OPEN ACCESS

Scholars International Journal of Obstetrics and Gynecology

Abbreviated Key Title: Sch Int J Obstet Gynec
ISSN 2616-8235 (Print) | ISSN 2617-3492 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Original Research Article

Impact of Elevated Serum Ferritin on Maternal and Fetal Outcome in Gestational Diabetes Mellitus

Dr. Umme Salma Shilpi[1*], Dr. Mst. Ismat Zerin[2], Dr. Mossa Nupur Aktar[3], Dr. Marfoonnahar Smriti[4], Dr. Tahurun-Nesa[5], Dr. Sanjana Rahman[6], Dr. Popy Rani Kundu[7], Dr. Najmatun Jikria[8]

[1]Indoor Medical Officer, Department of Obstetrics and Gynaecology, Kurmitola General Hospital, Dhaka, Bangladesh
[2]Registrar, Department of Obstetrics and Gynaecology, Kurmitola General Hospital, Dhaka, Bangladesh
[3]Assistant Registrar, Department of Obstetrics and Gynaecology, Shaheed M. Mansur Ali Medical College Hospital, Sirajganj, Bangladesh
[4]Registrar, Department of Obstetrics and Gynaecology, Mugda Medical College and Hospital, Dhaka, Bangladesh
[5]Medical officer, Department of Obstetrics and Gynaecology, Mugda Medical College and Hospital, Dhaka, Bangladesh
[6]Assistant Surgeon, Department of Obstetrics and Gynaecology, DNCC Covid Hospital, Dhaka, Bangladesh
[7]Indoor Medical Officer, Department of Obstetrics and Gynaecology, Specialized Hospital, Khulna, Bangladesh
[8]Medical officer, Naogao Sadar Hospital, Naogao, Bangladesh

DOI: https://doi.org/10.36348/sijog.2024.v07i11.008 | **Received:** 16.10.2024 | **Accepted:** 21.11.2024 | **Published:** 27.11.2024

***Corresponding author:** Dr. Umme Salma Shilpi
Indoor Medical Officer, Department of Obstetrics and Gynaecology, Kurmitola General Hospital, Dhaka, Bangladesh

Abstract

Background: Gestational diabetes mellitus (GDM) is associated with significant maternal and fetal complications, including preterm delivery, macrosomia, and neonatal hypoglycemia. Elevated serum ferritin levels, a marker of inflammation and oxidative stress, may exacerbate these risks. This study was aims to determine if serum ferritin elevation is a marker of adverse maternal and fetal outcome in pregnancies complicated by GDM. ***Method:*** A case control study was conducted in the Department of Obstetrics and Gynecology, Dhaka Medical College, Dhaka from September 2020 to August 2021. 42 pregnant women at 2nd 3rd trimester attended for antenatal care diagnosed as GDM was selected as cases and 42 non-diabetic pregnant women matching with cases by age and gestational age was selected as control are included this study. GDM was diagnosed by oral glucose tolerance test (OGTT). The serum ferritin level of these patients was measured. ***Results:*** Elevated serum ferritin was significantly associated with GDM ($p<0.05$). GDM women had higher rates of obesity ($p=0.005$), preterm delivery (30.9% vs. 16.6%) and term delivery was less in case group (69.05%) than controls (83.33%) . In neonates of GDM mothers macrosomia rates were 26.19% in case group and 14.3% in control group. Hypoglycemia was 16.6%, respiratory distress 11.9% and NICU admissions 21.4% ($p<0.05$ vs controls). ***Conclusion:*** Elevated serum ferritin is a strong predictor of adverse maternal and neonatal outcomes in GDM pregnancies. These findings suggest that ferritin could serve as a biomarker for identifying high-risk pregnancies. Incorporating ferritin screening into antenatal care may facilitate early risk stratification and targeted interventions.

Keywords: Gestational diabetes mellitus, Serum ferritin, maternal outcomes, neonatal outcomes, preterm delivery.

INTRODUCTION

Gestational diabetes mellitus (GDM) is a common complication of pregnancy, specifically hyperglycaemia first identified after 20 weeks of gestation. GDM is diagnosed in up to about 10 to 15% of pregnancies worldwide and the rates vary across populations as a result of differences in risk factors and diagnostic criteria [1,2]. And it is associated with potentially significant maternal and fetal morbidity (increased risk of hypertensive disorders, cesarean delivery, preterm birth, and long-term development of type 2 diabetes) [3,4]. Furthermore, GDM is associated with fetal complications, including macrosomia, neonatal hypoglycemia, respiratory distress and future metabolic disorders which predispose to the neonatal health [5, 6].

Serum ferritin is a key indicator of body iron status, and is also an acute phase reactant that rises correspondingly in response to systemic inflammation [7]. Hyperferritinemia, which has been shown to be associated with insulin resistance, GDM hallmark, and oxidative stress, beta cell dysfunction associated with glucose intolerance, may provide another detrimental contributing factor to the disorder [8]. Several other studies have indicated that women with a higher serum ferritin level during pregnancy are at greater risk for developing GDM [9-11]. However, among its role in GDM development, elevated ferritin levels have been associated with adverse maternal and fetal outcomes, like preeclampsia, preterm delivery, and neonatal complications [12,13].

Maternal hyperglycemia and the corresponding metabolic changes affect fetal outcomes in GDM pregnancies. Fetal overgrowth (macrosomia), a major predictor of delivery complications and neonatal morbidity, increases following chronic intrauterine exposure to hyperglycemia [14]. Complications due to GDM in neonates include respiratory distress and hypoglycemia and neonates born to mothers with GDM are more likely to necessitate NICU admission [15]. Recent evidence points to additional contributions of abnormal maternal ferritin to these outcomes through its promotion of placental dysfunction and fetal oxidative stress, both of which compromise fetal growth and development [16, 17].

Although serum ferritin is increasingly identified as a marker for GDM and its associated complications, little is known regarding the specific effects of elevated ferritin on improving or worsening of maternal and fetal outcomes in resource poor circumstances. The risks are compounded with GDM in Bangladesh where the prevalence of GDM is about 9.7% and limited access to antenatal care and routine biochemical screening [9]. Improving maternal and neonatal health outcomes in such settings requires addressing these gaps.

The objective of this study is to determine if elevated serum ferritin levels are associated with maternal and fetal outcomes for pregnancies complicated by GDM. We try to clarify the role of serum ferritin in predicting adverse outcome by analyzing parameters such as birth weight, preterm delivery, neonatal complications, and maternal characteristics. The findings may inform targeted interventions to manage high risk pregnancies and care for women with GDM.

Objective

The objective of this study were to evaluate the impact of elevated serum ferritin on maternal and fetal outcome in gestational diabetes mellitus.

METHODOLOGY & MATERIALS

Case control study was conducted in the Department of Obstetrics and Gynecology, Dhaka Medical College, Dhaka from September 2020 to August 2021. 42 pregnant women at 2nd 3rd trimester attended for antenatal care diagnosed as GDM was selected as cases and 42 non-diabetic pregnant women matching with cases by age and gestational age was selected as control in this study. GDM was diagnosed by oral glucose tolerance test (OGTT). The serum ferritin level of these patients was measured.

Inclusion criteria

I. Diagnosed case of GDM
II. Pregnant women who have given consent to participate
III. Single tone pregnancy.

Exclusion criteria

I. Pre-gestational diabetes
II. Pregnancy with severe anaemia
III. Acute or chronic renal disease
IV. Acute or chronic liver disease

Data Collection: Patients were selected purposively according to the availability of the patients. Detailed Obstetric and medical history and clinical information were obtained by preformed structured questionnaire.

Blood Sampling Methods: Maternal blood sample was drawn from the ante-cubital vein. 3 milliliters blood was drawn with proper aseptic precautions. The blood sample was transferred into a clean, dry test tube and taken to the laboratory. Blood samples were centrifuged for 10 minutes at a rate of 4000rmp.

Ethical Consideration: There was minimum physical, psychological, social and legal risk during history taking, physical examination and investigation. Proper safety measures were ensured in every steps of the study. Ethical clearance was obtained from the authority of DMCH to undertaken the present study. All the patients was informed about the study design, the underlying hypothesis and the right for the participants to withdraw themselves from the projects at any time. Informed written consent was obtained from each subject who voluntarily provide consent to participate in the study.

Statistical Analysis of Data: Statistical analysis of the results were obtained by using windows based computer software device with Statistical Packages for Social Science (SPSS-22). The results presented in tables and diagrams. Comparison of means made by using Student t-test, Mann-Whitney U-test. Categorical data was analyze by Chi-square Test. Odd ratio with 95% confidence interval and Pearson's correlation test was utilized between serum ferritin (ng/ml) with fasting plasma glucose (mmol/L) and post paradial plasma glucose (mmol/L) and p value.

RESULT

Table-1: Distribution of respondents by baseline characteristics

Variables		Case Group		Control Group		P-value
		n=42	%	n=42	%	
Age(years)	<18	4	9.5	3	7.1	0.387
	18-30	28	66.7	32	76.2	
	>30	10	23.8	7	16.7	
mean± SD		27.44±3.21		25.72±2.83		
BMI	Normal	3	7.1	14	33.3	0.005
	Overweight	22	52.4	20	47.6	
	Obese	17	40.5	8	19	

Table 1 shows that among the GDM detected patient, most of them (66.7%) were aged between 18 to 30 years. Similarly, most of the non-GDM patients (76.2%) were also aged between 18-30 years of age. No significant difference was found between the age of the GDM and non GDM patients (P = 0.387). It also shows that obese mother were more frequent in GDM detected group. The association of BMI with GDM was statistically significant (P<0.05).

Table-2: Comparison of Hemoglobin (g/dl) parameters between cases and controls (case=42, control=42)

Case/Control	n	Mean ± SD	p-value
Case	42	12.8 ± 11.4	0.375
Control	42	10.1 ± 0.9	

P value obtained from independent sample t test.

A low hemoglobin level was observed in control group compared to case group, although the difference between the groups did not turn to significant (p=0.375).

Gravida: Gravidity of the study sample was categorized into 'Primigravida' and 'Multigravida'. 18 (42.9%) GDM patients had been pregnant once and 24 (57.1%) more than once. In case of normal patient, 20 (47.6%) had been pregnant once and 22 (52.4%) more than once.

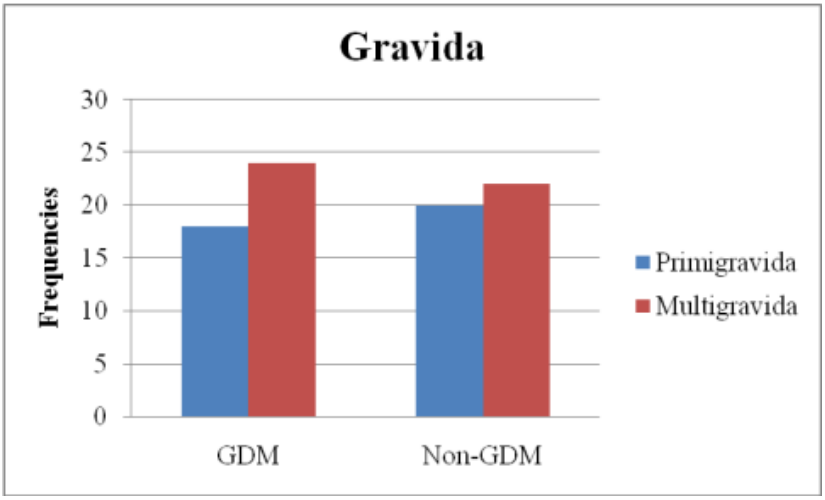

Figure-1: Gravida of the study groups

Gestational weeks

Most of the GDM patients (46.67%) were diagnosed at a gestational age of 25 to 32 weeks.

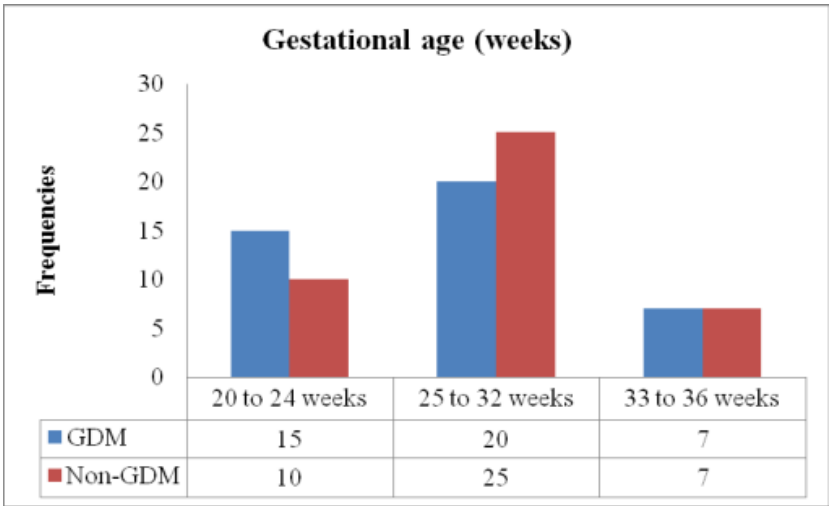

Figure-2: Gestational age (weeks) of the study groups

Table-3: Comparison of Birth Weight Between GDM and Non-GDM Groups

Group	n	Mean Birth Weight (kg) ± SD	Low Birth Weight (<2.5 kg) (%)	Macrosomia (>4 kg) (%)	p-value
Case	42	3.8 ± 0.5	9(21.42%)	11(26.19%)	<0.05
Control	42	3.4 ± 0.4	5(11.9%)	6(14.28%)	

In neonates GDM mothers had higher mean birth weight (3.8 ± 0.5 kg) than neonates born to non GDM mothers (3.4 ± 0.4 kg). The GDM group had 26.19% macrosomia (> 4 kg) and 14.28% macrosomia in the non-GDM group. However, a statistically significant ($p < 0.05$) difference was noted between birth weight (<2.5 kg) between the non GDM group 5(11.9%) and those in the GDM group 9(21.42%). The differentiation of GDM effects on fetal growth is this, and is associated with increased risk of overgrowth and undergrowth depending on the spectrum of the maternal status.

Table-4: Preterm Delivery Rates in GDM and Non-GDM Groups

Group	n	Preterm Delivery (<37 weeks) (%)	Term Delivery (≥37 weeks) (%)	p-value
Case	42	13(30.95%)	29(69.05%)	<0.05
Control	42	7(16.6%)	35(83.33%)	

Preterm delivery rate was notably higher in the GDM group (30.9%) compared to non-GDM group (16.6%). There was a significant difference ($p < 0.05$) between the GDM group and non-GDM counterparts in term deliveries (≥ 37 weeks) (69.1% vs 83.3%), while GDM was associated with significantly reduced terminal deliveries ($p < 0.05$). These results suggest that GDM may predispose pregnancies to preterm delivery and associated neonatal complications and healthcare burden.

Table-5: Neonatal Complications in GDM and Non-GDM Groups

Complications	Case(n=42)	Control(n=42)	P-value
Hypoglycemia	7 (16.6%)	1 (2.4%)	<0.05
Respiratory Distress	5 (11.9%)	1 (2.4%)	<0.05
NICU admission	9 (21.42%)	2 (4.8%)	<0.05

Complications in neonates born to mothers with GDM were significantly more common than those born to non-GDM mothers. In GDM group hypoglycemia was seen in 16.6% neonates, whereas 2.4% in the controls. As many as 11.9% of neonates in the GDM group and 2.4% in the non-GDM group exhibited respiratory distress. The GDM group also increased incidences of NICU admissions, 21.4%, compared to 4.8% in the non-GDM group. The findings on risk of neonatal complications underscore elevated risk in pregnancies complicated by GDM with statistically significant difference in all parameters ($p < 0.05$).

DISCUSSION

The aim of this study was to examine the association between maternal serum ferritin levels and adverse maternal and neonatal outcomes when there is a pregnancy complicated by gestational diabetes mellitus (GDM). The data suggest a strong correlation between GDM and high ferritin levels, maternal obesity and poor

pregnancy outcomes, suggesting that ferritin may be an indicator of a high risk pregnancy.

Maternal obesity was significantly associated with GDM, and the prevalence of overweight and obese participants in the GDM group was significantly higher than that in controls (52.4% and 40.5%, respectively). The findings are reinforced by the statistical significance ($p = 0.005$) with higher BMI associated with GDM. Increased obesity can worsen insulin resistance and systemic inflammation contributing to the metabolic derangements characteristic of GDM. In fact, elevated levels of serum ferritin, which signal increased iron stores in the body, and systemic inflammation may also exacerbate these effects by elevating oxidative stress and leading to placental dysfunction and worsening of maternal outcomes [4,9].

In GDM, neonatal outcomes were markedly worse than controls. For neonates born to mothers with GDM, the mean birth weight was significantly higher than the mean birth weight of neonates born to control mothers (3.8 ± 0.5 versus 3.4 ± 0.4 kg) and the incidence of macrosomia was significantly increased (26.2% vs 14.3%). This is consistent with evidence that maternal hyperglycemia is associated with fetal overgrowth due to excess fetal insulin secretion and fetal adipose tissue deposition [12]. In the GDM group, low birth weight (<2.5 kg) was less common (21.4% vs. 11.9%, $p<0.05$). Thus, we conclude that while GDM promotes macrosomia, the degree of maternal hyperglycemia may affect the extent of fetal growth, suggesting differential risk of overgrowth or undergrowth, depending on maternal metabolic condition.

GDM patients had preterm delivery rates higher than control patients (30.9%, vs. 16.6%, $p < 0.05$), which is consistent with the known risks of hyperglycemia and systemic inflammation. It is likely that elevated ferritin levels (>400 µg/L, as an acute phase reactant) lead to this same result, through inflammatory processes that disrupt uteroplacental blood flow and subsequently result in early labour onset [6]. Similarly, the prevalence of respiratory distress syndrome (RRDS) in neonates from GDM was higher (11.9% vs 2.4%, $p < 0.05$) when compared to control (non-GDM) neonates.

Complications for neonates born to GDM mothers also appeared at a significantly increased rate; hypoglycemia (16.6% vs. 2.4%, $p <0.05$, and NICU admissions (21.4% vs. 4.8%, $p <0.05$). The hyperinsulinemia that occurs in response to maternal hyperglycemia in utero may persist, but drive hypoglycemia in GDM neonates. The increased NICU admission rates reflect the greater healthcare burden for GDM pregnancies, and suggest the importance of effective antenatal management strategies to reduce these risks [7,16].

The study also showed that ferritin serves a function beyond being an iron storage marker. Elevated ferritin level is associated with GDM related outcomes, which indicate ferritin overproduction could be a marker and a mediator of systemic inflammation and oxidative stress. Overall, it would seem that ferritin's dual role especially implicates it in the pathophysiologic role of placental dysfunction and poor outcomes for the neonate based on prior studies showing hyperferritinemia associated with preeclampsia, preterm labor and abnormalities of fetal growth [15].

These findings from a clinical perspective suggest that routine screening of serum ferritin in GDM pregnancies would offer very useful information for stratification of maternal and neonatal complication risk. Ferritin screening may be integrated into antenatal care protocols for early intervention strategies including glycemic optimization, inflammation reduction as well as fetal monitoring. It is particularly relevant in resource limited settings like Bangladesh with increasing prevalence of GDM, and limited access to comprehensive antenatal care [10].

Finally, this study demonstrates the strong association between maternal and neonatal adverse outcomes and increased serum ferritin in pregnancies with GDM. Ferritin, which is elevated, acts as both a marker and contributor to systemic inflammation and oxidative stress and increases risks associated with maternal hyperglycemia. Integrating these pathways through care approaches could improve perinatal outcomes and decrease burden on health care in DM GDM populations.

CONCLUSION

Results of this study highlight the relevance of association between increased serum ferritin levels and negative maternal and fetal outcomes found in pregnancies with gestational diabetes mellitus (GDM). Strong positive correlation with poor neonatal outcomes (macrosomia, hypoglycemia, respiratory distress, increased NICU admissions) as well as maternal complications (preterm delivery, obesity) was seen with elevated ferritin in the neonatal population. Together, these findings indicate that maternal hyperglycemia as well as accompanying inflammation are associated with adverse outcomes and with ferritin as a candidate biomarker and mediator of these risks.

LIMITATIONS AND RECOMMENDATIONS

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community. These findings should be validated in larger, multicenter cohorts. This led to a need for development of a simple tool for stratifying risk: routine screening of serum ferritin levels in a pregnant woman with GDM.

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