

Analysis of Serum Ferritin Levels in Pregnant Women with Gestational Diabetes Mellitus versus Healthy Pregnant Women: A Cross-sectional Study

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ABSTRACT

Introduction: Gestational Diabetes Mellitus (GDM) is a disease that is linked to a variety of disturbances in the carbohydrate metabolism, specifically recognised during pregnancy. It is crucial to detect gestational diabetes at an early onset because if the developing foetus is exposed to abnormal carbohydrate metabolism can lead to morbidity, such as macrosomia and unexplained Intrauterine Death (IUD).

Aim: To compare serum ferritin levels in pregnant women with and without GDM.

Materials and Methods: This was a cross-sectional study conducted at Father Muller Medical College Hospital, Mangaluru, Karnataka, India, from December 2018 to July 2020. Antenatal patients were studied under two groups: those diagnosed with GDM (test group) during routine antenatal check-ups (n=62) and another group of non GDM antenatal mothers (n=62). Serum ferritin levels from venous blood were estimated for both GDM

and non GDM mothers between 24 and 34 weeks of gestation and analysed for the association between the groups using t-test.

Results: The mean gestational age was 30.85±2.51 weeks in the GDM group and 30.23±2.29 weeks in the non GDM group (p=0.1744). The mean Body Mass Index (BMI) in the GDM group was significantly higher (25.06±1.55 kg/m²) compared to the non GDM group (24.73±1.81 kg/m²) (p=0.0023). Haemoglobin levels were similar between groups (p=0.3610). Serum ferritin was significantly higher in the GDM group (33.14 ng/mL) compared to the non GDM group (30.18 ng/mL) (p=0.003).

Conclusion: The GDM is likely associated with higher serum ferritin levels compared to non GDM mothers. The increase in ferritin levels appeared to be independent of haemoglobin status. However, the high levels of ferritin observed in GDM group could be linked to higher BMI values rather than higher blood glucose levels. This indicates that serum ferritin levels in GDM mothers may be due to maternal fat and obesity, serving as an inflammatory marker.

Keywords: Body mass index, Inflammation, Maternal haemoglobin, Pregnancy-related oxidative stress, Pre-eclampsia

INTRODUCTION

The GDM is a condition characterised by disruptions in carbohydrate metabolism, first identified during pregnancy. The global prevalence of GDM is increasing, with rates reported to be as high as 14%. Typically, GDM develops after 24 weeks of gestation and resolves after delivery [1]. The processes responsible for GDM are still not completely understood. It is postulated that the possible reason for developing GDM is the presence of systemic inflammation, as evidenced by abnormally high levels of C-reactive Protein (CRP) and interleukins in the serum of individuals with GDM [2,3]. Iron is a micronutrient required by the human body and has various effects on a pregnant female. It also plays several roles in the outcome of a pregnancy. Studies have shown that when there is an overload of iron in a pregnant woman's body, it tends to reduce the placental circulation, which can predispose her to developing pre-eclampsia due to decreased placental perfusion, low birth weight in the baby due to reduced nutrient and blood supply, and preterm birth [4]. The predisposition to developing diabetes mellitus with an increase in iron intake has been proved in various studies. It is suggested that when a normal individual takes excessive amounts of iron in the food; the chances of developing type 2 diabetes mellitus are significantly increased [5,6].

Serum ferritin is one of the important storage proteins that play a fundamental role in the metabolism [7]. Iron, as an element, is also considered one of the factors required for oxidative stress. It is also considered a positive acute phase reactant, as the concentration

increases in the body during various acute and chronic diseases [8]. The complications arising in GDM are often preventable if, detected early and adequately. There is conflicting data regarding whether elevated serum ferritin is an independent risk factor for diabetes mellitus in pregnancy, or whether the higher levels of serum ferritin and the resulting inflammation are responsible for the effects [9]. Estimating serum ferritin levels and examining its correlation in GDM patients may therefore help identify the causative factors of GDM and its obstetric outcomes, which was the reason for conducting present study. The present study aimed to compare serum ferritin levels in pregnant women with and without GDM.

MATERIALS AND METHODS

This was a cross-sectional study conducted at Father Muller Medical College Hospital Mangaluru, Karnataka, India, from December 2018 to July 2020. Institutional ethical committee clearance was obtained (Ref: FMMCIEC/CCM/665/2018). Antenatal patients were studied in two groups: those diagnosed with GDM in their ongoing pregnancy during routine antenatal check-ups, and another group of non GDM antenatal mothers. GDM was diagnosed using the criteria established by the American College of Obstetricians and Gynaecologists (ACOG) [10].

Inclusion criteria:

- Antenatal patients diagnosed with GDM during their ongoing pregnancy (gestational age 24 weeks and beyond).
- Non GDM antenatal mothers included as controls for comparison.

Exclusion criteria:

- Patients with pregnancy-induced hypertension.
- Those with placental abruption.
- Pregnancies complicated by Intrauterine Growth Restriction (IUGR).
- Cases with oligohydramnios.
- Patients with systemic acute or chronic medical disorders associated with pregnancy, including respiratory, renal, hepatic, or cardiovascular conditions.
- Known cases of type 1 or type 2 diabetes.
- Pregnant women with known systemic infections.

Sample size: The sample size was calculated based on a study conducted by Pandey R et al., [11]. The minimum required sample size was 120; however, the total number of study population included in the study was 124 after meeting the inclusion and exclusion criteria. A sample size of 62 per group was included in the study.

Study Procedure

General physical and Obstetric examinations was done. The gestational age was calculated from the date of the Last Menstrual Period (LMP) and confirmed by an ultrasound scan in early pregnancy. Informed written consent was taken from all patients. Routine Antenatal Care (ANC) investigations were done. Venous blood samples were collected from both the GDM and non GDM groups during their routine antenatal check-ups. Ferritin levels were measured using a standardised biochemical assay to assess iron stores in the body.

STATISTICAL ANALYSIS

The IBM Statistical Package of Social Sciences (SPSS) version 25.0 was used for statistical analysis. The collected data were analysed by frequency, percentage mean, and standard deviation. Additionally, tests such as the paired t-test were applied.

RESULTS

The mean age of the test group (GDM) was 27.32±3.60 years, which was comparable to the mean age of control group (non GDM), which was 26.61±4.54 years [Table/Fig-1]. The number of primigravidae in the test group (GDM) was 18 (29.03%) which was comparable to that of the control group (non GDM) which were 22 (35.48%) [Table/Fig-2]. The mean gestational age in the test group (GDM) was 30.85 weeks, which was comparable to that of the control group (non GDM), which was 30.23 weeks [Table/Fig-3]. The mean BMI in the test group (GDM) was 25.06±1.55 kg/m², which was significantly higher compared to that of the control group (non GDM), which was 24.73±1.81 kg/m² [Table/Fig-4]. The mean haemoglobin level in the test group (GDM) was 11.5000±1.1373 mg/dL, which was comparable to that in the control (non GDM) group, which was 11.3294±1.0947 mg/dL [Table/Fig-5]. The mean serum ferritin level in the test group (GDM) was 33.14 ng/mL, which was significantly high compared to that in the control group (non GDM), which was

Group	Mean±SD	p-value
Test group (GDM)	27.32±3.60 years	0.2085
Control group (non GDM)	26.61±4.54 years	

[Table/Fig-1]: Age distribution of the study population.
95% CI from -1.83 to 0.41; t=1.2712; Standard error of difference=0.558

Parity	Test group (GDM) (n=62)	Control group (non GDM) (n=62)	p-value
Primigravida	18 (29.03%)	22 (35.48%)	0.06
Multigravida	44 (70.97%)	40 (64.52%)	

[Table/Fig-2]: Parity of the study population.
95% CI from 24.93 to 28.17, t=91.6008, standard error of difference=0.212; Paired t-test result two-tailed p-value equals 0.06 statistically not significant

30.18 ng/mL, with p-value of 0.003 [Table/Fig-6]. The mean ferritin level was found to increase with an increase in BMI in both the GDM and non GDM groups [Table/Fig-7].

Group	Mean±SD	p-value
Test group (GDM)	30.85±2.51 weeks	0.1744
Control group (non GDM)	30.23±2.29 weeks	

[Table/Fig-3]: Gestational age of the study population.
95% CI from -1.54 to 0.29; t=1.3742; standard error of difference=0.458

Group	Test group (GDM)	Control group (Non GDM)	p-value
Weight (mean±SD)	69.81±3.98 kg	65.79±5.11 kg	0.54
Height (mean±SD)	154.40±1.97 cm	154.08±3.13 cm	0.18
BMI (mean±SD)	25.06±1.55 kg/m ²	24.73±1.81 kg/m ²	0.0023

[Table/Fig-4]: Comparison of Body Mass Index (BMI) between the GDM and non GDM groups.
95% CI -0.90 to 0.25; t=1.1348; Standard error of difference=0.046

Group	Mean±SD	p-value
Test group (GDM)	11.5000±1.1373 mg/dL	0.3610
Control group (non GDM)	11.3294±1.0947 mg/dL	

[Table/Fig-5]: Haemoglobin level.
95% CI -0.5414 to 0.2001; t=0.9204; standard error of difference=0.185

Group	Mean±SD	p-value
Test group (GDM)	33.14±25.6293 ng/mL	0.003
Control group (non GDM)	30.18±26.0442 ng/mL	

[Table/Fig-6]: Serum ferritin level.
95% CI -10.0195 to 9.6914; t 0.0333; Standard error of difference=4.929

BMI	Average ferritin levels in GDM	Average ferritin levels in non GDM
18.5-25 kg/m ²	11.46 ng/mL	10.42 ng/mL
25-30 kg/m ²	30.35 ng/mL	32.56 ng/mL
>30 kg/m ²	39.017 ng/mL	34.50 ng/mL

[Table/Fig-7]: Average ferritin levels compared with BMI range.

DISCUSSION

In present study, the demographic factors between the study and control group were comparable, except for BMI. A higher mean BMI value was observed in the test (GDM) group compared to that of the control (non GDM) group. Gibson KS et al., in their retrospective study, found that demographic factors were comparable, including pre-pregnancy BMI [12]. They also found higher maternal weight gain in overweight and obese individuals. The BMI measured in present study was from the pregnancy period, rather than the pre-pregnancy measurement. The increased BMI value observed in present study could thus be attributable to increased maternal weight gain.

In present study, the mean serum ferritin in the test group was significantly higher than in the control group (non GDM). Amiri FN et al., in their prospective study done on pregnant women in early gestation, found that women who developed GDM had a higher concentration of serum ferritin than women who did not develop GDM [13]. They also estimated the risk level and concluded that the risk of GDM with high levels of serum ferritin was 1.4-fold higher than that for subjects with lower concentrations. Similar studies by Amiri FN et al., and Sharifi F et al., also showed a higher risk of GDM with higher serum ferritin values [13,14]. Lao TT et al., observed that women who developed GDM had a higher levels of serum ferritin (140.77±8.17 ng/mL) compared to those who did not develop GDM (82.56±29.6 ng/mL) [15].

They concluded that high serum ferritin can be regarded as a good predictor for the development of GDM. A study by Chauhan P also showed that the levels of ferritin were significantly higher in

the GDM mothers ($38.1 \pm 4.6 \mu\text{g}/\text{L}$) compared to control group ($33.5 \pm 2.7 \mu\text{g}/\text{L}$) [16]. Das C et al., observed that those who developed GDM had higher levels of serum ferritin ($55.1 \pm 28.9 \text{ ng}/\text{mL}$) compared to those who did not develop GDM ($31.3 \pm 18.7 \text{ ng}/\text{mL}$) [17]. In present study, the mean haemoglobin levels compared between the two groups were similar, with no significant difference. Ferritin is a cellular storage protein for elemental iron. Usually, lower haemoglobin levels are associated with a decrease in serum ferritin levels, particularly in iron deficiency states. However, in present study, it was seen that the levels of serum ferritin were higher while the haemoglobin levels were comparable between the two groups. This could explain why the serum ferritin, as an inflammatory marker, was found to be higher in GDM mothers. Sharifi F et al., observed that the comparison of haemoglobin levels in the GDM group and the non GDM group was statistically not significant, as found in present study [14]. Lao TT et al., in their study, found that the group with highest haemoglobin had a high serum ferritin and iron concentration and subsequently had a significantly higher incidence of GDM as well [15]. They also concluded that a high maternal haemoglobin is an independent risk factor for GDM, reflecting better nutritional status as suggested by increased iron status.

The mean BMI value measured during pregnancy was significantly higher in GDM group compared to non GDM group. Bowers K et al., observed in their study that higher dietary intake of red meat, including saturated fats and dietary cholesterol, can lead to higher BMI and GDM [18]. Hence, higher BMI value observed in the test group in present study could be related to dietary fat component. However, it could be a confounding factor for the interpretation of higher ferritin values in GDM patients. They performed a subgroup analysis which explained that there could indeed a positive association between BMI and ferritin levels.

Das C et al., found in their study that elevated serum ferritin levels were significantly and positively correlated with pre-pregnant BMI and skinfold measurements [17]. They suggested that there might be a possible link between elevated serum ferritin and low-grade inflammation mediated by maternal fat mass and obesity. Also, subgroup analysis comparing blood glucose levels through GCT values with serum ferritin levels in their study and they found no linear increase or decrease in mean ferritin value were compared with rise GCT values. This suggests the possibility that an increase in BMI contributed to the higher ferritin levels in the GDM group, rather than the carbohydrate intolerance during pregnancy.

Limitation(s)

The pre-pregnancy BMI was not calculated. Further research can be done considering this confounding factor (pre-pregnancy BMI) into account while evaluating the correlation between ferritin and GDM.

CONCLUSION(S)

In present study, the rise in ferritin levels seemed to be unrelated to haemoglobin status. The elevated ferritin levels seen in the GDM group may be more closely linked to increased BMI rather than to the diabetic condition itself during pregnancy. This suggests that serum ferritin, as an inflammatory marker, was higher in mothers with GDM due to factors associated with maternal fat and obesity.

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