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The association of serum ferritin levels in predicting the outcome in GDM pregnancies

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Abstract
Background: The incidence of gestational diabetes mellitus has seen a rising trend. There is evidence that by estimation of serum ferritin levels in patients with gestational diabetes mellitus it is possible to predict the obstetric outcome.
Methods: The incidence of gestational diabetes mellitus has seen a rising trend. There is evidence that by estimation of serum ferritin and GCT levels in patients with gestational diabetes mellitus it is possible to predict the obstetric outcome.
Results: 248 cases into two groups 124 GDM and 124 Healthy non complicated pregnancies that served as controls. The mean age was 24.12years and 25.31 years (GDM and non - GDM). The mean serum ferritin levels in GDM was 68. 14 ng/ml ± 15. 63ng/ml which was significantly high compared to that of non GDM which was 30. 18 ng/ml ± 06. 02 ng/ml.
Conclusion: In this study, we concluded that GDM is likely to be associated with high serum ferritin levels compared to non GDM mothers and by evaluation of serum ferritin levels it is possible to predict the outcome of the mother and the newborn.

Keywords: Gestational diabetes mellitus (GDM), serum ferritin, outcome, newborn, maternal

Introduction
Among the exclusive pregnancy related complications gestational diabetes mellitus is the commonest one. The incidence of gestational diabetes mellitus has seen a rising trend. It is estimated that gestational diabetes mellitus can be found in approximately 14 % of all pregnancies [1]. Gestational diabetes mellitus is a disorder that occurs as a result of an impaired tolerance to the carbohydrate metabolism. The disease occurs with a varying severity and is detected first during the time of pregnancy [2-4]. Gestational diabetes mellitus has its onset most often after the 24th week of gestation and the disease tends to subside following childbirth [5].
The cause of concern with gestational diabetes mellitus is that; the onset of gestational diabetes mellitus coincides with the period of maximum growth of the fetus during the period of gestation. One of the important mechanisms that is used to explain the development of gestational diabetes mellitus is that of oxidative stress and systemic inflammation associated with obesity [6, 7].
One among the factors responsible for generation of free radicals and cause inflammation is found to be the presence of abnormally high amount of elemental iron [8, 9]. There is evidence that by estimation of serum ferritin levels in patients with gestational diabetes mellitus it is possible to predict the obstetric outcome to a fairly correct extent, yet there are a few lacunae as there are still to be answered especially in the Indian population. Hence we evaluated the association of serum ferritin measured in mid pregnancy to predict the risk of developing gestational diabetes mellitus and maternal and neonatal morbidity.

Materials and Methods
Source of data: This case control study was conducted at Ks HedgeCollege Hospital from December 2016 to July 2020. It was conducted on antenatal patients 20-40 years of age with Gestational age was between 12 weeks- 40 weeks who were diagnosed as GDM by The American College Of Obstetricians and Gynecologist (ACOG)in their present pregnancy during their antenatal check up and non GDM antenatal mothers. The control group with uncomplicated normoglycemic antenatal women with gestational age between 12 weeks -40 weeks with above criteria were randomly chosen in each group we had 124 cases.

We excluded gestational hypertension known patients of Type 1 or type 2 diabetes mellitus and those with other systemic diseases. ACOG recommendation for Diagnosing GDM [17].

Table 1: ACOG recommendation for diagnosing GDM

ACOG criteria	Status of glucose
Fasting	105mg/dl
1 h	190mg/dl
2h	165mg/dl
3 h	145mg/dl

Detailed clinical history was taken from the patient who visited for regular ANC checkup and screened and were included in the study defined by the inclusion and exclusion criteria. The The gestational age was calculated from the date of the LMP and confirmed by an ultrasound scan in early pregnancy. Serum ferritin levels were collected between 24 and 28weeks. The ferritin and the GCT values were co related. The data collected data was analyzed by SPSS software version 23 comparison of ferritin levels in the study population was done with the control group.

Results

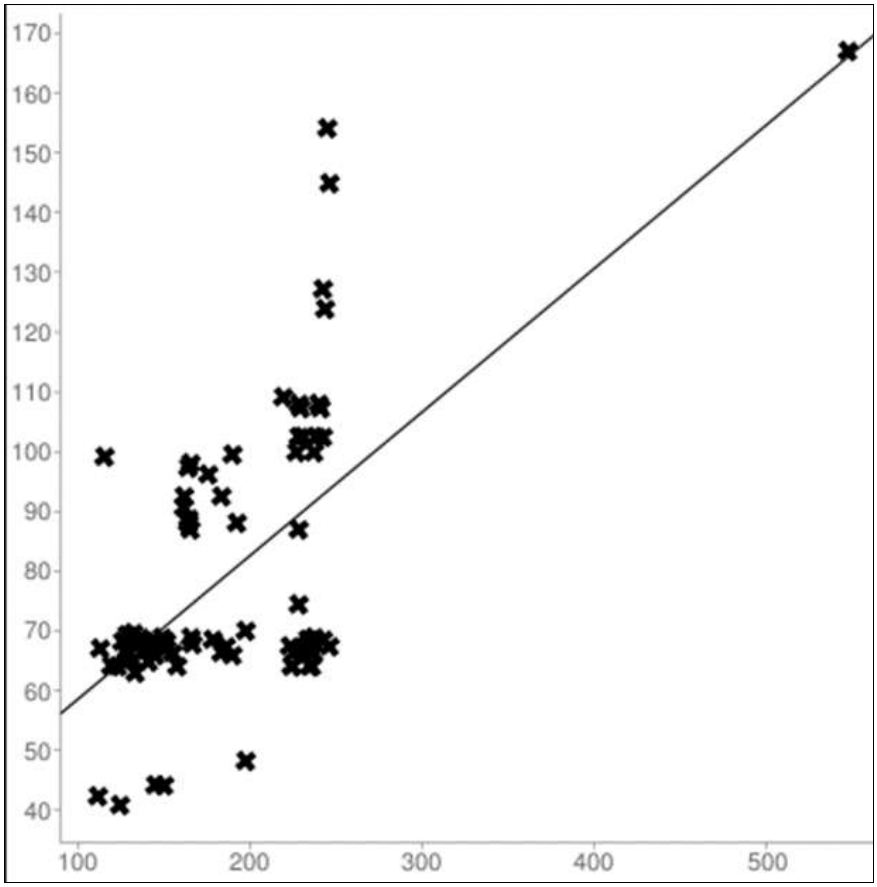
The study population was matched with that of controls with respect to parity, age and period of gestation. The mean age of the participant in GDM was 24.12 years and was comparable with that of non GDM which was 25.31 years. The number of primigravida who had GDM was86 cases (69.35%) which was comparable with non GDM which was 89 cases (71. 77%.). The mean gestational age of GDM was 25.85 weeks which was comparable with non GDM which was 26.23 weeks. The mean serum ferritin levels in GDM was 68. 14 ng/ml ± 15. 63ng/ml which was significantly high compared to that of non GDM which was 30. 18 ng/ml ± 06. 02 ng/mlIn this study, we concluded that GDM is likely to be associated with high serum ferritin levels compared to non GDM mothers. The increase in ferritin levels appears independent of hemoglobin status. High ferritin levels observed in GDM group could be positively associated with higher BMI values (29.73 GDM v/s 23.45 non GDM). This could explain that the serum ferritin as a inflammatory marker was found higher in GDM mothers due to maternal fat and obesity factor.

Table 2: Relation of elevated range of gct value andmean ferritin values

GCT	Mean ferritin levels (ng/ml)
141- 160 mg/dl	39. 71 (ng/ml)
161-180 mg/dl	42. 3 (ng/ml)
181-200 mg/dl	46. 11 (ng/ml)
201-220 mg/dl	46. 86 (ng/ml)
221-240 mg/dl	59. 38(ng/ml)
241-260mg/dl	64. 6 (ng/ml)
>261 mg/dl	78. 07 (ng/ml)

Table 3: Mean ferritin values in the groups

Group	Mean + SD	P value
Test group (GDM)	79.19 ng/ml ± 15. 63ng/ml	
control group (non GDM)	30. 18 ng/ml ± 06. 02 ng/ml	0. 0001
95% CI - -10. 0195 to 9. 6914, t3.33, df = 59standard error of difference = 4. 929		



Graph 1: Scatter plot of the linear regression

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) group which was 30. 18 ng/ml with P value of 0. 003. Correlation coefficient (r): 0.614 which is statistically significantp < 0.001, alsothere appears to be a linearpositive correlation between the GCT values and the ferritin levels. Mean GCT ($\bar{x}$): 185.77906976744 Mean (ferritin) ($\bar{y}$): 79.076860465116 Intercept (a): 34.42899109974 Slope (b): 0.24, Regression line equation: y=34.42899109974+0.24056868400616x There is A linear correlation between GCT values and mean ferritin levels.

Discussion

Pregnancy is considered as a unique situation in which there is a requirement of feeding two people. It is a state in which there exist a physiological equilibrium such that adequate nutrition is provided to both the mother and the developing foetus.

When the speciality of pregnancy is that as period of gestation increases there is a progressive increase in the insulin resistance and hence pregnancy is considered as a diabetogenic state Factors responsible for insulin diabetogenic state are increase in the insulin resistance increasing the lipolysis and increase in gluconeogenesis.

In India, the incidence of gestational diabetes can be as high as 40 to 60% and he went on to state that it will keep on rising attributed that the increase and the reflection of the increasing obesity and metabolic syndrome among women [1].

"Gestational diabetes mellitus is defined as any degree of. glucose intolerance with onset or first recognition during pregnancy (WHO, ACOG).(2) It includes women whose glucose tolerance returns back to normal after pregnancy and those who will develop type 2 diabetes, with persistent glucose intolerance [10]."

The criteria [11, 12]

The criteria that is used to diagnose gestational diabetes mellitus includes:

The FPG is more than 126 mg/dL

The PBG is more than 200mg/dL following a 75 gram oral glucose load. RBG is more than 126 mg/dL in the existence of symptoms that are attributed to diabetes mellitus.

The prevalence of GDM

It is estimated that globally the prevalence of gestational diabetes mellitus ranges between 2.4% percent in countries like Denmark [13] Ambrish Mithal *et al*. evaluated the prevalence of gestational diabetes mellitus in the various regions of India, and found the rate in urban areas of India to range between 4.6% and 14%, and in rural areas of India to range between 1.7% and 13.2% [14]. Savitri D. Kabad *et al*. in a study that was done in northern Karnataka state stated that prevalence of gestational diabetes mellitus in the region was 7.1% [15]. Poojita Tummalan *et al*. in a study that was done in Kolar district northern Karnataka state stated that prevalence of gestational diabetes mellitus in the region was 11.1% [16]. Shridevi AS *et al*. in a study that was done in Karnataka state stated that prevalence of gestational diabetes mellitus in the region was 11.5% [17].

The specialty of pregnancy is that as period of gestation increases there is a progressive increase in the insulin resistance and hence pregnancy is considered as a diabetogenic state Factors responsible for insulin diabetogenic state are increase in the insulin resistance increasing the lipolysis and increase in gluconeogenesis [4-6]. During pregnancy it is noted that there is an enhanced destruction of the hormone insulin by the maternal kidney and the placenta which secretes insulinase that is responsible for degrading the hormone, During pregnancy an increase in the destruction of lipids is also noted as a result of utilization of fatty acids for caloric needs for the mother and you could sparing for the foetus [5]. It was Pedersen Jorgen who stated that whenever there is better than hyperglycemia it in turn leads to fetal hyperglycemia which leads to stimulation of the beta cells of pancreas within the fetus. According to this theory that was named as the theory of hyperglycemic hyper insulinemla. Whenever there is maternal hyperglycemia causes hypertrophy of the foetus cells of the pancreas in the foetus in response to the maternal hyperglycemia which in turn causes fetal hyperglycemia [18]. The increased production of insulin in the fetus leads to deposition of higher amounts of adipose tissue that is responsible for macrosomia. These effects cause increase in the production of the hormone erythropoietin and reduction in the levels of surfactant. All this together make the child of a mother with gestational diabetes to have an increased incidence in the number of complications that occur during birth like traumatic delivery intrapartum asphyxia, and respiratory distress [5-9].

In our study the mean serum ferritin in the test group was significantly higher than the control group (non GDM). Soheilykhah, Sedigheh *et al*. [19]. In his prospective study done in pregnant woman in early gestation found that women who developed GDM had a higher concentration of serum ferritin than women who did not develop GDM. He 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 concentration. Similar studies by Amiri *et al*. [20], Sharifi *et al*. [21] also showed higher risk of GDM with higher serum ferritin values.

Galal and Salah [22] observed that those who developed gestational diabetes mellitus had a higher levels of serum ferritin 140.77±8.17 compared to those who did not develop gestational diabetes mellitus 82.56±29.6. They concluded that high serum ferritin can be regarded as a good predictor for the development of GDM.

In a study by Preethi Chauhan [23], also showed that the levels of ferritin was significantly higher in the gestational diabetes mellitus (38.1± 4.6 µgm/L) compared to that of control (33.5 ± 2.7µgm/L) Cinthya C Das *et al*. [24] observed that those who developed gestational diabetes mellitus had a higher levels of serum ferritin 55.1± 28.9ng/ml compared to those who did not develop gestational diabetes mellitus 31.3± 18.7 ng/ml.

Conclusion: In this study, we concluded that GDM is likely to be associated with high serum ferritin levels compared to non GDM mothers and by evaluation of serum ferritin levels it is possible to predict the outcome of the mother and the newborn..

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