specific to human pregnancy involves the onset of new hypertension after 20 weeks of pregnancy, impacting

one or more end organ systems, including the fetus.³ Globally, hypertensive diseases of pregnancy cause 14% of all maternal deaths, contributing to over 26% of maternal mortality in the Western world and 9% in Asia.⁴ Preeclampsia poses serious complications for both the woman and her child, potentially leading to cardiovascular disease later in life.^{5,6} According to the Daily Star (2014), the latest maternal mortality rate is 170/100,000 live births, as estimated by the United Nations (UN) and the world health organization (WHO) in 2014. Preeclampsia or eclampsia accounts for 20% of maternal mortality. In Bangladesh, preeclampsia is alarmingly common,

contributing to approximately 16% of maternal mortality.⁷ Ferritin, a widespread intracellular protein responsible for storing and releasing iron in a controlled manner, is produced by various living organisms, including bacteria, algae, plants, and animals.⁸ During pregnancy, serum ferritin concentration peaks around 12 weeks of gestation and decreases in the third trimester.⁹ The precise pathophysiology of preeclampsia remains unknown, but serum ferritin and iron levels are suggested as potential factors in its development. Free radicals produced from the cell membrane, rich in polyunsaturated fatty acids, and circulating lipoproteins initiate lipid peroxidation, leading to endothelial injury. The presence of catalytic amounts of transition metals, particularly iron, originating from the ischemic placenta due to the destruction of red blood cells in thrombotic, necrotic, and hemorrhagic areas, can generate highly reactive hydroxyl radicals through the Fenton reaction.¹⁰ Elevated ferritin levels are associated with an increased risk of preterm delivery and neonatal asphyxia, while lower ferritin levels are linked to a decreased risk of preeclampsia and pre-labor rupture of membranes.¹¹ The objective of this study was to assess the association of serum ferritin with preeclampsia and its severity.

METHODS

This case-control study was conducted in the department of obstetrics and gynaecology at Bangabandhu Sheikh Mujib medical university hospital and Dhaka medical college hospital, Dhaka, Bangladesh, spanning from July 2011 to June 2012. The study included a total of 100 pregnant women as study subjects, divided into two groups. The case group comprised 50 pregnant women with preeclampsia, while the control group consisted of 50 pregnant women without preeclampsia. Sample selection utilized a purposive sampling technique, and the study received approval from the ethical committee of the mentioned hospitals. Before data collection, proper written consent was obtained from all participants. The study's exclusion criteria comprised pregnant individuals with iron deficiency anemia, hemoglobinopathies, known cases of liver disease, chronic hypertension, renal disease, gestational diabetes, diabetes mellitus, a history of preeclampsia, multiple pregnancies, and those who did not provide consent to participate. Data analysis was conducted using the SPSS version 23.0 program, with a $p < 0.05$ considered as the threshold for statistical significance.

RESULTS

In this study, concerning gestational age, 82% of the cases and 72% of the control group were preterm (<37 weeks) ($p=0.235$). Observations revealed that 42% of cases and 50% of controls were primigravida, with the remaining in each group being multigravida ($p=0.422$). In terms of the distribution of cases by the grading of proteinuria, among the 50 cases, 50% had mild proteinuria (1+), 20% had moderate proteinuria (2+), and the remaining 30% had

severe proteinuria (3+). In the current study, regarding severity, 64% of preeclampsia cases were classified as mild, while 36% were categorized as severe preeclampsia. In this study, the mean serum ferritin in the case group was significantly higher compared to the control group ($p < 0.001$). However, there was no significant difference between the cases and control groups in terms of the levels of hemoglobin and hematocrit ($p=0.761$ and $p=0.231$, respectively). In this study, over three-quarters (76%) of the case group showed elevated serum ferritin (>20 ng/ml), in contrast to 44% in the control group ($p=0.001$). The probability of having elevated serum ferritin in women with preeclampsia was estimated to be 4 times higher (95% CI=1.7-9.5) than that in normal pregnant women. In this study, the mean serum ferritin level was 192.8 ng/ml in the severe preeclampsia group, 86.1 ng/ml in the mild preeclampsia group, and 21.7 ng/ml in normal pregnant women, indicating that the severity of preeclampsia correlates with higher serum ferritin levels ($p < 0.001$).

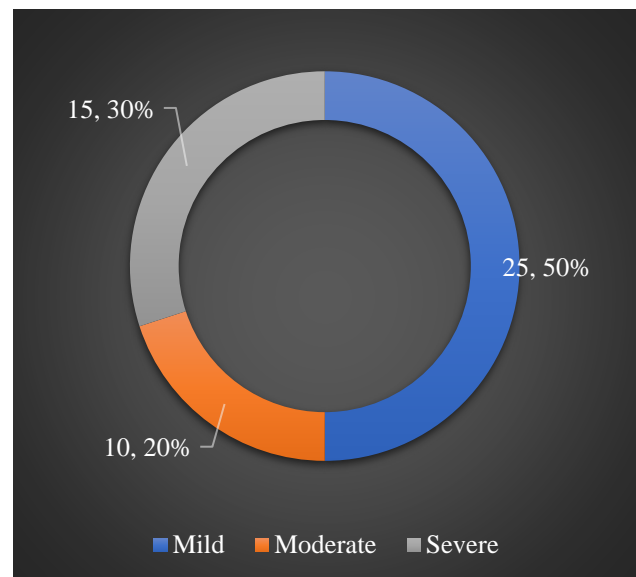


Figure 1: Grading of proteinuria (Case).

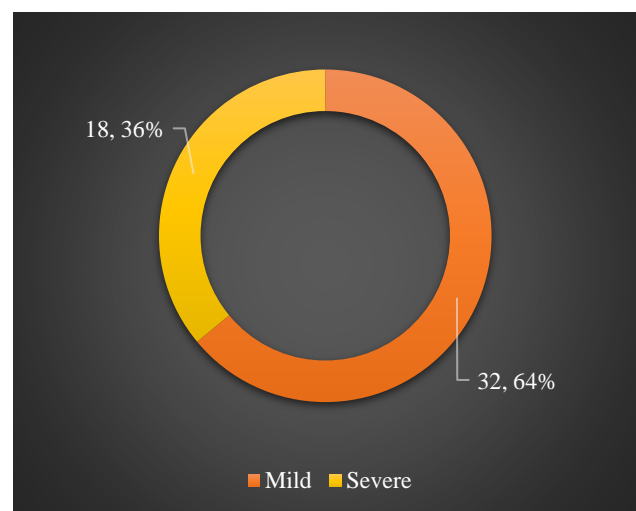


Figure 2: Severity of preeclampsia (Case).

Table 1: Gestational age distribution.

Gestational age	Case, (n=50)		Control, (n=50)		P value
	N	%	N	%	
<37 weeks	41	82	36	72	0.235
≥37 weeks	9	18	14	28	

Table 2: Comparison of gravidity between cases and controls.

Gravida	Case, (n=50)		Control, (n=50)		P value
	N	%	N	%	
Primigravida	21	42	25	50	0.422
Multigravida	29	58	25	50	

Table 3: Association between hematological parameters and preeclampsia.

Parameters	Case, (n=50)		Control, (n=50)		P value
	Mean ± SD		Mean ± SD		
Hemoglobin level (g/dl)	10.9±0.8		11.0±0.9		0.761
Hematocrit (%)	32.4±1.8		31.6±1.5		0.231
Serum ferritin (ng/ml)	124.5±24.8		21.7±1.4		<0.001

Table 4: Estimation of risk of having raised serum ferritin in preeclamptic women.

Parameters (ng/ml)	Case, (n=50)		Control, (n=50)		OR (95% CI)	P value
	N	%	N	%		
> 20	38	76	22	44	4.0 (1.7-9.5)	0.001
≤ 20	12	24	28	56		

Table 5: Association between severity of preeclampsia and serum ferritin.

Severe preeclampsia, (n=18)	Mild preeclampsia, (n=32)	Control, (n=50)	P value
192.8±44.7	86.1±27.8	21.7±1.4	<0.001

DISCUSSION

In this study, 82% of cases and 72% of controls were preterm (<37 weeks of gestation) ($p=0.235$). Another study found that 89.4% of preeclamptic women had preterm gestational age, with a mean of 34.65 ± 1.53 weeks in cases and 35.08 ± 1.73 weeks in controls ($p>0.05$).¹² Additionally, 42% of cases and 50% of controls were primigravida ($p=0.422$), aligning with findings by Paul et al where 65.0% had primigravida in cases and 70.0% in controls ($p>0.05$).¹³ In the present study, 50% of cases had mild proteinuria, 20% had moderate proteinuria, and 30% had severe proteinuria. Based on severity, 64% of preeclampsia cases were mild, and 36% were severe. In a previous study, the majority (94.1%) of patients with severe preeclampsia, 63.3% with mild preeclampsia, and 36.2% in the control group had serum ferritin levels >120 ng/ml.¹² The differences were statistically significant ($p<0.05$) between preeclampsia severities and serum ferritin levels. The mean serum ferritin in the case group was significantly elevated compared to the control group ($p<0.001$). No significant differences were found between cases and control groups in terms of hemoglobin and hematocrit levels ($p=0.761$ and $p=0.231$). This aligns with similar findings in a study by Zafar and Iqbal.¹⁴ In the

current study, over three-quarters (76%) of the case group had elevated serum ferritin (>20 ng/ml), compared to 44% in the control group ($p=0.001$). The likelihood of elevated serum ferritin in women with preeclampsia was estimated to be 4 times higher (95% CI=1.7-9.5) than in normal pregnant women. In a study by Taheripanah, none of the normal women had abnormal ferritin levels, while 45.5% of preeclamptic patients had abnormal ferritin levels, a higher percentage than observed in our study.¹⁵ The mean serum ferritin levels in this study demonstrated that the severe preeclampsia group had a level of 192.8 ng/ml, the mild preeclampsia group had 86.1 ng/ml, and normal pregnant women had 21.7 ng/ml, indicating a correlation between higher severity of preeclampsia and elevated serum ferritin levels ($p<0.001$). The changes in serum ferritin levels at different gestational ages in both case and control groups are depicted. Another study reported significantly different mean serum ferritin levels in case and control groups, with values of 100.03 ± 123.52 µgm/L and 31.53 ± 20.86 µgm/L, respectively ($p<0.001$).¹⁶

Limitations

This study was conducted at a single center and involved a relatively small sample size. Additionally, the study was

conducted over a brief period. Therefore, it's important to note that the findings of this study may not accurately represent the overall situation across the entire country.

CONCLUSION

Elevated serum ferritin levels emerge as a significant characteristic in preeclamptic cases compared to normal pregnant women. The probability of experiencing elevated serum ferritin in preeclampsia is notably four times higher than in the normal pregnancy population. Furthermore, a positive correlation exists between the severity of preeclampsia and higher serum ferritin levels. These findings emphasize the potential role of serum ferritin as a biomarker in the context of preeclampsia, offering insights into both its diagnostic and prognostic implications. Further research may shed light on the mechanisms underlying this association and whether monitoring serum ferritin levels could be a valuable aspect of managing and predicting the severity of preeclampsia.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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