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Association of elevated serum ferritin levels in mid-pregnancy and the risk of gestational diabetes mellitus

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Abstract
Gestational Diabetes Mellitus is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy, according to WHO guidelines. serum ferritin, is a major storage protein of iron. It is also a acute phase reactant which increases in inflammatory conditions. Studies have shown a positive relation between insulin resistance and serum ferritin levels.
The role of serum ferritin as an inflammatory marker is used in this study and its levels are measured in mid pregnancy to predict the risk of developing GDM, thereby making it as a tool for early diagnosis and prevention.
Aim: To determine the association between moderately elevated Serum Ferritin levels in mid-pregnancy and risk of onset of Gestational Diabetes Mellitus.
To investigate the effect of a higher level of maternal serum Ferritin and thereafter describe a generic framework for combining this screening information with designing a prophylactic intervention in the future.
Materials and methods
Study Centre: Department of Obstetrics and Gynecology, Madras Medical College, Chennai
Duration of: One year
Study Design: Prospective study
Sample Size: 100
Results: Among th 100 pregnant women in this study, only 37 had GDM diagnosed at some point of time in the current pregnancy. In that 37 women, 22 were started on insulin and 15 were on medical nutrition therapy out of 37 who developed GDM, about 18 had ferritin values between 60-90 ng/ml, and 6 had values above 90 ng/ml. and in this 6 women women with serum ferritin >90, 5 were started on insulin
Conclusion: Serum ferritin levels, apart from iron store action, is a good predictor of developing GDM. Elevated serum ferritin concentrations, at early gestational weeks, is associated with increased risk of developing GDM. This association is mediated by fat mass of the mother and obesity, at least in part.

Keywords: Serum Ferritin, BMI and GDM

Introduction
Gestational Diabetes Mellitus is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy, according to WHO guidelines.
Gestational Diabetes Mellitus is "any degree of glucose intolerance that either starts during pregnancy or is newly diagnosed in pregnancy" as per ACOG (American College of. Obsterics and Gynecology). It includes women, whose glucose tolerance, is normal after pregnancy and those with type 2 diabetes with persistent glucose in intolerance developed later The GDM incidence is nowadays increasing due to life style changes, increased obesity and metabolic syndrome prevalence. The trend towards modern life style, older age at child birth, changing eating habits and reduced physical activity has now lead to increased GDM incidence. History of diabetes in family (like father, mother, maternal uncle and aunts, and in siblings too). In addition to all above factors, ethnicity also plays a role in the development and risk of GDM. Our Indian ethnicity is more prone for developing Diabetes in the Gestational period. Moreover as India is in the trend towards adoption of western life style among youngsters, this risk factor adds an additional impact in the development of GDM.
The incidence of GDM is increasing globally and is now 20% to 27% of all pregnancies. According to Indian diabetic federation, in 2015, two out of every five diabetic women, are of reproductive age, accounting for women over 60 million worldwide. According to this estimate, 16.2% of live births, who delivered in 2015 had some form of, hyperglycemia in pregnancy. In that GDM accounted for 85.1%. Gestational diabetes affects one in seven births. For a successful pregnancy outcome, the longitudinal changes, that takes place, in carbohydrate metabolism during pregnancy plays an integral role.

Gestational diabetes mellitus is an important cause of perinatal mortality and morbidity. The complications occurring due to GDM are preventable if screening and diagnosis is done at an early stage as possible.

The complications arising in GDM is mostly preventable if adequate control of blood sugar levels are maintained throughout the pregnancy. As it is always good that prevention is better than cure, it is better to prevent its occurrence than to deal with it after its onset. Gestational diabetes poses short term as well as long-term effects on the health of both the mother and the child. Hence early diagnosis and treatment is necessary to decrease the risks.

High frequency of GDM among Indian women needs early diagnosis of GDM. There is no specific biochemical test so far available that can predict the risk of developing GDM other than the blood sugar tests with OGCT, OGTT etc. Recent studies have shown a positive correlation between moderately elevated serum ferritin levels in mid trimester of pregnancy and increased risk of GDM.

Insulin resistance plays a key role in GDM and there is a systemic inflammation, indicated by higher levels of C-reactive protein & interleukin-6. Adipocytes in adipose tissue can secrete pro inflammatory cytokines in obesity which is also associated with insulin resistance. serum ferritin, is a major storage protein of iron. It is also a acute phase reactant which increases in inflammatory conditions. Studies have shown a positive relation between insulin resistance and serum ferritin levels.

The role of serum ferritin as an inflammatory marker is used in this study and its levels are measured in mid pregnancy to predict the risk of developing GDM, thereby making it as a tool for early diagnosis and prevention.

Aim of the study

To determine the association between moderately elevated Serum Ferritin levels in mid-pregnancy and risk of onset of Gestational Diabetes Mellitus.

Objective of the study

To investigate the effect of a higher level of maternal serum Ferritin and thereafter describe a generic framework for combining this screening information with designing a prophylactic intervention in the future.

Materials and Methods

Study Centre: Department of Obstetrics and Gynecology, Madras Medical College, Chennai

Duration: One year

Study Design: Prospective study

Sample Size: 100

Inclusion Criteria

- Pregnant women in gestational age 16 to 24 weeks as calculated by LMP and dating scan

Exclusion Criteria

Pregnant women with

- Anemia (Hb<11gm/dl),
- Pre-eclampsia,
- Type 1 and type 2 diabetes
- Hematological disorders (sickle cell anemia, hemoglobinopathy, thalassemia)
- Auto immune disorders(SLE, rheumatoid arthritis)
- Hepatitis, Any fever
- Any local and systemic infection

100 women attending the antenatal clinic in 16-24 weeks of gestation (as selected by inclusion criteria and exclusion criteria) were enrolled in the study. Data was collected from the study participants after explaining about the study to them and getting their informed consent. To avoid selection bias, the participants were chosen based on a randomised approach. The questionnaire for data collection was filled by the principal investigator by interviewing the participant in person. The participants were interviewed in person, during their routine antenatal visit to ensure their comfort and to have their fullest cooperation.

Venous blood samples were obtained from the patient between16 to 24 weeks' gestation to measure serum ferritin level by fully automated bidirectionally interfaced chemi-luminescent immuno-assay. serum Ferritin levels measured are grouped in quintiles.

The reference value for serum Ferritin in pregnancy is 12-150ng/ml. The serum ferritin observed in 100 study population are grouped in quintiles and number of GDM mothers diagnosed in each quintile is studied

OGTT

FBS level oral intake of 100 gms glucose measuring blood glucose level at 1, 2 and 3 hrs.

Patients are considered to have GDM if 2 or more values of the 4 exceed described in carpenter & Coustan Criteria (American diabetes association 2009)

Blood Glucose	Carpenter & coustan cut-off
FBS	>95mg/dl
POST 1 HR	>180mg/dl
POST 2 HR	>155mg/dl
POST 3 HR	>140mg/dl

Observation and analysis

Table 1: Independent Samples Test

		N	Mean	Std. Deviation	Std. Error Mean	t value	p value
S. Ferritin	Risk Factors	28	57.8157	27.52998	5.20268	5.492**	p<0.0001
	No Risk Factors	72	32.0715	17.97718	2.11863		

The p-value of risk factors association with raised derum ferritin levels was found to be <0.001 and is significant.

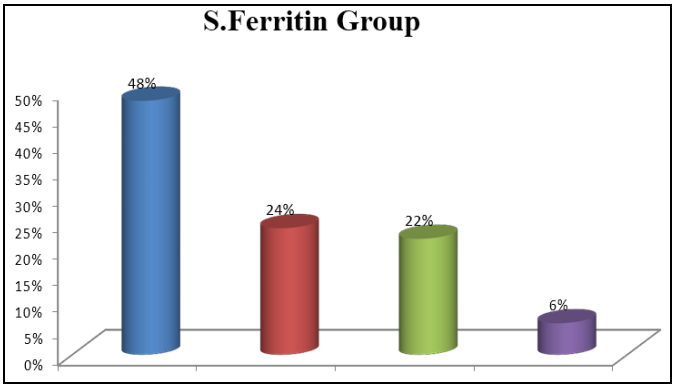

Diagram 1: S. Ferritin levels of the study group

Table 2: S. Ferritin and GDM

			GDM		Total
			No	Yes	
S. Ferritin Group	<30	Count	44	4	48
		% within GDM	69.8%	10.8%	48.0%
	30-60	Count	15	9	24
		% within GDM	23.8%	24.3%	24.0%
	60-90	Count	4	18	22
		% within GDM	6.3%	48.6%	22.0%
	Above 90	Count	0	6	6
		% within GDM	0.0%	16.2%	6.0%
Total		Count	63	37	100
		% within GDM	63%	37%	100.0%

Pearson Chi-Square=46.099** p<0.001

There was significant association between GDM and ferritin levels in this study group

Table 3

			GDM		Total
			No	Yes	
S. Ferritin Group	<30	Count	2	2	4
		% within GDM	9.1%	13.3%	10.8%
	30-60	Count	1	8	9
		% within GDM	4.5%	53.3%	24.3%
	60-90	Count	14	4	18
		% within GDM	63.3%	26.7%	48.6%
	Above 90	Count	5	1	6
		% within GDM	22.7%	6.7%	16.2%
Total		Count	22	15	37

Pearson Chi-Square=12.801** *p*<0.001

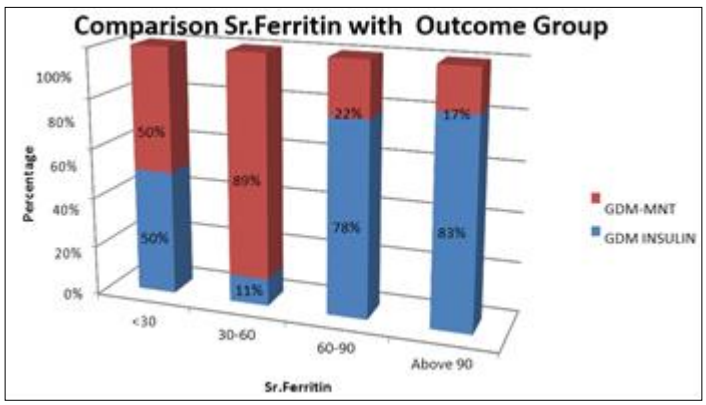

Diagram 2

Discussion

This prospective study, with 100 population of randomly selected pregnant women, attending the tertiary care centre for antenatal check up, was studied for elevated serum ferritin levels and the subsequent risk of developing GDM.

The study population showed significant correlation of BMI and elevated ferritin range, with subsequent development of GDM. This showed that there is a positive association between body fat mass and chronic low grade inflammation in the body. This triggers increased s. ferritin synthesis, thus making s. ferritin a good marker of inflammation. So it is clear that obesity plays important role in the development of diabetes., with marker of raised ferritin.

There seemed to be positive correlation between presence of history of PCOS and risk of GDM, with elevated ferritin range. This seems to prove that insulin resistance and hyperinsulinemia of PCOS favours the development of GDM. Serum ferritin levels too, increases in hyperinsulinemia. Other risk factors associated were, BOH, prev GDM, family history of GDM, all showed a positive association with increased ferritin levels.

Conclusion

Diabetes mellitus is a common disorder in India. It is not uncommon to encounter GDM in pregnant women of Indian population. GDM is associated with, increased perinatal mortality and morbidity, if not controlled properly. Preconception counselling, early diagnosis at prompt stage, good glycemic control, monitoring of fetal well being., all plays a significant role in improving the perinatal outcome.

It is essential to offer universal screening for pregnant women in India, as Indians are at risk of developing diabetes due to ethnicity.

Early diagnosis is the first and foremost determinant of the outcome of the pregnancy.

Glycemic control must be optimum., and achieved by daily self monitoring, adequate diet control and exercise, and by use if insulin and OHA's. Antepartum fetal well being monitoring is essential. It is done by ultrasound and biophysical profile monitor. Intrapartum fetal monitoring is very essential for good perinatal outcome.

Early diagnosis by serum markers, which are easy to predict the risk of developing GDM, should be widely used for easy diagnosis. Serum ferritin in this study had a significant correlation with development of GDM. High ferritin range is at risk of GDM. Routine use of monitoring of serum ferritin levels, during the antenatal visit in the mid trimester should be carried out, for early prediction of developing GDM.

Serum ferritin levels, apart from iron store action, is a good predictor of developing GDM. Elevated serum ferritin concentrations, at early gestational weeks, is associated with increased risk of developing GDM. This association is mediated by fat mass of the mother and obesity, at least in part. This data in this study suggests a possible link, between high serum ferritin and low grade inflammation and insulin resistance in pregnancy., which creates the risk of developing GDM.

Though significant association was analysed in this study, between serum ferritin in higher levels and risk of developing GDM, still larger studies are required to prove this association in a significant large population. Study on fetal outcome to be emphasised in further studies.

References

1. American Diabetes Association: Gestational diabetes mellitus. Diabetes Care. Definition and diagnosis of

diabetes mellitus and intermediate yperglycemia".World health organization. 2001; 23(Supp1 1):S77-S79.
2. Longitudinal changes in basal hepatic glucose production and suppression during insulin infusion in normal pregnant women. Am J Obstet Gynecol. 1992; 167:913-9.
3. Kalhan SC, D'Angelo LJ, Savin SM, Adam PAJ. Glucose production in pregnant women at term gestation. Sources of glucose for human fetus. J Clin Invest. 1979; 63:388-94.
4. Kalhan S, Rossi K, Gruca L, Burkett E, O'Brien A. Glucose turnover and gluconeogenesis in human pregnancy. J Clin Invest. 1997; 100:1775-81.
5. DiGiacomo JE, Hay WW Jr. Regulation of placental glucose transfer and consumption by fetal glucose production. Pediatr Res 1989; 25:429-434.
6. Hay WW Jr, DiGiacomo JE, Meznarich HK, *et al*. Effects of glucose and insulin on fetal glucose oxidation and oxygen consumption.
7. Ehrenberg HM, Mercer BM, Catalano PM: The influence of obesity and diabetes on the prevalence of macrosomia. Am J Obstet Gynecol. 2004; 191:964-968.
8. American Diabetes Association, authors. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2006; 29:S.
9. American College of Obstetricians and Gynecologists Committee on Practice Bulletins—Obstetrics. ACOG Practice Bulletin, authors. Clinical management guidelines for obstetrician-gynecologists. Number 30, September 2001 (replaces Technical Bulletin Number 200, Decembe1994).
10. Gestational diabetes. Obstet Gynecol. Marion DW. Screening and diagnosis of gestational diabetes mellitus. [Accessed August 29, 2008]. UpToDate Web site. 2001; 98:525-538.