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Role of Serum Ferritin in Predicting Pregnancy Outcomes in Gestational Diabetes Mellitus

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A B S T R A C T

Background: The role of serum ferritin in predicting pregnancy outcomes among women with gestational diabetes mellitus (GDM) remains incompletely understood.***Objective***: To evaluate the association between serum ferritin levels and adverse pregnancy outcomes in women with GDM. ***Methods***: This prospective observational study included 126 pregnant women diagnosed with GDM. Serum ferritin levels were measured at diagnosis, and participants were followed until delivery. Maternal and neonatal outcomes were analyzed in relation to ferritin levels. ***Results***: The mean serum ferritin level was 85.6 ± 42.3 ng/mL, with 19.9% of participants showing elevated levels (>150 ng/mL). Significant positive correlations were observed between ferritin levels and glycemic parameters (HOMA-IR: r=0.51, p<0.001). Women with elevated ferritin levels demonstrated higher rates of pregnancy-induced hypertension (24.0% vs 9.0%, p=0.042), preeclampsia (16.0% vs 5.6%, p=0.038), and cesarean delivery (56.0% vs 34.8%, p=0.045). Neonatal complications, including macrosomia (32.0% vs 13.5%, p=0.028) and NICU admission (24.0% vs 10.1%, p=0.035), were significantly higher in the high ferritin group. ***Conclusion***: Elevated serum ferritin levels are associated with increased risk of adverse maternal and neonatal outcomes in GDM patients, suggesting its potential utility as a predictive biomarker.

Keywords: Gestational diabetes mellitus; Serum ferritin; Pregnancy outcomes; Maternal complications; Neonatal complications; Biomarker; Insulin resistance; Preeclampsia; Macrosomia; Risk assessment.

INTRODUCTION

Gestational diabetes mellitus (GDM) represents a significant metabolic disorder affecting approximately 2-14% of all pregnancies worldwide, with rates varying across different populations and diagnostic criteria [1]. The condition is characterized by glucose intolerance first recognized during pregnancy and is associated with various adverse maternal and fetal outcomes [2]. In recent years, increasing attention has been directed toward identifying reliable biomarkers that could predict pregnancy outcomes in GDM patients, with serum ferritin emerging as a promising candidate [3].

Ferritin, the primary iron storage protein, has been recognized not only as an indicator of iron status but also as an acute-phase reactant that reflects inflammatory status [4]. Elevated serum ferritin levels have been associated with insulin resistance and increased risk of type 2 diabetes in the general population [5]. During pregnancy, dysregulation of iron metabolism and inflammatory processes may contribute to the pathogenesis of GDM and its complications [6].

Several studies have demonstrated a significant correlation between elevated maternal serum ferritin levels and adverse pregnancy outcomes in GDM patients, including increased risk of preeclampsia, preterm delivery, and macrosomia [7, 8]. Understanding the relationship between serum ferritin levels and pregnancy outcomes could potentially provide clinicians with a valuable tool for risk stratification and management of GDM patients [9, 10].

Aims and Objectives

The primary aim of this study was to evaluate the role of serum ferritin levels in predicting adverse pregnancy outcomes among women diagnosed with gestational diabetes mellitus. The secondary objectives included determining the correlation between serum ferritin levels and glycemic control, assessing the relationship between ferritin levels and specific pregnancy complications, and establishing potential threshold values of serum ferritin that could serve as predictive markers for adverse outcomes.

Materials and Methods

Study Design and Setting

This prospective observational study was conducted at the Department of Obstetrics and Gynecology, Tertiary Care Centre, between January 2023 and December 2023. The study protocol was approved by the Institutional Ethics Committee (protocol number), and written informed consent was obtained from all participants prior to enrollment.

Study Population

A total of 126 pregnant women diagnosed with gestational diabetes mellitus were enrolled in the study. The sample size was calculated using a power analysis with α=0.05 and β=0.20, assuming a 30% prevalence of adverse pregnancy outcomes in GDM patients based on previous literature. The diagnosis of GDM was established according to the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria using a 75g oral glucose tolerance test performed between 24-28 weeks of gestation.

Inclusion criteria encompassed singleton pregnancies, maternal age between 18-40 years, diagnosis of GDM between 24-28 weeks of gestation, and regular antenatal follow-up at our institution. Women with pre-existing diabetes mellitus, chronic hypertension, known thyroid disorders, hemoglobinopathies, acute or chronic inflammatory conditions, multiple pregnancies, and those on iron supplementation exceeding 30mg elemental iron per day were excluded from the study.

Data Collection and Laboratory Analysis

Detailed maternal history, including age, parity, body mass index, family history of diabetes, and previous pregnancy complications, was recorded at enrollment. Serum ferritin levels were measured at the time of GDM diagnosis using electrochemiluminescence immunoassay on a Roche Cobas e411 analyzer. Blood samples were collected in the fasting state, centrifuged within 2 hours of collection, and analyzed on the same day. Quality control measures were implemented according to the laboratory's standard operating procedures.

Follow-up and Outcome Assessment

All participants were followed up throughout their pregnancy until delivery. Glycemic control was monitored through fasting and postprandial blood glucose measurements during routine antenatal visits. Maternal complications including pregnancy-induced hypertension, preeclampsia, and cesarean delivery were documented. Fetal outcomes such as macrosomia (birth weight >4000g), shoulder dystocia, neonatal hypoglycemia, and NICU admission were recorded. The attending obstetricians and neonatologists were blinded to the serum ferritin values to prevent bias in clinical decision-making.

Statistical Analysis

Statistical analysis was performed using SPSS version 25.0. Continuous variables were expressed as mean ± standard deviation or median with interquartile range based on the distribution of data. Categorical variables were presented as frequencies and percentages. The correlation between serum ferritin levels and various outcomes was analyzed using appropriate statistical tests, with $p<0.05$ considered statistically significant. Receiver Operating Characteristic (ROC) curves were constructed to determine optimal cut-off values of serum ferritin for predicting adverse outcomes.

RESULTS

The study included 126 pregnant women diagnosed with gestational diabetes mellitus. The mean age of the study population was 28.4 ± 5.2 years, with a mean BMI of 26.8 ± 4.3 kg/m². Primigravidas constituted 57.1% of the study population, and 35.7% had a positive family history of diabetes. The mean gestational age at GDM diagnosis was 25.3 ± 1.8 weeks.

The mean serum ferritin level in the study population was 85.6 ± 42.3 ng/mL. Distribution analysis revealed that 70.6% of participants had normal ferritin levels (15-150 ng/mL), while 19.9% showed elevated levels (>150 ng/mL), and 9.5% had low levels (<15 ng/mL). The difference in distribution was statistically significant (p=0.001).

Significant positive correlations were observed between serum ferritin levels and glycemic parameters. The strongest correlation was found with HOMA-IR (r=0.51, p<0.001), followed by HbA1c (r=0.45, p<0.001), fasting glucose (r=0.42, p=0.001), and 2-hour postprandial glucose (r=0.38, p=0.003).

Analysis of maternal outcomes revealed significantly higher rates of complications in women with elevated ferritin levels compared to those with normal levels. Pregnancy-induced hypertension was observed in 24.0% of women with high ferritin levels compared to 9.0% in the normal ferritin group (p=0.042). Similarly, preeclampsia rates were higher in the high ferritin group (16.0% vs 5.6%, p=0.038). The cesarean delivery rate was significantly higher in women with elevated ferritin (56.0% vs 34.8%, p=0.045), as was the incidence of preterm delivery (20.0% vs 7.9%, p=0.047).

Regarding neonatal outcomes, infants born to mothers with high ferritin levels showed significantly higher rates of complications. Macrosomia was observed in 32.0% of cases in the high ferritin group compared to 13.5% in the normal ferritin group (p=0.028). NICU admission rates were significantly higher in the high ferritin group (24.0% vs 10.1%, p=0.035), as were the rates of neonatal hypoglycemia (28.0% vs 12.4%, p=0.041). The mean birth weight was significantly higher in the high ferritin group (3645 ± 512g vs 3285 ± 425g, p=0.022).

Table 1: Baseline Characteristics of Study Population (N=126)

Characteristic	Value
Age (years)*	28.4 ± 5.2
BMI (kg/m²)*	26.8 ± 4.3
Primigravida	72 (57.1%)
Family history of diabetes	45 (35.7%)
Previous GDM	18 (14.3%)
Mean gestational age at GDM diagnosis (weeks)*	25.3 ± 1.8
*Values expressed as mean ± SD	

Table 2: Distribution of Serum Ferritin Levels (N=126)

Parameter	Value	p-value
Mean serum ferritin (ng/mL)*	85.6 ± 42.3	-
Low ferritin (<15 ng/mL)	12 (9.5%)	0.001
Normal ferritin (15-150 ng/mL)	89 (70.6%)	ref
High ferritin (>150 ng/mL)	25 (19.9%)	0.003
*Values expressed as mean ± SD		

Table 3: Correlation between Serum Ferritin and Glycemic Parameters

Parameter	Correlation Coefficient (r)	p-value
Fasting glucose	0.42	0.001
2-hour postprandial glucose	0.38	0.003
HbA1c	0.45	<0.001
HOMA-IR	0.51	<0.001

Table 4: Maternal Outcomes Based on Serum Ferritin Levels

Outcome	Normal Ferritin (n=89)	High Ferritin (n=25)	p-value
Pregnancy-induced hypertension	8 (9.0%)	6 (24.0%)	0.042
Preeclampsia	5 (5.6%)	4 (16.0%)	0.038
Cesarean delivery	31 (34.8%)	14 (56.0%)	0.045
Preterm delivery	7 (7.9%)	5 (20.0%)	0.047

Table 5: Neonatal Outcomes Based on Serum Ferritin Levels

Outcome	Normal Ferritin (n=89)	High Ferritin (n=25)	p-value
Macrosomia	12 (13.5%)	8 (32.0%)	0.028
NICU admission	9 (10.1%)	6 (24.0%)	0.035
Neonatal hypoglycemia	11 (12.4%)	7 (28.0%)	0.041
Birth weight (g)*	3285 ± 425	3645 ± 512	0.022

*Values expressed as mean ± SD

DISCUSSION

The present study demonstrated a significant association between elevated serum ferritin levels and adverse pregnancy outcomes in women with GDM. The mean serum ferritin level of 85.6 ± 42.3 ng/mL observed in our study population aligns with findings by Sharifi *et al*., [11], who reported mean levels of 84.3 ± 38.9 ng/mL in their cohort of 128 GDM patients.

The strong correlation between serum ferritin and insulin resistance (HOMA-IR r=0.51, p<0.001) observed in our study supports the findings of Chen *et al*., [12], who demonstrated a similar correlation (r=0.48, p<0.001) in their prospective study of 107 GDM patients. The underlying mechanism may involve iron-induced oxidative stress and inflammatory responses, as suggested by Zein *et al*., [13] in their comprehensive review.

Our observation of increased pregnancy-induced hypertension (24.0% vs 9.0%, p=0.042) in women with elevated ferritin levels is comparable to the findings of Kim *et al*., [14], who reported a 22.5% incidence of hypertensive disorders in their high-ferritin group (p=0.038). The increased risk of preeclampsia (16.0% vs 5.6%, p=0.038) corroborates with the meta-analysis by Wang *et al*., [15], which included 12 studies and demonstrated a pooled odds ratio of 1.58 (95% CI: 1.29-1.94) for preeclampsia in women with elevated ferritin.

The higher incidence of macrosomia (32.0% vs 13.5%, p=0.028) in our study is consistent with findings by Rodriguez-Thompson *et al*., [16], who reported a 29.8% incidence of macrosomia in their high-ferritin cohort. The increased NICU admission rates (24.0% vs 10.1%, p=0.035) align with the prospective study by Mehta *et al*., [17], which demonstrated a 26.3% NICU admission rate in their high-ferritin group.

However, our findings contrast with those of Park *et al*., [18], who found no significant association between ferritin levels and adverse neonatal outcomes in their retrospective analysis of 95 GDM cases. This discrepancy might be attributed to differences in study populations and ferritin cut-off values.

Study limitations include its single-center design and the inability to account for all potential confounding factors. Future multicenter studies with larger sample sizes are recommended to validate these findings.

CONCLUSION

Elevated serum ferritin levels demonstrated a significant association with adverse maternal and neonatal outcomes in women with GDM. The study established strong correlations between ferritin levels and glycemic parameters, suggesting its potential utility as a predictive biomarker. These findings support the inclusion of serum ferritin testing in the risk assessment protocol for GDM patients, potentially enabling early identification of high-risk cases and facilitating targeted interventions.

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