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Maternal Serum Ferritin and Pregnancy Outcomes: A Comparative Analysis between Preterm and Term Labor

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Abstract

Background: Preterm labor remains a leading cause of neonatal morbidity and mortality worldwide. Emerging evidence suggests that maternal iron status, particularly elevated serum ferritin levels, may be associated with preterm labor through mechanisms involving inflammation or oxidative stress. ***Methods:*** This case-control study was conducted at the Department of Obstetrics & Gynaecology, Dhaka Medical College Hospital, from June 2022 to May 2023. A total of 88 pregnant women were enrolled, with 44 cases in the preterm labor group and 44 in the term labor (control) group. Maternal serum ferritin levels were measured and compared between the two groups. Sociodemographic and obstetric data were also analyzed. Statistical significance was determined using appropriate tests, with a p-value < 0.05 considered significant. ***Results:*** The mean maternal age was 25.59 ± 5.80 years in the preterm labor group and 24.56 ± 5.41 years in the term group ($p = 0.076$). A higher proportion of preterm labor cases were multiparous (59.1%), whereas most term deliveries were in primiparous women (52.3%), though this was not statistically significant ($p = 0.285$). Serum ferritin levels were significantly elevated in the preterm labor group (89.09 ± 106.07 ng/mL) compared to the term group (32.13 ± 31.40 ng/mL), with a p-value of 0.004. A significant negative correlation was found between ferritin levels and gestational age ($r = -0.313$, $p < 0.05$). ***Conclusion:*** Elevated maternal serum ferritin levels are significantly associated with preterm labor and inversely correlated with gestational age. Serum ferritin may serve as a potential biomarker for identifying women at risk of preterm delivery.

Keywords: Preterm labor, Maternal serum ferritin, Iron status, Pregnancy, Gestational age, Inflammation.

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INTRODUCTION

Preterm labor, defined as childbirth occurring before 37 completed weeks of gestation, remains a major global obstetric challenge and a leading cause of neonatal morbidity and mortality. According to the World Health Organization (WHO), approximately 15 million babies are born prematurely each year, and preterm birth complications are responsible for nearly 1 million deaths annually [1]. In low- and middle-income countries like Bangladesh, the burden of preterm birth is particularly significant due to limited access to advanced neonatal care and preventive strategies [2].

Multiple etiological factors contribute to preterm labor, including infections, uterine anomalies, cervical insufficiency, multiple gestation, and various maternal medical conditions [3]. In recent years, growing attention has been directed toward the role of maternal nutritional and biochemical markers in predicting pregnancy outcomes [3]. Among these, serum ferritin, a key indicator of iron stores and inflammation, has emerged as a potential biomarker linked to preterm

birth [4].

Ferritin is an iron-storage protein primarily synthesized by the liver, playing a critical role in iron metabolism. During pregnancy, maternal iron requirements increase significantly to support fetal development and maternal hematological expansion [5]. Although iron deficiency anemia has traditionally been a focus in maternal health, accumulating evidence suggests that elevated serum ferritin levels may also be associated with adverse pregnancy outcomes, including preterm labor [6]. This paradoxical relationship may be due to ferritin's dual function as both an iron reserve and an acute-phase reactant that increases during systemic inflammation or infection [7].

Several studies have reported inconsistent findings regarding the association between maternal serum ferritin levels and the risk of preterm delivery [8]. Some have suggested that high ferritin concentrations may indicate underlying inflammation or oxidative stress, both of which can contribute to premature uterine contractions and cervical changes [9]. Others have emphasized that both low and high ferritin levels could negatively affect pregnancy outcomes, highlighting the need for a balanced iron status during gestation.

Given the limited data from South Asian populations, particularly in the Bangladeshi context, further investigation is warranted [10]. Understanding the association between maternal serum ferritin levels and preterm labor may help identify at-risk pregnancies earlier and improve clinical decision-making through targeted interventions [11].

The study aimed to compare maternal serum ferritin levels between women with preterm and term labor and assess their relationship with gestational age and pregnancy outcomes. By evaluating this association, the study seeks to provide evidence on whether serum ferritin can serve as a predictive biomarker for preterm birth in the Bangladeshi population.

METHODOLOGY & MATERIALS

This case-control study was conducted at the Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital (DMCH), from June 2022 to May 2023. A total of 88 pregnant women were enrolled using purposive sampling, with 44 women in the case group who presented with preterm labor and 44 women in the control group who had term labor. Eligible participants were aged between 18 and 35 years, had singleton pregnancies, and presented with regular uterine contractions along with cervical dilatation and effacement greater than 2 cm. The case group included women with gestational age between 28 and <37 weeks, while the control group consisted of women with gestational age ≥37 weeks. Women with anemia, iron overload, chronic infections, multiple pregnancies, polyhydramnios, diabetes mellitus, preeclampsia, hepatic or renal disease, a history of preterm labor due to incompetent cervix, intrauterine fetal death, or known fetal anomalies were excluded.

Data collection was carried out using a structured questionnaire that included sociodemographic information, medical and obstetric history, and relevant clinical findings. Blood samples were obtained from the antecubital vein under aseptic conditions prior to delivery. Serum ferritin levels were measured using a two-step Chemiluminescent Microparticle Immunoassay (CMIA), which provides accurate and sensitive quantification of ferritin concentrations. All necessary safety precautions, including the use of gloves, lab coats, and protective eyewear, were observed during sample handling.

Statistical analysis was performed using SPSS version 25. Continuous variables were analyzed using the Mann–Whitney U test, and categorical variables were compared using the Chi-square test. The correlation between serum ferritin levels and gestational age was assessed using the Spearman correlation test. A p-value of less than 0.05 was considered statistically significant. Ethical approval for the study was obtained from the Institutional Review Board of Dhaka Medical College Hospital. Informed written consent was taken from all participants prior to data collection.

RESULTS

Table-I: Sociodemographic characteristics of the study participants (n=88)

Characteristics	Pre-term labor (N=44)	Term labor (N=44)	p-value
	Frequency (%)	Frequency (%)	
Age (in years)			
18-26	24 (54.5)	32 (72.7)	0.076^{ns}
27-35	20 (45.5)	12 (27.3)	
Mean±SD	25.59±5.80	24.56±5.41	$^{b}0.331^{ns}$

Data presented frequency, percentage, and mean ± SD over columns. P-value reached through a chi-square test for categorical variables and [b]Mann-Whitney U test, where continuous data was not normally distributed.
s=significant
ns=non-significant

Table-I shows that, age of the preterm pregnancy (25.59±5.80) and term pregnancy (24.56±5.41) was not statistically different ($p > 0.05$).

Table II: Obstetric characteristics of the study participants (n=88)

Characteristics	Pre-term labor (N=44)	Term labor (N=44)	p-value
	Frequency (%)	Frequency (%)	
Parity			
Primiparous	18 (40.9)	23 (52.3)	0.285^{ns}
Multiparous	26 (59.1)	21 (47.7)	

Data presented as frequency and percentage over columns. P-value reached through a chi-square test for categorical variables.
s=significant
ns=non-significant

Table II shows that, majority of the pre-term pregnant women 26 (59.1%) was multiparous.

Table-III: Comparison between preterm and full-term regarding biochemical data (n=88)

Characteristics	Pre-term labor (N=44)	Term labor (N=44)	p-value
	Mean ± SD	Mean ± SD	
Serum Ferritin	89.09±106.07	32.13±31.40	^{b}**0.004**^{s}

Data presented as mean ± SD over columns. P-value reached through ^{b}Mann-Whitney U test, where data was not normally distributed.
s=significant
ns=non-significant

Table-III shows that, serum ferritin was statistically significant between both groups ($p < 0.05$).

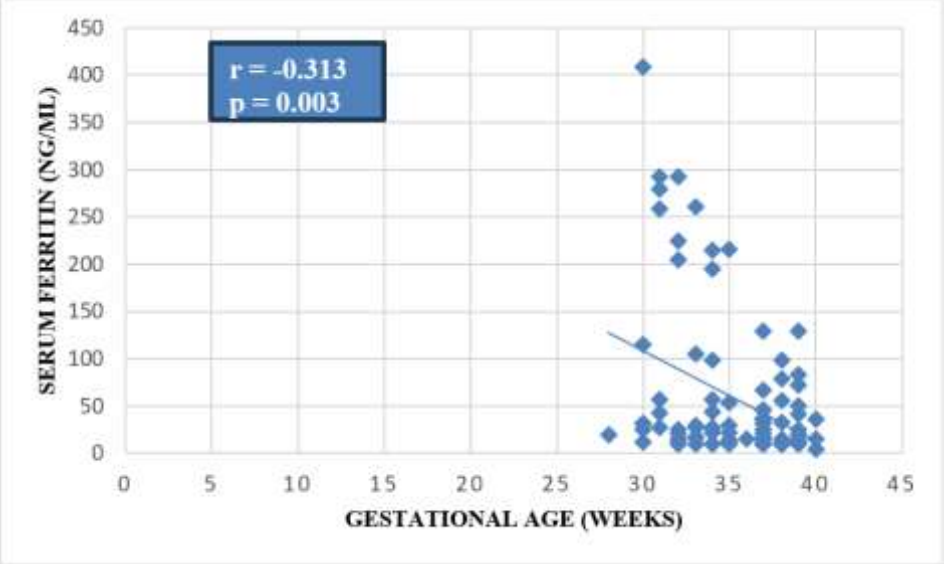

Figure-1: Relationship between serum ferritin levels and gestational age (n=88)
R^2 linear = 0.139

Figure-1 shows that serum ferritin level increases with decreased gestational age; the relationship is negative but weak ($r = -0.313$) and also statistically significant ($p < 0.05$).

DISCUSSION

This study investigated the association between maternal serum ferritin levels and the risk of preterm labor. Our findings revealed that women in the preterm labor group had significantly higher mean serum ferritin levels (89.09 ± 106.07 ng/mL) compared to those who delivered at term (32.13 ± 31.40 ng/mL), with a statistically significant p-value of 0.004. Furthermore, we observed a weak but statistically significant negative correlation ($r = -0.313$, $R^2 = 0.139$) between serum ferritin levels and gestational age, indicating that elevated ferritin levels were associated with earlier delivery.

Our results align with the findings of El-Shahawy *et al.*, who also reported significantly higher serum ferritin levels in women presenting with preterm labor, suggesting a possible role of elevated ferritin as a

predictive marker [12]. Similarly, Khambalia *et al.*, highlighted that altered iron status, particularly elevated serum ferritin in early pregnancy, was associated with adverse outcomes including preterm birth [13]. In addition, Rahmati *et al.*, in a meta-analysis, concluded that both iron deficiency and elevated iron markers can be linked with preterm birth, underscoring the complexity of iron metabolism in pregnancy [14].

Interestingly, while iron deficiency anemia is classically associated with poor pregnancy outcomes, emerging evidence has pointed toward elevated ferritin as a marker of subclinical inflammation, which may contribute to spontaneous preterm labor. This notion is supported by Khezri *et al.*, who found a significant association between maternal anemia and preterm birth, but also noted that iron overload might reflect an inflammatory state detrimental to pregnancy continuation [15].

In our study population, although there was no significant difference in parity or age between the groups ($p = 0.285$ and $p = 0.076$, respectively), 59.1% of preterm labor cases were multiparous, and 72.7% of term deliveries occurred in women aged 18–26 years. These trends, although not statistically significant, are consistent with studies that have observed a higher prevalence of preterm labor in multiparous women and older maternal age groups [16, 17].

Further supporting our results, Oskovi-Kaplan et al., emphasized that untreated maternal anemia and iron imbalance, including both deficiency and excess, may lead to poor neonatal outcomes, including preterm birth [18]. Moreover, Iqbal and Ekmekcioglu, in their meta-analysis, stressed the importance of maintaining optimal maternal iron status to reduce the risk of adverse pregnancy outcomes [19].

It is important to consider that serum ferritin is an acute phase reactant and may be elevated in the presence of infection or inflammation. As suggested by Gomes *et al.*, and Hornaday *et al.*, elevated maternal biomarkers, including ferritin, may reflect underlying inflammatory processes that predispose women to spontaneous preterm labor [20, 21]. Thus, elevated ferritin in our study may not solely indicate iron overload, but also an ongoing subclinical inflammatory state.

The findings of our study are further contextualized by Rahman *et al.*, who, in a Bangladeshi cohort, found that elevated maternal plasma ferritin levels were inversely associated with neonatal size at birth [22]. This supports the inverse relationship we observed between serum ferritin levels and gestational age.

Limitations of the study

The cross-sectional design restricts causal inference, and the sample size, though adequate, may limit generalizability. Furthermore, potential confounders such as infections, chronic inflammation, and iron supplementation history were not fully accounted for. Future studies should adopt longitudinal designs with larger, more diverse populations to validate ferritin's predictive role and establish standardized cut-off values.

CONCLUSION

In conclusion, our findings indicate that elevated maternal serum ferritin levels are significantly associated with preterm labor, and a negative correlation exists between ferritin levels and gestational age. These results suggest that serum ferritin may serve as a potential marker for identifying women at risk for preterm delivery. Further research incorporating inflammatory markers and longitudinal monitoring is warranted to better elucidate the mechanisms involved and to guide iron supplementation policies in pregnancy.

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