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Original Research Article

Association of serum ferritin with gestational diabetes mellitus

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ABSTRACT

Background: Gestational diabetes mellitus (GDM) is the most common metabolic disorder during pregnancy and is associated with increased maternal and neonatal morbidities. High serum ferritin levels have been linked to type 2 diabetes and GDM development in pregnant women. The present study was designed to evaluate the association of serum ferritin with GDM.
Methods: A case-control study was conducted in the Department of Obstetrics and Gynecology of Dhaka Medical College from September 2020 and August 2021. Pregnant women in their second or third trimester diagnosed with GDM served as case, whereas non-diabetic pregnant women were selected as control. Serum ferritin levels were measured and compared between the groups.
Results: Mean serum ferritin levels were significantly higher in the GDM group (124.97±53.78 ng/ml) than in the control (83.50±25.73 ng/ml, $p<0.05$). Positive correlations were observed between serum ferritin and fasting glucose ($r=0.643$, $p<0.05$) and 2-hours after glucose intake ($r=0.524$, $p<0.05$) in GDM patients. The serum ferritin level was little bit high at 25 to 32 weeks gestational age. High level of serum ferritin was more in case (42.9%) compared with that of control (14.3%). These findings are statistically significant ($p=0.004$). Respondents with high serum ferritin level have 4.50 times more chance to develop GDM (OR=4.50,95% CI=1.56-12.97).
Conclusions: Serum ferritin levels were markedly higher in women with GDM than in those without. Therefore, high serum ferritin level can be regarded as a significant risk factor for the development of GDM.

Keywords: GDM, Serum ferritin, Pregnancy, Biomarkers

INTRODUCTION

Gestational diabetes mellitus is a common metabolic disorder of pregnancy, defined as glucose intolerance first diagnosed or documented in pregnancy. The incidence of GDM has risen globally over the last few years and now affects 10-15 per cent of pregnancies according to WHO criteria.[1] GDM is diagnosed diagnostically based on fasting blood glucose of 5.1 to 6.9 mmol/l or 2h plasma glucose of 8.5 to 11.0 mmol/l following a 75g oral glucose load; the WHO 2013 guidelines.[2] These risks to maternal and fetal health include both potential complications during delivery and long-term metabolic consequences for mother and child.

According to the IDF, globally, hyperglycaemia effect 15.8 percent of pregnancies, with 83.6 percent linked to GDM.[3] Hyperglycemia in pregnancy cases can occur up to 86.8 percent in low- and middle-income countries with limited healthcare resources for antenatal. Prevalence of GDM is also high in Bangladesh at 9.7%, which indicates that there is great concern about this issue and developing

country where there is limited access to health care resources.[4] Classical risk factors for maternal development of GDM include maternal age >35 years; family history of type 2 diabetes; prior diagnosis of GDM or impaired glucose tolerance; obesity; and macrosomic infant.[5] With rising incidence of GDM worldwide we must pursue identification of potential biomarkers that may help to detect, assess the risk of, and manage GDM at its earliest stage possible.

A new biomarker of GDM is serum ferritin: an iron storage protein used to measure body iron reserves and to regulate iron metabolism.[6] By correlating bone marrow iron with ferritin levels, ferritin concentrations can also be used as an indirect indication of body iron stores. It is a positive acute phase reactant, whose level rises in inflammation or chronic disease.[7] Elevated ferritin levels were reported in chronic inflammatory conditions such as type 2 diabetes, metabolic syndrome and GDM.[8] Pertinent pathophysiologic similarities of insulin resistance in GDM also occur in metabolic syndrome characterized by metabolic syndrome which may be exacerbated by iron overload through oxidative stress related pathways.[6,9]

Elevated serum ferritin may be related to the development of GDM, through mechanisms related to insulin resistance – studies have shown this. Sometimes coupled with conditions such as hemochromatosis and chronic blood transfusions both linked to insulin resistance increased serum ferritin, indicative of hepatic iron overload are associated with increased serum ferritin, indicative of hepatic iron overload. One example is that women in the highest quartile of ferritin serum levels have a twofold greater risk of GDM.[6,10] Iron overload, however, may lead to oxidative stress, and consequent lipid peroxidation and pancreatic beta cell damage which may result in insulin secretion and sensitivity impairment that further increase the risk of GDM.[11] In addition, high ferritin levels are correlated with measured insulin resistance and glucose intolerance, indicating ferritin is a candidate risk factor for GDM.[12]

Since elevated ferritin might herald GDM, this connection could lead to new possibilities for the early identification of at-risk pregnancies. Advising the pregnant woman with GDM remains a high-risk condition for adverse maternal and fetal outcomes including macrosomia, increased perinatal morbidity and mortality and an increased tendency to develop type 2 diabetes following delivery.[13,14] This emphasises the necessity of preventive measures and early management, especially for resource limited settings where prevalence and magnitude of GDM are significantly high.[15]

The purpose of this study is to determine the relationship between serum Ferritin levels and GDM by comparing serum Ferritin of pregnant women with GDM to pregnant women without GDM. We seek to contribute to the expanding literature on role of iron metabolism in GDM by analysing the association between ferritin levels and GDM. The results of this study may be used to identify and assist in earlier disease (GDM) detection and improve risk stratification, which should lead to improvements in the management and outcome of pregnancies affected with GDM.

Objective

The objective of this study was to evaluate the association between serum ferritin with gestational diabetes mellitus.

METHODS

This case-control study was conducted at the Department of Obstetrics and Gynecology, Dhaka Medical College Hospital, Dhaka, from September 2020 to August 2021. A total of 84 pregnant women in the second and third trimesters who attended antenatal care outdoors were included in this study using a non-random purposive sampling method after fulfilling the inclusion and exclusion criteria. Among the population, 42 with GDM were included in the case group, and the remaining 42 without GDM were included in the control group.

Inclusion criteria

Diagnosed case of GDM, single-tone pregnancy, pregnant women who have given consent to participate

Exclusion criteria

Pre-gestational diabetes, multiple pregnancy (Twin pregnancy, triplet, qudriplet), pregnancy with severe anemia, for example, iron deficiency anemia, hemoglobinopathies. Acute or chronic renal disease, acute or chronic liver disease.

Data collection

Patients were purposively selected based on their availability. The purpose and procedure of the study were discussed with patients. Written consent was obtained from all participants. Detailed Obstetric and medical histories and clinical information were obtained using a structured questionnaire.

Study procedure

Through clinical examinations were performed on all patients. Blood was collected from the antecubital vein by using a sterile needle and syringe. The blood was placed on ice immediately after collection. The sample was allowed to clot and then centrifuged at 4000 revolutions per minute for 10 min. Serum ferritin concentration was measured via a particle-enhanced immune turbid metric method with a fully automatic analyzer and AXSYM ferritin, a microparticle enzyme immunoassay. Whenever possible, analysis was performed immediately. When there was a delay, samples were stored at 2-80 Celsius till further

analysis. For each and every subject separate data collection sheet was prepared.

Ethical considerations

There were minimum physical, psychological, social, and legal risks during history taking, physical examination, and investigation. Proper safety measures were ensured in every step of the study, and ethical clearance was obtained from the authority of the DMCH to undertake the present study. According to the Helsinki Declaration for Medical Research involving Human Subjects 1964, all patients were informed about the study design, underlying hypothesis, and right to withdraw from the projects at any time.

Statistical analysis

Statistical analysis of the results was performed using a Windows-based computer software device with Statistical Packages for Social Science (SPSS-22). The results are presented in tables and diagrams. Comparison of means was made using Student's t-test and Mann-Whitney U test. Categorical data were analyzed using the chi-squared test. Odds ratio with 95% confidence interval and Pearson's correlation test were used to compare serum ferritin (ng/ml) with fasting plasma glucose (mmol/l) and post-paradial plasma glucose (mmol/l), and a p value <0.05 was considered significant.

RESULTS

The hospital-based case control study was conducted in the Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital (DMCH), Dhaka to evaluate the association of serum ferritin level with gestational diabetes mellitus (GDM). The cases were pregnant women (42 respondents) diagnosed with GDM and controls were pregnant women (42 respondents) who did not have GDM.

Table 1: Patients demographic 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		
Education	Illiterate	0	0	1	3.3	0.378
	Primary	5	11.9	3	6.7	
	Secondary	18	42.9	12	30	
	Higher secondary	15	35.7	21	50	
	Graduate or above	4	9.5	5	10	
Occupation	Housewife	29	69	25	59.5	0.25
	Student	8	19	10	23.8	
	Service	4	9.6	2	3.3	
	Others	1	2.4	5	13.3	
Monthly income	Low income	4	9.5	4	9.5	0.796
	Lower middle income	18	42.9	16	38.1	
	Upper middle income	14	33.3	18	42.9	
	High income	6	14.3	4	9.5	

Table 2: Comparison of serum ferritin (ng/ml) between normal pregnant woman and GDM (cases=42, control=42).

Case/control	N	Mean±SD	P value
Case	42	124.97±53.78	0.000
Control	42	83.50±25.73	

Table 1 shows that most (66.7%) patients with GDM were aged between 18 and 30 years. Similarly, most 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 demonstrates that most of the participants, both in the GDM and non-GDM groups, completed secondary or higher secondary levels of education. No significant association was found between GDM and mother's level of education (p=0.378). Almost 70% of GDM patients were housewives by occupation of the study sample. No significant association was found between GDM and mother's occupation (p=0.250). Regarding monthly income, most of the patients in both the GDM and non-

GDM groups were in the lower and upper middle-income classes. No significant association was found between GDM and monthly income (p=0.796).

Table 2 shows a comparison of serum ferritin levels between normal pregnant patients and GDM patients. Since the data violated the normality assumption, the Mann-Whitney U test was conducted. A statistically significant difference was found (U=191.000, P=0.000). The mean serum ferritin level was lower in the control (83.50±25.73) than in the case group (124.97±53.78).

Table 3: Comparison of serum ferritin level at different gestational age between normal pregnant women and GDM patients (case =42, control =42).

Gestational age (weeks)	Case/control	N	Mean±SD	P value
20-24	Case	15	118.55±45.33	0.032
	Control	10	75.7±28.22	
25-32	Case	20	142.77±63.80	0.006
	Control	25	91.63±22.31	
33-36	Case	7	111.67±30.12	0.048
	Control	7	67.50±28.20	

Table 4: Odds for GDM with respect to serum ferritin.

Serum ferritin (ng/ml)	Case		Control		OR (95%CI)	P value
	n=42	%	n=42	%		
≥120	18	42.9	6	14.3	4.50 (1.56 -12.97)	0.004
<120	24	57.1	36	85.7		

Table 3 shows a comparison of serum ferritin (ng/ml) levels at different gestational ages between normal pregnant women and women with GDM. The study found that serum ferritin levels at different gestational ages were significantly different. However, at 25-32 weeks, it was found to be slightly higher than the others in the GDM groups.

Correlation between serum ferritin (ng/ml) and fasting blood glucose (mmol/l)

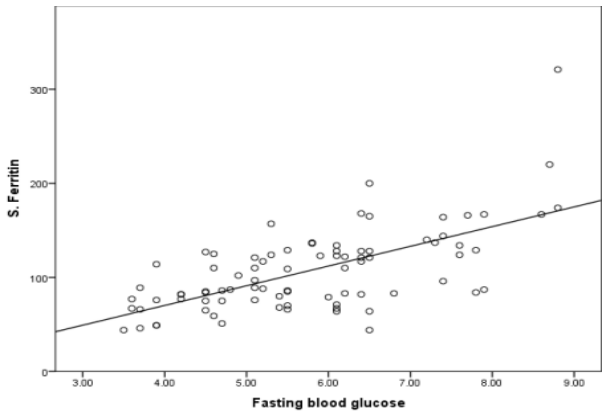

Figure 1: Correlation between serum ferritin (ng/ml) and fasting blood glucose (mmol/l).

Figure 1 shows the positive correlation between serum ferritin and fasting blood glucose. A liner correlation was evident between serum ferritin level and fasting blood glucose, and it is statistically significant (r=0.643, p=<0.05).

Correlation between serum ferritin (ng/ml) and 2 hours after 75 gm blood glucose (mmol/l)

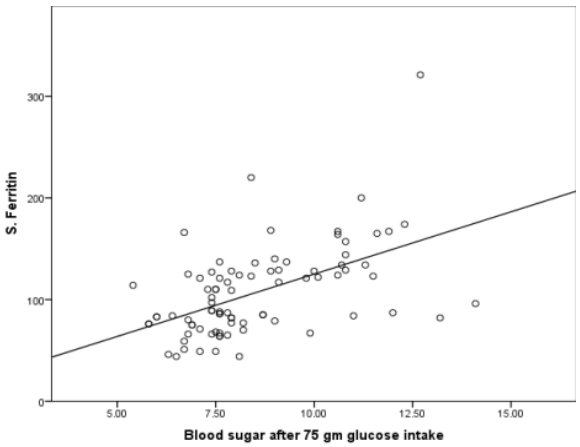

Figure 2: Correlation between serum ferritin (ng/ml) and blood sugar after 75 gm glucose intake (mmol/l).

Figure 2 shows positive correlation between serum ferritin and blood sugar after glucose intake. A liner correlation was evident between serum ferritin level and fasting blood glucose, and it is statistically significant (r=0.524, p=<0.05).

High level of serum ferritin was more in case (42.9%) compared with that of control (14.3%). These findings are statistically significant (p=0.004). Respondents with high serum ferritin level have 4.50 times more chance to develop GDM (OR=4.50,95% CI=1.56-12.97).

DISCUSSION

This study was carried out in the department of Obstetrics and Gynaecology, Dhaka Medical College Hospital, Dhaka to evaluate the association of serum ferritin level with gestational diabetes mellitus. The pregnant women (42respondents) diagnosed as GDM consider as cases and pregnant women (42 respondents) who don't have GDM consider as control. Poor health care infrastructure and wide spread public ignorance of nutrition causes a large number of uncontrolled DM with anemia in Bangladesh. Iron is frequently prescribed without knowing its status in the pregnant, hence a probability of getting pregnancy with iron overload in Bangladesh.[14]

However, in this study, we noted that between 18 and 30 years old, 66.7% of patients in the GDM case group and 76.7% in the control group. Mean age was 27.44±3.21 years in case group and 25.72±2.83 years in control group with non-significant difference between two (p>0.05). So, this similarity in age distribution parallels results from another study showing that both GDM and non GDM groups had similar age ranges with no differences that suggested that age is not an issues confounding factors associated with the association between serum ferritin and GDM risk.[5]

In this present study, it was observed that mean serum ferritin levels were 124.97±53.78 ng/ml in case group and 83.50 ±25.73 ng/ml in control group, which is significantly (P<0.05) in case group. Mahmood S et al. obtained in their study, mean serum ferritin level were 121.1 ±17.7 ng/ml in case group and 86.4 ±19.9 ng/ml in control group. Which is significantly elevated (P<0.05) in case group.[13] A study by Soheilykhah et al obtained that in pregnant women with GDM the serum ferritin level was found to be higher 41±35 and 35.5±30.7 in non GDM healthy pregnancy women and difference was statistically signified (P<0.05).[16]

In present study it was found that there was a positive correlation between elevated serum ferritin and fasting blood sugar. Level of fasting blood sugar value increases with increasing serum ferritin level (r=0.643, p=< 0.05). It also evident a highly significant linear correlation between serum ferritin and blood glucose two hours after 75 gm glucose ingestion (r=0.524, p=<0.05). Wang et al observed that there was a positive correlation between elevated serum ferritin and fasting blood sugar (r=0.461, p=<0.05). Yadav et al undertaken study was found that there was a positive correlation between ferritin and blood sugar (r=0.488).[17]

In this study 42.9% patients had serum ferritin level elevated in case group and 14.3% in control group. Elevated Serum ferritin level 4.5 times (95% CI 1.56 – 12.97) significantly (P<0.05) increase to develop GDM with compared to healthy pregnant women. Mahmood S et al. was observed that 65% patients had elevated serum ferritin in case group and 20% in control group. Serum ferritin was significantly (P<0.05) increased (3.1 times) developed GDM.[13]

In summary, this study demonstrates a strong correlation between high serum ferritin levels and increased potentiality of gestational diabetes mellitus. Results indicate that elevated ferritin may be associated with glucose intolerance in pregnancy through mechanisms of iron overload and oxidative stress. Ferritin level monitoring can potentially identify women at higher GDM risk and can aid in early intervention strategies to optimize maternal and fetal outcomes.

Limitations

This study was conducted in a single hospital with a small sample size. Therefore, the results may not be representative of the entire community. Additionally, serum ferritin was the sole marker of iron storage, without the assessment of other iron-related parameters, such as transferrin saturation or serum iron concentration, which may further clarify the role of iron metabolism in GDM. Future studies should include larger multicentre populations to enhance the generalizability of the results. It would also be beneficial to include a broader range of iron metabolism markers to provide a more comprehensive understanding of the relationship between the iron status and GDM. Further research should explore the potential benefits of monitoring and managing iron levels as a part of GDM prevention strategies, particularly in high-risk populations.

CONCLUSION

Gestational diabetes, the most common metabolic disorder during pregnancy, is a type of diabetes. The present study concluded that serum ferritin levels are significantly higher in women with GDM than in those without GDM. Thus, high serum ferritin levels may be considered a risk factor for the development of GDM.

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