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Original Research Article

High Serum Ferritin Levels: A Potential Risk Factor for Diabetes in Pregnancy

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Abstract:

Background: The most prevalent metabolic disease in pregnancy is gestational diabetes. Risk factors for gestational diabetes are not being fully recognised. Several studies have found a link between higher iron reserves and an increased chance of developing type II diabetes in non-pregnant people, which has led to grave worries about this possible risk factor in pregnancy also.

Objective: With the goal of measuring serum iron, TIBC, and ferritin levels in patients with diabetes in pregnancy and in pregnant women who appear to be in healthy conditions, this study seeks to determine if diabetes in pregnancy, including GDM, is connected with the iron status.

Method: A hospital-based observational, cross-sectional study involving 50 diabetes in pregnancy cases and 50 controls who appeared to be in good health was conducted. In both cases and controls, the mean serum ferritin, iron, and TIBC levels were assessed.

Results: In this study, we discovered that the mean serum ferritin levels in cases of pregnancy with diabetes were 200.7 ± 6.66, while they were 133.3 ± 6.04 in normal pregnant controls. This difference was statistically significant, indicating an increase in serum ferritin levels in DM patients compared to normal pregnant women. However, when the mean blood iron levels and mean Total Iron Binding Capacity values of cases and controls were examined, it became clear that there were no appreciable differences between the groups of patients with pregnancy-related diabetes and the controls in these parameters.

Conclusion: According to the current study's findings, a significant risk factor for the onset of gestational diabetes is a high plasma ferritin level. This could pose issues with the advice to all pregnant women to take routine iron supplements.

Keywords: Diabetes In Pregnancy, Iron Stores, Ferritin.

Introduction

The most prevalent metabolic condition during pregnancy is gestational diabetes [1]. Any degree of glucose intolerance that manifests during pregnancy is referred to as this [2]. Gestational diabetes mellitus is to blame for around 90% of instances of diabetes during pregnancy [3]. Women with GDM have an insulin resistance that they are unable to overcome by producing more insulin from their pancreatic beta cells. Pregnancy-related placental hormones and, to a lesser extent, larger fat deposits appear to influence insulin resistance [4]. The main contributors are cortisol and progesterone, but prolactin, estradiol, and human placental lactogen also play a role. There are dangers linked with gestational diabetes mellitus for both the mother and the foetus. Macrosomia, newborn hypoglycemia, perinatal mortality, congenital deformities, hyperbilirubinemia, polycythemia, hypocalcemia, and respiratory distress syndrome are some of the foetal problems [5]. The increased chance of getting diabetes after giving birth, hypertension, preeclampsia, and caesarean delivery are all examples of maternal complications [6]. As a result, approaches to effective prevention, accurate diagnosis, and successful treatment are advantageous. Risk factors for gestational diabetes are not being fully recognised. Nonetheless, there are some variables that can be thought of as potential risk factors for gestational diabetes mellitus, including older age, obesity, a history of prior GDM, hypertension, and higher haemoglobin and ferritin levels [7].

For humans, iron is a crucial micronutrient. Being a cofactor for numerous enzymes and a significant part of the body's oxygen transporter, iron plays a crucial role [8]. In biological systems, iron is thought to be a double-edged sword since both an iron deficit and an iron surplus can be damaging. Women who

are expecting are especially vulnerable to iron deficiency and the harmful effects that result from it [9]. Beta cell function and glucose regulation depend on adequate iron levels, but excess iron beyond what the body requires can increase oxidative stress [10]. Iron is a potent pro-oxidant, and greater than normal iron concentrations may cause reduced insulin secretion along with pregnancy-induced insulin resistance [11], however the precise molecular mechanism is unknown. Iron interferes with insulin's ability to prevent the liver from producing glucose [12]. Insulin resistance in the liver is the first anomaly that is frequently seen in cases of iron overload. Peripheral hyperinsulinemia results from decreased hepatic extraction and metabolism of insulin [13]. Insulin affects the uptake and storage of iron in cells by increasing the transferring receptors on the cell surface [14]. It's still unclear whether a patient with diabetes has too much iron because of increased insulin resistance.

A growing body of evidence from both animal and human studies has sparked grave concerns regarding the connection between higher iron reserves and a higher risk of developing type 2 diabetes in non-pregnant people [15]. The link between increased iron storage during pregnancy and gestational diabetes mellitus (GDM), a frequent pregnancy condition linked to a number of negative health consequences for both mother and child, is unclear, according to the available research. Very few prospective studies have looked at these correlations with longitudinal assessments of iron status. Prospective studies examining the relationship between iron status during pregnancy and the risk of GDM are few and inconsistent in their findings.

Objectives:

The aim of this study is to find out whether diabetes in pregnancy including GDM is associated with the iron status with the following objectives:

1. To measure the serum iron, TIBC, and ferritin levels in patients having diabetes in pregnancy.
2. To measure the above parameters in apparently healthy pregnant women as controls.
3. To compare and find out if there is any relationship of the above in pregnant mothers with diabetes and healthy controls.

Materials and Methods

The study was conducted in the Dept of Biochemistry and OBG, IPGMER, Kolkata for more than a year with 50 cases and 50 apparently healthy pregnant controls. Inclusion criteria of cases included patients with diabetes in pregnancy aged 20 to 35 years with otherwise uncomplicated current pregnancy. Patients aged <20, >35 years, patients with PIH, APH, BOH, heart disease and patients having haemoglobinopathies or h/o blood transfusions were excluded from the study.

It was a Observational, Cross sectional, hospital based study. Informed consent from cases and controls were taken. Record of history and clinical examinations noted. Then Collection of 5 ml venous blood was done, centrifuged at 3500 rpm for 5 mins to collect plasma and stored at -20 deg Celcius. The Parameters studied were Serum ferritin, Serum Iron, TIBC. Ferritin estimation was done by ELISA method, TIBC estimation by TIBC test system in Rx autoanalyzer and Serum iron by Spectophotometric analysis of ferrous ion in Iron test system suitable for use in Rx autoanalyser. Data Analysis was done by statistical software Minitab version-18.

Results and Analysis:

All numerical variables are normally distributed checked by Kolmogorov- Smirnov normality test. Mean ± SD were used to express the data. The null hypothesis was rejected by P-value < 0.05.

Table 1: Clinical and Biochemical Parameters of the Study Subjects:

Characteristics	Diabetes in pregnancy cases (n=50)	Healthy pregnant controls (n=50)	p-Value*
Age (years)	23.9 ± 2.8	23.6 ± 2.3	0.620
Gestational age (wks)	25.12 ± 0.98	25.14 ± 0.96	0.919
Height (cm)	153.3 ± 2.1	153.6 ± 2.2	0.438
Weight (kg)	63.5 ± 5.1	63.8 ± 4.7	0.777
Urea (mg/dl)	25.6 ± 6.05	25.9 ± 5.46	0.822
Creatinine (mg/dl)	0.886 ± 0.21	0.882 ± 0.21	0.927
T.bilirubin (mg/dl)	0.754 ± 0.17	0.780 ± 0.25	0.553
Serum iron (µg/dl)	110.7 ± 28.0	108.3 ± 35.7	0.711
TIBC (mcg/dl)	432.0 ± 57.9	431.6 ± 57.6	0.967

*T test done. P<0.05 considered significant at 95% CI

There is no statistically significant difference in the age, mean gestational age, mean weight and height of cases and controls. The mean urea, creatinine levels in cases and controls were also similar. The mean serum iron levels and the mean Total Iron Binding Capacity values of cases and controls were compared by 2 pair-sample t-test and it was seen that

there is no significant differences in these parameters between pregnancy with diabetes patients and control groups.

Table 2: Comparison of Serum Ferritin Values Between Cases and Controls:

Characteristics	Diabetes in pregnancycases (n = 50)	Normal pregnant controls (n = 50)	p-value#*
serum ferritin (ng/ml)	200.7 ± 6.66	133.2 ± 6.04	<0.001

*T test done. P<0.05 considered significant at 95% CI

In this study we found that the mean serum ferritin levels in pregnancy with diabetes cases is 200.7 ± 6.66 and for normal pregnant controls is 133.3 ± 6.04. 2-sample t-test shows significant increase in serum ferritin levels in cases, p- value is < 0.001 which is statistically significant indicating a rise in serum ferritin levels in diabetic pregnant patients in comparison to normal pregnant women.

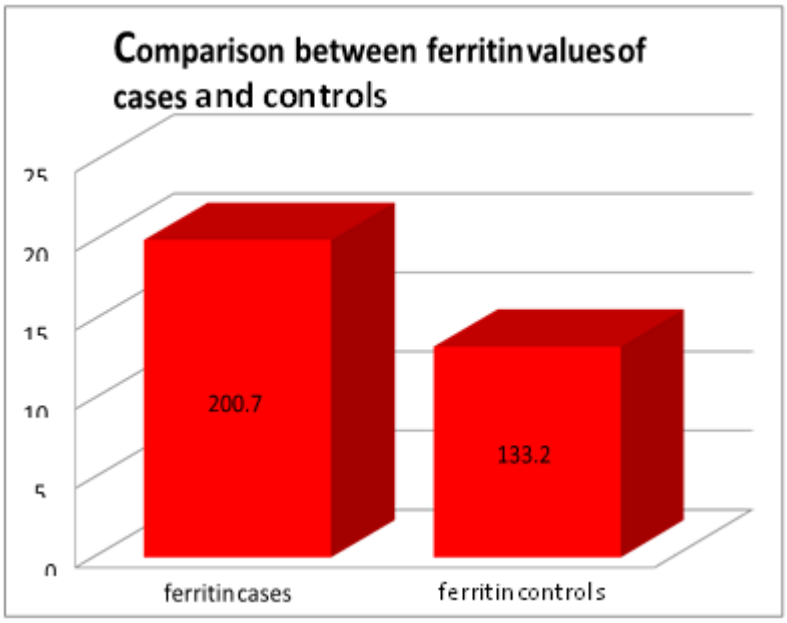

Figure 1: Comparison of Serum ferritin levels between cases and controls

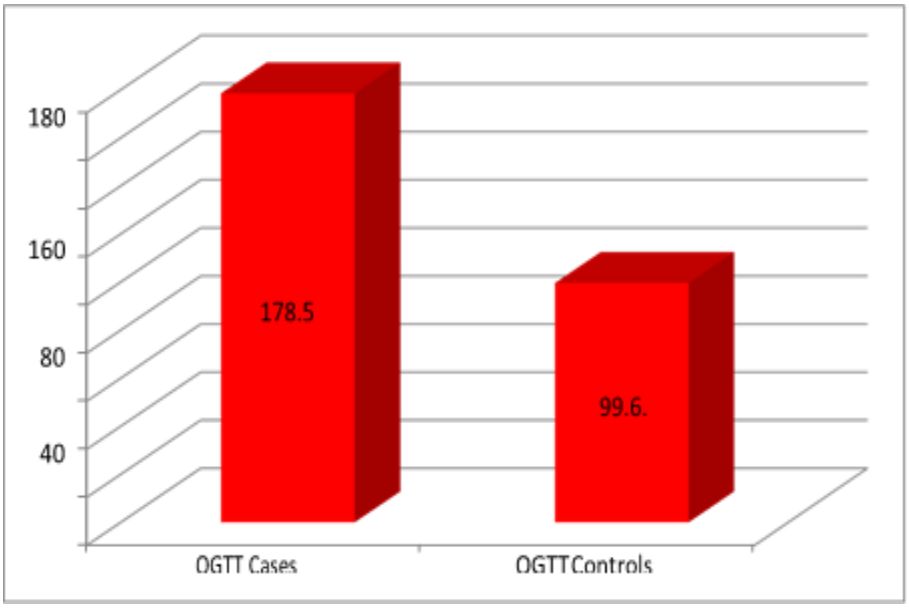

Figure 2 : Comparison of OGTT values between cases and controls

The OGTT values in pregnancy with diabetes cases are 178.5 ± 13.5 and 99.6 ± 9.8 in healthy pregnant controls. The OGTT values are interpreted following the DIPSI guidelines.

Correlation Studies: Pearson correlation between OGTT values and serum ferritin values shows a coefficient of 0.556 indicating a positive correlation with p-value <0.001.

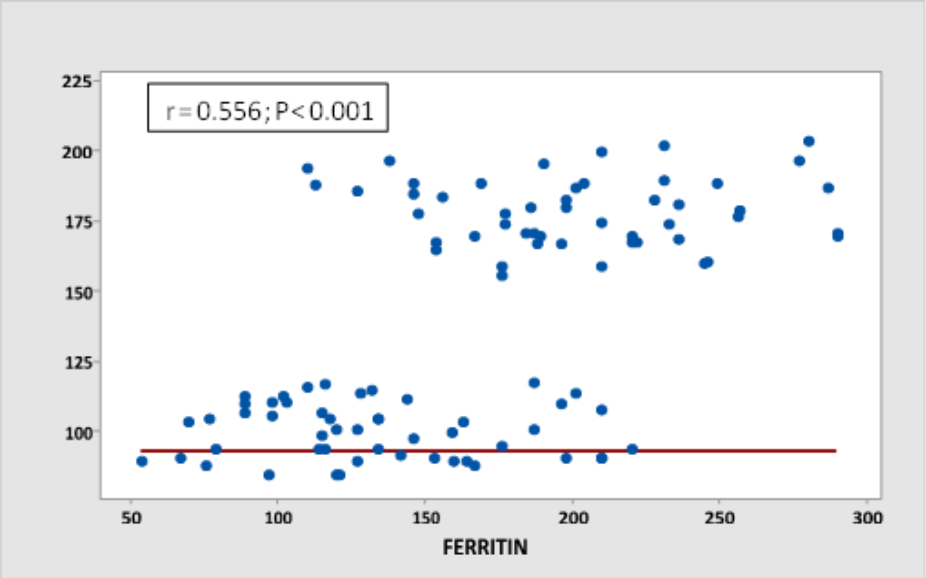

Figure 3: Scatter plot of Ogtt Values (mg/dl) vs ferritin

Correlation studies also done between serum iron levels and OGTT values but it showed a very weak positive correlation. On the other hand, Correlation observed by Pearson correlation between TIBC values and OGTT values showed a very weak negative correlation.

Discussion:

In this study, pregnant women with diabetes had significantly greater blood ferritin levels than pregnant women in the control group who appeared to be healthy. Several investigations have demonstrated a correlation between elevated diabetes incidence and increased iron reserves in the general population [16]. Ferritin has received the greatest attention among iron biomarkers when it comes to GDM. In the study by Scholl et al., women with high ferritin levels represented the risk of acquiring type II diabetes roughly three times within the next 10 years, without being connected with other risk factors such as body mass index, age and race [17]. Another study observed no differences in the serum iron levels or total iron binding ability to transferrin between GDM-affected women and the control group. Nevertheless, women with GDM had significantly higher ferritin levels [18]. Between the two groups in this investigation, there was no discernible change in serum iron levels or total iron binding capacity.

Studies that have shown a significant positive connection between OGTT results and serum ferritin levels (figure 3-) have an r-value of 0.556 and a p-value of 0.001. Studies on the relationship between serum TIBC and OGTT results reveal a very weak non-significant negative association, whereas those on the relationship between serum iron levels and OGTT results reveal a very weak non-significant positive correlation.

In a Hong Kong study, controls without anaemia or diabetes were chosen at random from the population at risk and compared to non-anemic gravidas who developed GDM during pregnancy. During 28–31 weeks of gestation, cases with GDM had significantly greater unadjusted blood ferritin, iron, transferrin saturation, and postnatal haemoglobin concentrations than controls [19].

Since Kayet al. initially investigated the potential relationship between ferritin and DM in 1993, additional research on the topic was concentrated[20]. High levels of ferritin were found in diabetics in a 1999 study by Ford and his colleagues on 9486 diabetic people in the United States. Serum ferritin may be a sign of insulin resistance, according to Fernandez and Kim et al 's 1998 study [21] on the correlation between serum ferritin and diastolic blood pressure, HDL, glucose area under the curve, and insulin sensitivity. According to Jiang et al. [22], iron overload results in the hydroxyl radical's development, which damages cells and promotes insulin resistance. Hyperferritinemia is a comorbidity of diabetic nephropathy and vascular dysfunction in poorly managed DM patients. The results of a different investigation within the Fetal Growth studies of the Eunice Kennedy Shriver National Institute of Child Health and Human Development [23] revealed that high iron reserves may have a role in the onset of GDM as early as the first trimester.

The suggestion of routine iron supplementation for pregnant women who are iron-deficient poses possible issues. When iron stocks are sufficient in women, taking iron supplements with vitamin C causes free radical overproduction, lipid membrane damage, delayed growth, and increased carcinogenesis [24]. Increased iron administration also impacts insulin secretion, boosts lipid oxidation, decreases muscle glucose uptake and consumption, and enhances liver gluconeogenesis, which increases insulin sensitivity and predisposes to GDM [25].

The results of the current study point to elevated plasma ferritin as a substantial risk factor for the onset of gestational diabetes, notwithstanding the study's small sample size. Moderately increased ferritin levels may be useful for clinical and public identification of high-risk group for GDM.

Conclusion

The Department of Biochemistry at the Institute of Post Graduate Medical Education & Research, SSKM Hospital, Kolkata, collaborated with the Department of Obstetrics and Gynecology on this study. Diabetic pregnant patients were chosen from the indoor and outdoor sections of the Department of Obstetrics and Gynecology, samples were obtained according to schedule, and biochemical parameter analysis was completed in the Department of Biochemistry.

The purpose of the study was to look into the connection between GDM risk and body iron status. This study's goals were to measure the levels of serum iron, ferritin, and total iron binding capacity (TIBC) in pregnant diabetic women and compare them to pregnant women who appeared to be healthy.

By using an ELISA kit, serum ferritin levels from patients and controls were assessed (Accubind, TOSOH INDIA PVT. LTD). The relevant Randox test kits in Rx autoanalyzers were used to evaluate the serum iron levels and TIBC values in the patients and controls. The analysis of the results reveals that the blood ferritin level was significantly higher in pregnant women with diabetes (200.7 + 6.66) than it was in the control group (133.2 + 6.04). Thus, a substantial risk factor for the development of gestational diabetes is a high ferritin level. In the two groups, there was no discernible change in serum iron levels or total iron binding capacity.

These results imply that having a high plasma ferritin level can be a substantial risk factor for the onset of gestational diabetes. Moderately elevated ferritin levels may be helpful in identifying high-risk GDM populations in both clinical and public settings. This could present issues with the advice to pregnant women to take routine iron supplements.

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