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Original Research Article

Association of maternal serum ferritin level with preterm labor

Popy R. Kundu[1]*, M. Nupur Aktar[2], Umme S. Shilpi[3], Tanzin Hossain[3], Rubab Sarmin[4], Sarna Tarafder[5], Jannatul F. Chowdhury[6], Khadiza A. Sumi[7]

[1]Department of Obstetrics and Gynaecology, Specialized Hospital, Khulna, Bangladesh
[2]Department of Obstetrics and Gynaecology, Upazila Health Complex, Daganbhuiyan, Feni, Bangladesh
[3]Department of Obstetrics and Gynaecology, Kurmitola General Hospital, Dhaka, Bangladesh
[4]Department of Obstetrics and Gynaecology, Upazila Health Complex, Chowgacha, Jashore, Bangladesh
[5]Department of Obstetrics and Gynaecology, Dhaka Medical College, Dhaka, Bangladesh
[6]Department of Obstetrics and Gynaecology, Sarkari Karmachari Hospital, Dhaka, Bangladesh
[7]Department of Obstetrics and Gynaecology, 250 Bed General Hospital, Chandpur Sadar, Chandpur, Bangladesh

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***Correspondence:**
Dr. Popy R. Kundu,
E-mail: paul.tanmoy12@gmail.com

ABSTRACT

Background: Preterm labor is a significant contributor to neonatal morbidity and mortality worldwide. Identifying reliable biomarkers for predicting preterm birth can improve maternal and neonatal outcomes. Serum ferritin, an acute-phase reactant and iron storage protein, may play a role in the pathophysiology of preterm labor. This study aimed to evaluate the association between maternal serum ferritin levels and preterm labor.
Methods: A case-control study was conducted in the Department of Obstetrics and Gynaecology at Dhaka Medical College Hospital from June 2022 to May 2023. A total of 88 pregnant women were enrolled using purposive sampling, including 44 with preterm labor (cases) and 44 with term labor (controls). Sociodemographic, obstetric, and biochemical data were collected, and maternal serum ferritin levels were measured. Data were analyzed using statistical package for the social sciences (SPSS) version 25, and comparisons between groups were made using the Mann-Whitney U test and Chi-square test where appropriate.
Results: There was no significant difference in maternal age between the two groups. However, serum ferritin levels were significantly higher in the preterm group (89.09±106.07 ng/ml) compared to the term group (32.13±31.40 ng/ml) ($p=0.004$). A weak but statistically significant negative correlation was observed between serum ferritin levels and gestational age ($r=-0.313$, $p<0.05$).
Conclusions: Elevated maternal serum ferritin levels are significantly associated with preterm labor. Serum ferritin may serve as a useful biomarker for identifying women at risk of preterm delivery, allowing for timely interventions to prevent adverse pregnancy outcomes.

Keywords: Preterm labor, Serum ferritin, Biomarker, Pregnancy, Maternal health

INTRODUCTION

Preterm delivery is a major global health concern, associated with significant short- and long-term physical, emotional, psychological, and financial consequences. It refers to childbirth occurring before 37 completed weeks of gestation and is a leading cause of neonatal morbidity and mortality.[1] Preterm labor is clinically diagnosed when there are regular uterine contractions accompanied by cervical changes, such as dilation or effacement, or when a woman presents with cervical dilation of at least 2 cm. However, fewer than 10% of women diagnosed with preterm labor actually deliver within seven days, highlighting the complexity of predicting outcomes. It is important to note that spontaneous labor is not the sole contributor to preterm birth; many cases arise from

preterm premature rupture of membranes (PROM) or medical conditions that necessitate early delivery.[2]

Globally, approximately 15 million babies are born preterm each year, accounting for 11% of all live births, with around 90% of these occurring in low- and middle-income countries. The burden is particularly high in Africa and Asia, which together contribute to approximately 85% of global preterm births. Prematurity accounts for about 75% of perinatal mortality and 50% of long-term morbidity, posing a considerable challenge to healthcare systems, especially in resource-limited settings.[3] While the pathophysiology of preterm labor remains incompletely understood, increasing evidence supports the role of subclinical infections and chronic intrauterine inflammation in its development.[4]

Multiple risk factors have been associated with preterm labor, including a history of previous preterm birth, abortion, multifetal pregnancy, vaginal bleeding, moderate to severe anemia, cervical insufficiency or surgery, uterine anomalies, assisted reproductive techniques, low socioeconomic status, poor weight gain, and substance abuse.[4-14] Among these, infection and inflammation have been identified as key contributors, especially in spontaneous cases. It has been hypothesized that subclinical infections may elevate maternal serum ferritin levels, which in turn are associated with an increased risk of preterm PROM and labor.[9]

Ferritin, an intracellular iron-storage protein, plays a vital role in maintaining iron in a soluble and non-toxic form. Beyond its role in iron metabolism, ferritin is also an acute-phase reactant that increases during inflammatory processes.[11] Elevated serum ferritin levels have been documented in various inflammatory and infectious conditions, suggesting its potential utility as a biomarker in pregnancy complications. Given the central role of inflammation in the initiation and progression of preterm labor, serum ferritin may serve as a predictive marker for this condition.[7,13] Several studies have suggested a significant association between elevated maternal ferritin levels and preterm birth, although data from specific populations remain limited.

Despite growing interest in this area, limited research has explored the association between maternal serum ferritin levels and preterm labor in our regional context. Therefore, this study aims to investigate whether elevated maternal serum ferritin levels are associated with an increased risk of preterm labor, providing further insight into its potential role as a predictive marker in high-risk pregnancies.

METHODS

The study was a case-control design conducted from June 2022 to May 2023 at the Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital (DMCH). The study population consisted of 88 pregnant women, with 44 cases having preterm labor and 44 controls with normal term labor.

Inclusion criteria

Participants were selected using purposive sampling, and the inclusion criteria for cases included pregnant women aged 18–35 years with singleton pregnancies, between 28 to <37 weeks of gestation, regular uterine contractions, cervical dilatation and effacement >2 cm, and consent to participate. The control group included pregnant women aged 18–35 years with singleton pregnancies and a gestational age >37 weeks, regular uterine contractions, cervical dilatation and effacement >2 cm, and consent to participate.

Exclusion criteria

Women with anemia, iron overload, preexisting chronic infections, multiple pregnancies, polyhydramnios, diabetes mellitus, preeclampsia, liver or renal disease, previous preterm labor due to incompetent cervix, intrauterine fetal death, or known fetal abnormalities were excluded.

Data were collected using a structured questionnaire that included obstetric and medical history, clinical examination, and hematological investigations. Blood samples were drawn from the antecubital vein under sterile conditions, and serum ferritin levels were measured using a two-step immunoassay technique, chemiluminescent microparticle immunoassay (CMIA), which detects ferritin levels through chemiluminescence. Safety precautions such as wearing gloves, lab coats, and safety glasses were adhered to during sample collection and handling.

Statistical analysis was performed using statistical package for the social sciences (SPSS) software. The Mann-Whitney U test was used for continuous variables, and the Chi-square test was used for categorical data. A Spearman correlation test assessed the relationship between serum ferritin levels and preterm labor. A p value of <0.05 was considered statistically significant. Ethical approval was obtained from the institutional review board, and informed written consent was acquired from all participants.

RESULTS

Table 1 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 2 shows that serum ferritin was statistically significant between both groups (p<0.05).

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).

Table 1: Socio demographic 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 2: 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

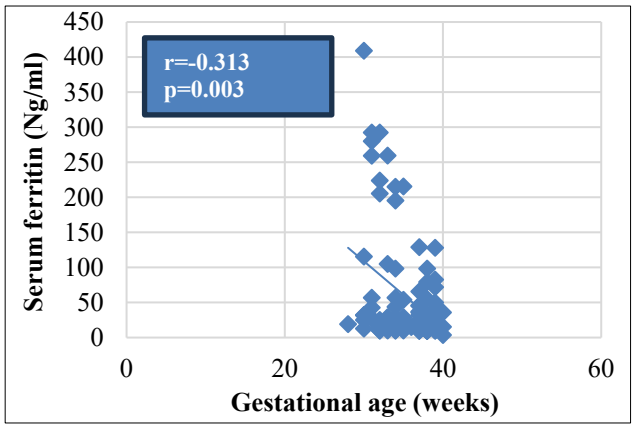

Figure 1: Relationship between serum ferritin levels and gestational age (n=88).

R2 linear=0.139

DISCUSSION

The present study was conducted to evaluate the association between maternal serum ferritin levels and preterm labor. This analytical case-control study was carried out in the Department of Obstetrics and Gynaecology at Dhaka Medical College Hospital, where pregnant women with preterm labor were considered as the case group and those with term labor as the control group.

Ferritin, an iron storage protein synthesized by various tissues including the liver, spleen, bone marrow, and placenta, is also released by infiltrating leukocytes during inflammatory responses. Given its dual role in iron metabolism and inflammation, serum ferritin has emerged as a potential biomarker for predicting preterm labor. The primary objective of this study was to determine whether elevated maternal serum ferritin levels are associated with preterm birth.

We observed that 54.5% patients belonged to age 18-26 years in case group and 72.7% in control group. No significant difference was found between the age of preterm and term labor patients (p>0.05).

In this present study it was observed that mean age was (25.59±5.80) years in case group and (24.56±5.41) years in control group. The difference was statistically not significant (p>0.05) between two groups. In a study it was fund that the case and control were almost similar in terms of age.[15] Mohamed et al observed that mean age in preterm and term group was (27.5±4.31) and (26.2±4.81) years respectively.[15] Our finding was similar to Siddika et al, where the difference of mean maternal age was statistically not significant.[16] Siddika et al observed that mean age of case and control (26.35±4.56) and (24.25±3.60) years respectively.[16]

We found that, among hemoglobin, PCV, TIBC and serum ferritin, only serum ferritin is statistically significant between both groups (p<0.05). Serum ferritin in preterm group (89.09±106.07) and term group (32.13±31.40). Our finding was similar with Mohamed et al, Siddika et al, Jahedbozorgan et al, and Abdel-Malek et al.[15-18]

Malek et al showed that serum ferritin level at week 30 of gestation was significantly higher in preterm group (76.3±29.4 ng/ml) than in the control group (20.2±5.0 ng/ml).[18] Jahedbozorgan et al concluded that serum ferritin level was significantly higher in preterm group (71.7±41.1 ng/ml) than in term group (35.1±20.2 ng/ml).[17] Mohamed et al highlighted that mean serum ferritin level in women with preterm and normal term delivery was (254.62±165.19 ng/ml) and (110.81±63.05 ng/ml) respectively which was much higher from our findings but statistically significant.[15]

We observed 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). Our finding was almost similar with Weintraub et al, where they found no significant correlation between serum

ferritin concentrations and gestational age at birth (Pearson correlation coefficient r=-0.093; p=0.522).[19]

So, serum ferritin 20.58 ng/ml could be proposed as a potential helpful marker to predict preterm labor.

Limitations

Despite careful planning and execution, this study had several limitations. The sample size was relatively small, which may limit the generalizability of the findings. Additionally, the study was conducted in a single tertiary hospital, which might not adequately represent the broader population. Due to limited resources and logistical constraints, purposive sampling was used, introducing the possibility of selection bias that could affect the results. Moreover, only serum ferritin was measured as a predictive biomarker for preterm labor, while other potentially relevant inflammatory and hematologic markers were not assessed.

CONCLUSION

The findings of this study demonstrate that elevated maternal serum ferritin concentrations are significantly associated with spontaneous preterm delivery among the Bangladeshi population. This suggests that serum ferritin may serve as a useful biomarker for identifying women at risk of preterm birth. Early detection of elevated ferritin levels could provide an opportunity for timely intervention, potentially reducing the risk of preterm delivery and its associated complications. Therefore, incorporating serum ferritin measurement into routine antenatal screening could be beneficial in predicting and preventing adverse pregnancy outcomes related to preterm labor.

Recommendations

To obtain more conclusive and generalizable results, future studies should be conducted with larger sample sizes across multiple healthcare centers. National-level multicenter prospective studies are recommended to better understand the relationship between serum ferritin and preterm labor across diverse populations. Random sampling methods should be employed to minimize selection bias.

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