IRON STORES AND ITS RELATIONSHIP WITH GESTATIONAL DIABETES MELLITUS – A CROSS SECTIONAL STUDY

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Abstract: **Background & objectives:** The incidence of Gestational Diabetes Mellitus (GDM) worldwide is on an increase with approximately 40 percent between 1989 and 2004. Iron overload is found to contribute for the pathogenesis of GDM. In this study Haemoglobin and Serum Ferritin levels are as an index of Iron overload and its relationship with GDM is assessed. **Methods**: Pregnant women are divided into 2 groups those with GDM and another without GDM by screening for Glucose challenge test. Blood sugar after 12 hours of fasting and 2 hours Post prandial is done for diagnosis of GDM. Haemoglobin and Serum Ferritin levels of both groups are also estimated and compared. **Results**: Mean serum Ferritin level of pregnant women with GDM (30.83 +/-20.61) was high than those without GDM(23.48+/-10.91). Median serum Ferritin level was comparable (20.950+/-23.8 vs 20.050+/-13.2).The difference is not statistically significant (p– 0.264).The mean haemoglobin value among pregnant women with GDM (11.70+/- 1.247) was significantly higher than the pregnant women without GDM(10.29+/- 1.221). This is statistically significant also (p– 0.00).Interpretation & **Conclusions**: It seems that routine administration of iron supplements to all pregnant women without estimating Iron stores needs more evaluation since a positive relationship has been found between GDM and increased serum Ferritin level and a statistically significant relationship between Haemoglobin level and GDM.

Key Words: Haemoglobin, Serum Ferritin, GDM, Pregnant women

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Introduction:

The incidence of Gestational Diabetes Mellitus (GDM) is increasing rapidly worldwide. Women with Gestational Diabetes Mellitus have type 2 diabetes (Insulin resistance state). Incidence of diabetes complicating pregnancy has increased approximately 40 percent between 1989 and 2004. [1] It is also estimated that this incidence will increase 165 percent by 2050. There are many factors that influence the pathogenesis of GDM. In many recent studies, it is found that serum Ferritin has a positive correlation with GDM. Women who developed GDM have a higher concentration of serum Ferritin than women who do not develop GDM. In a developing country like India all pregnant women are supplemented with iron without investigating the iron status. This is because iron deficiency anemia is one of the important problem in developing countries. But now it is estimated that increased iron load in a pregnant women is linked to maternal complications like GDM [2].We measure serum Ferritin level to estimate the iron overload in pregnant Women. We know serum Ferritin is one of the acute phase protein, the concentration of which increased in acute infections. Pregnant women may be prone for acute infections, this may account for the increased serum Ferritin. But we have studies that suggest the possible link between elevated serum Ferritin and low grade inflammation.[2,3] Studies also associate elevated serum Ferritin concentration with increased risk of GDM, independent of C-reactive protein (acute phase protein) and BMI. This study tries to co-relate elevated serum ferritin concentration with gestational diabetes mellitus in one of the tertiary care center in Kerala, south India.

Material and Methods:

A total of 60 pregnant women of gestational age 16-32 weeks are chosen. This included 30 subjects with normal pregnancy and without GDM and 30 subject with normal pregnancy and with GDM. Their Haemoglobin and serum Ferritin levels are assessed.

Inclusion Criteria : Pregnant females between 16-32 weeks of gestation and the females are on Iron supplementation

Exclusion Criteria :

1. Acute and chronic infections
2. History of malignancy
3. Previous history of Diabetes mellitus

4. History of seizure
5. History of renal disease
6. History of liver disease
7. History of drug abuse
8. Women with iron deficiency anaemia

Sample Size Calculation : According to Camden study[2] the sample size of at least 30 in each arm in order to have 80% power of detecting this difference at the 5% level of significance. This is based on a standard deviation of 13 degrees.

Methodology : Pregnant women of gestational age 16-32 weeks is included in the study after getting ethical clearance and Institutional Research clearance from Govt medical college, Thrissur. They are divided into 2 groups women with GDM and women without GDM. This is done by screening the subject for Glucose challenge test by asking them to take 75 gm of glucose and the 2hr OGTT was taken. Diagnosis of GDM is done by estimating Fasting blood sugar after atleast 12 hours of fasting and Post prandial blood sugar after 2 hours of meal. Pre pregnant weight is used to calculate approximate value of body mass index (BMI). Haemoglobin and Serum Ferritin of both groups are estimated and compared. Estimation of plasma glucose is by Glucose oxidase peroxidase method. Estimation of serum Ferritin by two site sand wich immunoassay using Direct chemiluminomeric technology. Analysis was done by software SPSS version 20.

Result:

Analysis was done by software SPSS version 20.

The results obtained are discussed further

Normal values : (According to WHO recommendation) .[6-9]

GCT : <140mg/ dl

FBS : 110-125mg/dl

Haemoglobin : 11g/dl [10].

Serum Ferritin : 10-230ng/ml(5-216pmol/l) .[11]

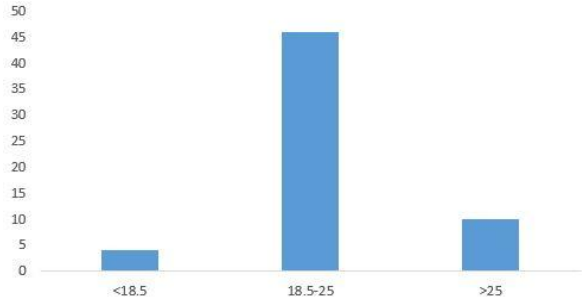
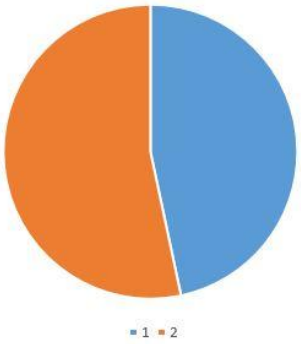


Figure : 1
Distribution According to the BMI of the pregnant women
Most of the subjects are not obese



1. Hb <11g/dl
2. Hb >11g/dl

Figure : 2
Distribution According to the Haemoglobin level of the pregnant women

Variable	Category	Mean+/-SD	T value	P value
Haemoglobin	Pregnant women with GDM	11.70+/-1.247	4.436	0.000
	Pregnant women without GDM	10.29+/-1.221		

Table 1 Comparison of Haemoglobin with diabetes mellitus : Student t test

The mean haemoglobin value among pregnant women with GDM(11.70+/- 1.247) was significantly higher than the pregnant women without GDM(10.29+/- 1.221). This is statistically significant also(P – 0.00)

	Diabetes mellitus	Number	Mean Rank	Sum of Ranks
S. Ferritin	0	30	33.02	990.5
S. Ferritin	1	30	27.98	839.5

Code 0 : Pregnant ladies with GDM
Code 1 : Pregnant ladies without GDM
S. Ferritin : Serum Ferritin

Table 2 Comparison of serum ferritin with diabetes mellitus : Mann-Whitney Test

Mean serum Ferritin level of pregnant women with GDM(30.83 +/-20.61) was higher than those without GDM(23.48+/-10.91). Median serum Ferritin level was comparable(20.950+/-23.8 vs 20.050+/-13.2). The difference is not statistically significant(P – 0.264)

Discussion: Analysis of haemoglobin with GDM was done by student's t-test. The mean haemoglobin value among pregnant women with GDM(11.70+/- 1.247) was significantly higher than mean haemoglobin value among the pregnant women without GDM(10.29+/- 1.221). This is statistically significant also(P – 0.00). Comparison of serum Ferritin with GDM was done by Mann Whitney, a Non Parametric analysis. The mean serum Ferritin level of pregnant women with GDM(30.83 +/- 20.61) was high than those without GDM(23.48+/- 10.91). Median serum Ferritin level was comparable(20.950+/-23.8 vs 20.050+/-13.2).The difference is not statistically significant($\mathcal{P}$ – 0.264). Joseph Scott Gabrielsen et.al [12,13]proved the pathophysiology behind the iron stores and GDM. Increased Iron stores causes oxidative stress induced damage to Adipocytes by producing free radicals. One of the stress specific gene is FOXO1. FOXO1 gene is specific for Adipocytes is found to reduce the Adiponectin transcription.[14,15] Hence the release of Adiponectin into circulation is reduced contributing for the Insulin resistance. Physiologically Adiponectin cause Insulin sensitive state.

In our study comparison between BMI and GDM was not analyzed. Studies shows significant correlation between iron stores (Ferritin and Hemoglobin) and GDM independent of BMI and other confounding factors like positive family history, C-reactive protein (a marker of inflammation) etc.[2] Serum Ferritin, the storage form of iron is also a marker of inflammation. Thus Ferritin-insulin resistance could be due to increased iron stores or inflammation or both. Most of the studies investigating serum Ferritin also measured other markers of acute phase reaction including CRP and fibrinogen. There are studies which suggest that measuring of inflammatory markers had little effect on iron-insulin resistance. This gives the evidence of Ferritin-insulin resistance relationship independent of inflammation.[2] In this study all confounding factors were not included

Most of the studies which investigated the iron stores not only measured Haemoglobin and serum Ferritin but also serum iron, total iron binding capacity and transferrin saturation.

Since other forms of iron are not measured the precise information regarding the iron stores is not available. Hence this is a drawback of this study compared to the other studies.

In this study we categorized pregnant women with GDM by measuring OGCT and FBS. Many of the upcoming study measured Hb A1c as useful indicator for diagnosing GDM. Alex Fong et al [16] analyzed Hb A1c as the early indicator of GDM. An HbA1c level of 5.7-6.4% is an effective means of identifying patients at the highest risk of developing GDM. It may be most prognostic in an obese population. Its efficacy has been demonstrated when the sample is drawn during the first trimester and may be effective up to 20 weeks of gestation. This information may help the clinicians target the patients who will benefit the most

Limitation of the study :

1. Sample size is very low
2. TIBC and Transferrin saturation levels were not measured
3. Serum Insulin level is not measured to justify insulin resistance as the pathology under GDM (due to increased iron stores)
4. Confounding factors were not estimated
5. Study should be done in different parts of India

Conclusion: It seems that routine administration of iron supplements to all pregnant women without estimating Iron stores needs more evaluation since a significant relationship has been found between GDM and increased Haemoglobin level. Clinicians should consider the unwanted supplementation of Iron for pregnant women without estimating the Iron storage state.

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