Journal of Cardiovascular Disease Research
ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 9, 2021

ORIGINAL RESEARCH

Assessment of Serum ferritin, CRP and insulin levels as predictor biomarker of Gestational Diabetes Mellitus in first trimester of pregnancy at a tertiary care centre: A Longitudinal Study

Dr. Md. Masum Rizwee[1], Dr. Sandeep Kumar Sharma[2]

[1]Assistant professor, Department of Biochemistry, Kanti Devi Medical College, Hospital and Research Centre, Mathura, Uttar Pradesh, India
[2]Professor and Head of Department, Department of Biochemistry, Kanti Devi Medical College, Hospital and Research Centre, Mathura, Uttar Pradesh, India

Corresponding Author: Dr. Md. Masum Rizwee
Assistant professor, Department of Biochemistry, Kanti Devi Medical College, Hospital and Research Centre, Mathura, Uttar Pradesh, India
Email: masumrizwee2k6@gmail.com

Received Date: 14 June, 2021 Acceptance Date: 10 August, 2021

ABSTRACT

Background: Gestational diabetes mellitus (GDM) is a type of diabetes that develops during pregnancy. The present study was conducted to evaluate serum ferritin, CRP, and insulin levels in the first trimester of pregnancy.

Materials and Methods: 96 antenatal mothers in the first trimester with singleton pregnancies were studied. Waist-hip ratio and body mass index (BMI) were recorded.

Results: The age group of 18–24 years had 39 subjects with GDM and 7 without GDM. The age group of 25–31 years had 42 subjects with GDM and 6 without GDM. 59 subjects with GDM and 10 without GDM had ferritin levels ≥31.35 ng/mL.22 subjects with GDM and 3 without GDM had ferritin levels <31.35 ng/mL. 50 subjects with GDM and 7 without GDM had ferritin levels ≥3.6 mg/L. 31 subjects with GDM and 6 without GDM had ferritin levels <3.6 mg/L. Antenatal mothers with a higher concentration of CRP (OR = 1.6) and waist-hip ratio (OR = 2.9) in the first trimester were at greater risk of developing GDM. Parameters such as ferritin, insulin, plasma glucose, CRP, and haemoglobin were measured.

Conclusion: The authors detected higher first-trimester CRP, ferritin, and HOMA-IR levels among women diagnosed with GDM at 24-28 weeks of gestation.

Keywords: CRP, Ferritin, Insulin, Gestational Diabetes Mellitus

Introduction

Gestational diabetes mellitus (GDM) is a type of diabetes that develops during pregnancy. It is characterised by high blood sugar levels that occur for the first time during pregnancy and typically resolve after childbirth.[1] GDM occurs when the body cannot produce enough insulin to meet the increased insulin needs during pregnancy, leading to elevated blood glucose levels.[2] Women who are overweight or obese, have a family history of diabetes, or belong to certain ethnic groups (such as Hispanic, African American, Native American, South Asian, or Pacific Islander) are at higher risk of developing GDM. Advanced maternal age (over 35 years), previous history of gestational diabetes, or polycystic ovary syndrome (PCOS) also increase the risk.[3] Although the primary cause of gestational diabetes is insulin resistance brought on by pregnancy hormones such as progesterone, cortisol, and human placental lactogen (somatomamotropin), the etiopathogenesis of the condition is yet unknown.[4] Reviews of the literature, however, also imply that gestational diabetes mellitus might be type 2 diabetes mellitus, which is distinguished by metabolic abnormalities brought on by β cell

malfunction. Mothers have a 20% chance of developing type 2 diabetes later in life.[5] The development of GDM has been linked to the interaction of several risk factors, including obesity, macrosomia in a prior pregnancy, rising maternal age (>35 years), and a family history of type 2 diabetes in first-degree relatives.[6]

Aims and objectives: The present study was conducted to evaluate serum ferritin, CRP, and insulin levels in the first trimester of pregnancy.

Materials and Methods

The present longitudinal prospective study comprised 96 (ninety six) antenatal mothers in first trimester with singleton pregnancy, conducted at the Department of Biochemistry in collaboration between the Department of Biochemistry and the Department of Obstetrics and Gynaecology, Kanti Devi Medical College, Hospital and Research Centre, Mathura, Uttar Pradesh, India. The study took place from June 2020 to May 2021 after receiving approval from the Institutional Ethics Committee. All gave their written consent to participate in the study. Data such as name, age, etc. was recorded.

Inclusion criteria: The study included pregnant women who visited the prenatal outpatient department in the first trimester of their singleton pregnancy and had no previous history of diabetes mellitus or gestational diabetes.

Exclusion criteria: The study excluded pregnant women who had a history of iron deficiency anaemia, hemoglobinopathy, a haematological problem, polycystic ovary syndrome (PCOS), cardiovascular diseases, multiple pregnancies, infection, or fever.

The sample size was calculated based on a formula used for the cohort study: $n = (Z/e)^2$, where Z = 1.96 (two-tailed) at 95% confidence interval (CI), and e= allowable error around the reported incidence of the event of interest (here, it is the prevalence of GDM = 20%). Considering 20% = 0.2 error, the sample size was 96 (approximately).

During the first trimester, anthropometric measures such as skin fold thickness, waist-hip ratio, and body mass index (BMI) were done in each of the antenatal mothers during first trimester. Estimates were made of blood parameters such as ferritin, insulin, plasma glucose, CRP, hemoglobin, and hemocrit. The methods used for estimating plasma glucose and CRP were immunoturbidimetry and hexokinase.[7] Insulin and serum ferritin were estimated using Roche Cobas e411 electrochemiluminiscence.[8]

Statistical analysis: The data thus obtained were subjected to statistical analysis using Microsoft Excel 2016 and IBM Statistical Package for Social Sciences (SPSS) version 22.0. Continuous data was expressed as mean ± S.D. The binary logistic regression was done, and Odd's ratio was calculated to assess the risk with the predictive biomarkers. The performance parameters like sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratio of ferritin and CRP were calculated. A P value < 0.05 was considered significant.

Results

The mean age of participants who developed diabetes was 26.58 ± 3.79 years, and that of participants who did not develop diabetes was 24.05 ± 4.50 years [Table 1].

Table I: Age wise distribution of patients

Age groups (years)	With GDM	Without GDM	Total
18-24	39	7	46
25-31	42	8	50
Mean age in years (Mean ± SD)	26.58±3.79	24.05±4.50	

Table I shows that the age group of 18–24 years had 39 subjects with GDM and 7 without GDM. The age group 25–31 years had 42 subjects with GDM and 8 without GDM.

Table II: Distribution of cases based on ferritin concentration

Ferritin level	With GDM	Without GDM	P value
≥31.35 ng/mL	59	10	0.001
<31.35 ng/mL	22	3	

Table II, figure 1, shows that 59 subjects with GDM and 10 without GDM had ferritin levels ≥31.35 ng/mL. 22 subjects with GDM and 3 without GDM had ferritin levels <31.35 ng/mL. The difference was significant (P< 0.05).

Figure 1: Distribution of cases according to cut off ferritin level (75th percentile)

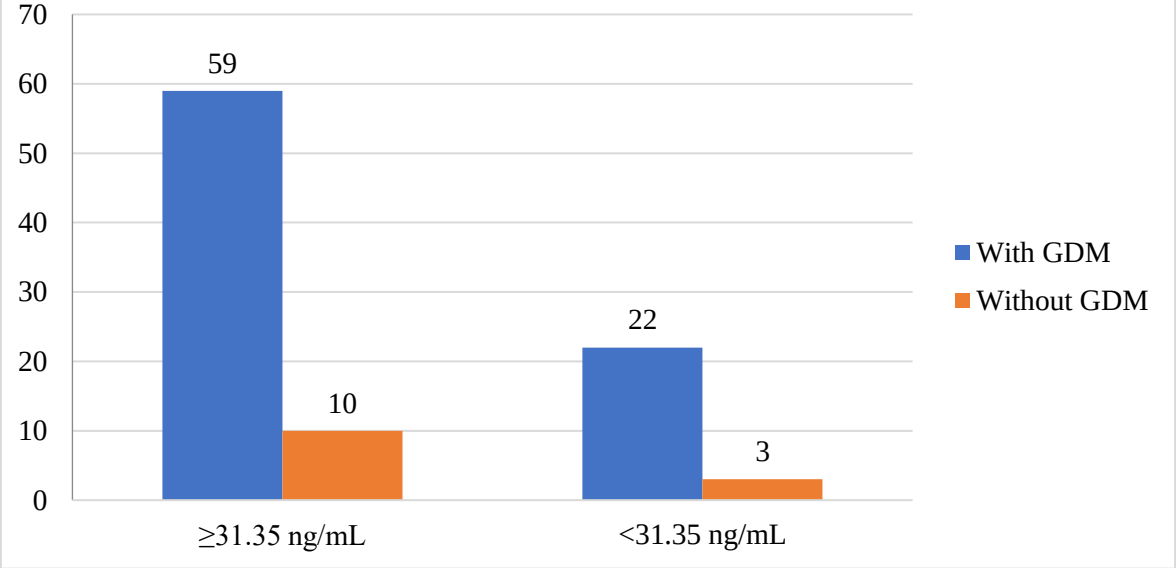

Table III: Distribution of cases based on CRP concentration

CRP level	With GDM	Without GDM	P value
≥3.6 mg/L	50	7	0.01
<3.6 mg/L	31	6	

CRP = C- reactive protein; GDM = Gestational Diabetes Mellitus

Table III shows that 50 subjects with GDM and 7 without GDM had a ferritin level of ≥3.6 mg/L. 31 subjects with GDM and 6 without GDM had ferritin levels <3.6 mg/L. The difference was significant (P< 0.05).

Table IV: Risk factors for Gestational Diabetes Mellitus (GDM)

Risk	OR (95% Cl)
Ferritin	1.3
C-reactive protein	1.6
Insulin resistance (HOMA-IR)	2.7
Waist-hip ratio	2.9

Table IV shows that antenatal mothers with a higher concentration of CRP (OR = 1.6) and waist-hip ratio (OR = 2.9) in the first trimester were at greater risk of developing GDM.

Discussion

Most pregnant women are screened for gestational diabetes mellitus between 24 and 28 weeks of gestation using a glucose challenge test (GCT) or an oral glucose tolerance test (OGTT).[9,10] If the initial screening test is positive, further diagnostic testing is done to confirm the diagnosis. Untreated or poorly controlled gestational diabetes mellitus can lead to various complications for both the mother and the baby.[11,12] These may include macrosomia (large birth weight), birth injuries, preterm birth, preeclampsia, caesarean delivery, hypoglycaemia (low blood sugar) in the newborn, and an increased risk of developing type 2 diabetes later in life for both mother and child.[13,14] We found that age group 18-24 years had 39 subjects had GDM and 7 without GDM. The age group 25- 31 years had 42 subjects with GDM and 8 without GDM. Chakraborty et al.[15] detected whether estimation of serum ferritin, C-reactive protein, and insulin in the first trimester can predict the subsequent occurrence of GDM and whether susceptible mothers can be managed cautiously to prevent foetal-maternal complications. The mean age of participants who developed diabetes (n = 12) was 25.75±2.92 years and those who did not develop diabetes (n = 68) were 23.91±3.74 years. There was 15% prevalence of GDM in study population. The median concentration of serum ferritin and CRP was significantly higher in patients who developed GDM (n = 12) among the study population (n = 80). The sensitivity of serum ferritin {83.33% (95% confidence interval=51.59-97.91%)} was higher in comparison to CRP {31.82% (95% CI=13.86-54.87%)}.

We observed that 59 subjects with GDM and 10 without GDM had ferritin levels ≥31.35 ng/mL. 22 subjects with GDM and 3 without GDM had ferritin levels <31.35 ng/mL. We found that 50 subjects with GDM and 7 without GDM had a ferritin level of ≥3.6 mg/L. 31 subjects with GDM and 6 without GDM had ferritin levels <3.6 mg/L. We found that antenatal mothers with a higher concentration of CRP (OR = 1.6) and waist-hip ratio (OR = 2.9) in the first trimester were at greater risk of developing GDM. Sharifi et al.[16] compared the serum ferritin concentrations of normal pregnant women with those of those with gestational diabetes mellitus (GDM) to determine the possible role of ferritin in predicting pregnancy outcome and the early development of postpartum glucose intolerance and diabetes mellitus. This case-control study consisted of 128 pregnant women (64 women with GDM and 64 age-matched healthy pregnant women) seen at a university hospital in Zanjan, Iran. Anthropometric measurements were determined, and serum ferritin, C-reactive protein, insulin, glycosylated haemoglobin (HbA1c), and haemoglobin levels were measured. Pregnancy outcomes were recorded in all subjects. In women with GDM, a diagnostic oral glucose tolerance test was performed eight weeks after delivery. Women with GDM had a higher concentration of serum ferritin (112±28.4 pmol/L in GDM versus 65±16.9 pmol/L in controls, P < 0.001). A positive correlation was found between serum ferritin levels and mid-pregnancy fasting plasma glucose and HbAlc levels. Although women in the highest quartile of serum ferritin had a greater than two-fold increased risk of GDM, no significant correlation was found between ferritin levels and early postpartum oral glucose tolerance test results.

Limitation of the study: The limitation of the study is the small sample size and short duration of study.

Conclusion

Authors found that there was higher first trimester CRP, ferritin and HOMA-IR levels among women diagnosed with GDM at 24-28 weeks of gestation. Therefore, the first trimester measurements of CRP, ferritin, and insulin help in the categorization of patients who have a substantial risk of developing GDM. Although the insulin levels measured during the first trimester did not differ significantly, the GDM group had a higher HOMA-IR, as shown by an odds ratio of 2.70. Repairing

damage after it has already occurred is more difficult than preventing it from happening in the first place. Therefore, for these patients, early intervention may result in a good perinatal outcome.

References

1. Wolf M, Sandler L, Hsu K, Vossen-Smirnakis K, Ecker JL, Tha dhani R. First trimester C-reactive protein and subsequent gestational diabetes. Diabetes Care. 2003; 26(3):819-24.
2. Romem Y, Artal R. C-reactive protein in pregnancy and in the postpartum period. Am J Obstet Gynecol. 1985; 151:380-83.
3. López Caudana AE, López Ridaura R, González Villalpando C, Lazcano Ponce EC, Casanuevay López EM, Hernández Avila M, et al. Prediction of alterations in glucose metabolism by glucose and insulin measurements in early pregnancy. Arch Med Res. 2011; 42(1):70-76.
4. Saisho Y, Miyakoshi K, Tanaka M, Shimada A, Ikenoue S, Kadohira I, et al. Beta cell dysfunction and its clinical significance in gestational diabetes. Endocr J 2010:57(11):973-80.
5. Grewal E, Kansara S, Kachhawa G, Ammini AC, Kriplani A, Aggarwal N, et al. Prediction of gestational diabetes mellitus at 24 to 28 weeks of gestation by using first-trimester insulin sensitivity indices in Asian Indian subjects. Metabolism 2012;61(5):715-20.
6. Ozgu-Erdinc AS, Yilmaz S, Yeral MI, Seckin KD, Erkaya S, Danisman AN. Prediction of gestational diabetes mellitus in the first trimester: Comparison of C-reactive protein, fasting plasma glucose, insulin and insulin sensitivity indices. J Matern Fetal Neonatal Med. 2015:28(16):1957-62.
7. Price CP, Trull AK, Berry D, Gorman EG. Development and validation of a particle enhanced turbidimetric immunoassay for C-reactive protein. J Immunol Methods. 1987; 99:205-11.
8. Lotz J., Hafner G., and Prellwitz W. Reference Study for Ferritin Assays. Kurzmitteilung Clin Lab. 1997;43(11):993-94
9. Clark CM, Qiu C, Amerman B, Porter B, Fineberg N, Aldasouqi S, et al. Gestational diabetes: Should it be added to the syndrome of insulin resistance? Diabetes Care. 1997; 20:867-71.
10. Babu GR, Tejaswi B, Kalavathi M, Vatsala GM, Murthy GV, Kinra S, et al. Assessment of screening practices for gestational hyperglycaemia in public health facilities: A descriptive study in bangalore, India. J Public Health Res. 2015; 9;4(1):448.
11. American Diabetes Association. Standards of medical care in diabetes- 2015. Diabetes Care. 2015;38:1-93.
12. Sain S, Mukhopadhyay P, Saha TK, Ghosh R. Gestational diabetes: How risky are the mothers of rural Bengal, India. Global Journal Of Medicine And Public Health. 2012;1(06):01-09.
13. American Diabetes Association: Gestational diabetes mellitus. Diabetes Care. 2018;42(Supp1):165-172.
14. Savvidou M, Nelson SM, Makgoba M, Messow CM, Sattar N, Nicolaides K. First Trimester Prediction of Gestational Diabetes Mellitus: Examining the Potential of Combining Maternal Characteristics and Laboratory Measures. Diabetes. 2010;59:3017-22.
15. Chakraborty M, Sil AK, Chakraborty S. Assessment of Serum Ferritin, CRP and Insulin Levels in First Trimester of Pregnancy as a Predictive Biomarker of Gestational Diabetes Mellitus: A Longitudinal Study. Journal of Clinical & Diagnostic Research. 2022 Jun 1;16(6).
16. Sharifi F., Ziaee A., Feizi A., Mousa Vinasab N., Anjomshoaa A., and Mokhtari P. Serum ferritin concentration in gestational diabetes mellitus and risk of subsequent development of early postpartum diabetes mellitus. Diabetes Metab Syndr Obes. 2010; 3:413–19.