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Original Research Article

Association of maternal serum triglycerides at term and macrosomia in gestational diabetes mellitus

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ABSTRACT

Background: Aim of the study was to determine association of maternal serum triglycerides (TG) at term and macrosomia in gestational diabetes mellitus (GDM).
Methods: A cross sectional study was carried out in the department of obstetrics and gynaecology, RIMS, Manipur. The study was conducted for 2 years duration from September 2019 to August 2021 and 85 singleton term pregnant women with GDM were included. All the patients were subjected to check fasting serum TG, FBS, PPBS. Descriptive statistics like mean, standard deviation and Inferential statistics like Chi-square test was used for comparing study variables between large for gestational age (LGA) and non LGA group. T-test was used to compare the mean values of age, pre-pregnancy BMI, pregnancy weight gain, OGTT, FBS, PPBS, fasting serum TG between LGA and non LGA group.
Results: The observed mean TG values in LGA and non LGA group in our study was 262.35±26.08 and 158.18±13.24 mg/dL respectively. The serum TG values in the LGA group mothers was significantly higher when compared to the non LGA group. The mean weight gain in pregnancy 15.17±1.82 and 9.60±1.47 in LGA and non LGA respectively. The mean BMI comparison among LGA and non LGA are 27.7±1.74 and 22.94±1.6 respectively.
Conclusions: It is observed that maternal fasting serum TG may be a strong predictor of foetal size irrespective of the glycemic status. Our study clearly pointed out the usefulness of measuring serum TG in GDM pregnancy. In addition to maternal hypertriglyceridemia, pre-pregnancy BMI, excessive weight gain in pregnancy significantly associated with foetal macrosomia in GDM mothers.

Keywords: GDM, Oral glucose tolerance test, LGA, BMI

INTRODUCTION

Gestational diabetes mellitus (GDM) defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy, is the most common metabolic condition during pregnancy and is increasing in prevalence worldwide.[1] Upto 22% pregnant women have GDM and this prevalence may be higher under newer diagnostic criteria.[2] In women with GDM, the physiological changes in insulin and lipids are exaggerated and may indicate underlying metabolic dysfunction that manifests during pregnancy.[3]

Currently the diagnosis and management of GDM is primarily on measurements of glucose metabolism. Although diabetic mothers with poor glycemic control are more likely to deliver macrosomia babies than mother with good glycemic control, strict glycemic control sometimes fails to prevent macrosomia.[4] Macrosomia is associated with serious complications to both mother and the foetus

like prolonged labor, caesarean delivery, postpartum hemorrhage, severe lacerations and foetal injuries, respiratory distress syndrome, hypoglycemia, hyperbilirubinemia respectively.[5]

Various studies shows that variation in birth weight which occur more often in diabetic pregnancies are not only determined by maternal glycemic state but other metabolic factors as well, in particular lipids may have an important influence. In fact the growth of the foetus depends on glucose, lipids and amino acids. The modified Pedersen-Freinkel hypothesis also includes maternal amino acids and lipids in addition to glucose.[6-10]

The rising level of TG observed even during normal pregnancies is the result of high serum estrogen concentration and increasing insulin resistance. Fatty acids derived from maternal TG cross the placenta and contribute to foetal macrosomia.[11] According to WHO, 41 million children under the age of five are known to be obese worldwide.[12] During pregnancy, foetal growth is influenced by the in-utero environment. Maternal nutrition plays a major role not only on the mother's own health, it also has a lasting impact on the normal growth and the well-being of the baby.[13]

Therefore, by identifying pregnancies at increased perinatal risk, macrosomia prediction allows for tailoring appropriate obstetric care. Macrosomia complicates significant proportion of diabetic pregnancies. The main purpose of this study is to determine the association of the maternal serum TG with macrosomia at term in GDM. So appropriate management and interventions could be employed if high risk cases are identified earlier.

METHODS

Study design

Study design was cross sectional study.

Study setting

The study was carried out in the department of obstetrics and gynaecology, Regional Institute of Medical Sciences, Imphal, India. The study was conducted for duration of two years beginning from September 2019 to August 2021, 85 term pregnant women with GDM were included in the study. Identity of the patient in relation to age, parity was taken. Body mass index of the patient before pregnancy and pregnancy weight gain has been recorded. Oral glucose tolerance test and blood sugar (Fasting and post-prandial) was done. All the patients were subjected to check fasting serum TG by collecting venous blood from antecubital vein under strict aseptic precautions after 12 hours of fasting. Serum TG was estimated using Randox reagent imola autoanalyzer, manufactured in 2007, United Kingdom. Data has been checked for consistency and completeness was analysed by using SPSS version 21.0 IBM. Descriptive statistics like mean, standard deviation, percentages and frequencies was used. Inferential statistics like chi-square test used for comparing age, parity, pre-pregnancy BMI, pregnancy weight gain, FBS, PPBS, mode of delivery, glycemic control between LGA and Non LGA group. T test was used to compare mean values of age, pre-pregnancy BMI, pregnancy weight gain, OGTT, FBS, PPBS, fasting serum TG between LGA and non LGA group. $P<0.05$ was considered as statistically significant.

Inclusion criteria

Any singleton term pregnant women with GDM admitted in the department of obstetrics and gynaecology, RIMS, Imphal were included.

Exclusion criteria

Patients with gestational hypertension or with other systemic diseases like overt DM, thyroid disorder in pregnancy or any chronic illness were excluded.

Sample size

(N) is calculated by using the formula,

$N= 4PQ/L^2$, where P=Prevalence of macrosomia in GDM mothers,

Q=100-P, L=Allowable margin of error, L=10%,

Taking p=25.8% from prevalence of foetal macrosomia in a study conducted by Karthiga Prabhu J, Anjalakshmi Chandrasekar and margin of error L=10%.[24]

Sample size (N)=77 Considering 10% of non response rate, the final calculated sample size N is 85.

RESULTS

In this cross-sectional study, 85 term pregnant women with GDM fulfilling the inclusion and exclusion criteria were taken up. It was carried out for period of 2 years (September 2019 to August 2021) in department of obstetrics and gynaecology, Regional Institute of Medical Sciences, Manipur, India.

Table 1: Background characteristics of patients, (n=85).

Patient characteristics	Mean ± SD
Age in completed (Years)	29.22±3.9
Pre-pregnancy BMI (Kg/m^2)	24.22±2.7
Weight gain in pregnancy (kg)	11.11±2.9
Screening OGTT value (mg/dL)	152.03±6.2
Fasting blood sugar (mg/dL)	95.99±7.1
Postprandial blood sugar (mg/dL)	127.94±19.1
Fasting serum triglyceride (mg/dL)	181.75±45.2
Birth weight (kg)	3.391±0.62

Table 1 shows mean values of age, pre-pregnancy BMI, weight gain in pregnancy, screening OGTT values, fasting and postprandial blood sugar values, fasting serum triglyceride values and birth weight of the baby of the study population.

Our study included the patients with age ranging from 21 years to 38years, with mean age of 29.22. Most of the study subjects were between 20-34years (88.20%). None of the subjects were found below 20 years. Maximum number of patients were multipara (74.10%), while 22 were nullipara (25.90%).

Out of 85 patients, 36.5% (n=31) had excessive weight gain and 20% (n=17) had poor weight gain. Maximum people (43.50%) had normal weight gain of 11-13 kg. Majority (61.20%) had normal BMI before pregnancy followed by overweight (34.10%) and obese (4.70%). None of the study subjects had BMI<18.5.

Most of the patients in the study had their FBS level more than the target level (≥95 mg/dL). Only 48.2% (n=41) had controlled FBS value. Out of 85 patients, 43 patients (50.6%) had PPBS value <120mg/dL and 42 patients (49.4%) had PPBS value ≥ 120 mg/dL. Based on treatment received by patients, maximum patients were on Oral hypoglycemic agents (65.90%) followed by insulin (21.2%) and medical nutritional therapy (12.9%). Maximum number of patients (n=51) had vaginal delivery followed by caesarean section (n=34). Babies born to the mothers in the study, majority were non-LGA (72.9%) followed by LGA (27.10%).

Figure 1 shows the distribution of fasting serum triglyceride levels according to Adult Treatment Panel III guidelines of national cholesterol education program. Maximum subjects (49.4%) were having normal triglyceride level followed by borderline triglyceride level (25.9%) and high triglyceride level (24.7%).

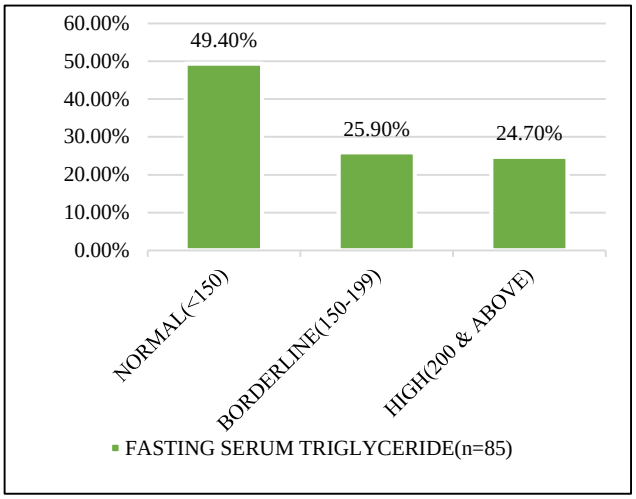

Figure 1: Distribution of patients based on fasting serum TG level, (n=85).

Table 2 shows the comparison of mean values between Non LGA and LGA group. Independent T test was applied. Mean values of age, OGTT, FBS, PPBS were not significant statistically whereas pre-pregnancy BMI and Pregnancy weight gain comparison showed statistically significant results.

Table 3 shows the mean value comparison of fasting serum triglyceride in non LGA and LGA group and the values are 158.1±13.24 and 262±26.08 respectively. The mean fasting serum TG in LGA group was higher when compared to the non LGA groups. The comparison shows statistically significant association between LGA and fasting serum triglyceride.

Table 2: Predictors of foetal macrosomia in GDM mothers, (n=85).

Predictive variables	Non LGA (Mean ± SD)	LGA (Mean ± SD)	Mean difference	95% CI	P value
Age (Years)	29.5±3.6	28.3±4.5	1.26	-0.6, -3.1	0.192
Pre-pregnancy BMI	22.94±1.6	27.70±1.74	-4.76	(-5.5, -3.93)	0.000
Pregnancy weight gain	9.60±1.47	15.17±1.82	-5.57	(-6.3, -4.8)	0.000
OGTT	152.1±5.3	151±8.3	0.46	-2.5-3.5	0.762
FBS	95.4±6.01	97±9.55	-1.86	-5.3-1.5	0.287
PPBS	126.5±17.74	131.7±22.3	-5.2	-14.4-4.05	0.267

Table 3: Fasting serum TG comparison, (n=85).

Predictive variables	Non LGA (Mean ± SD)	LGA (Mean ± SD)	Mean difference	95% CI	P value
Fasting serum triglyceride	158.1±13.24	262±26.08	-104.1	(-112.7, -5.63)	0.000

Table 4: Pre-pregnancy BMI comparison, (n=85).

Pre-pregnancy BMI (Kg/m^2)	Non LGA, n (%)	LGA, n (%)	P value
Normal	50 (96.2)	2 (3.8)	0.000
Overweight and obesity	12 (36.4)	21 (63.6)	

Table 4 shows the pre-pregnancy BMI comparison between LGA and Non LGA groups. Maximum number of patients had normal pre-pregnancy BMI in the study. Among the normal BMI category, 96.2% had non LGA babies and 3.8% had LGA babies. Among the overweight and obese category 63.6% had LGA babies and 36.4% had non LGA babies. Pre-pregnancy BMI comparison shows statistically significant results.

Table 5: Comparison based on mode of delivery, (n=85).

Mode of delivery	Non LGA, n (%)	LGA, n (%)	P value
Caesarean section	16 (47.1)	18 (52.9)	0.000
Vaginal delivery	46 (90.2)	5 (9.8)	

Table 5 shows the comparison of mode of delivery in non LGA and LGA groups. Vaginal delivery was observed to be very less in LGA group (9.8%). Caesarean section rate was also high in LGA group (52.9%). Comparison results based on mode of delivery was statistically significant.

Table 6: Comparison based on glycaemic control, (n=85).

Glycaemic control	Non LGA, n (%)	LGA, n (%)	P value
Controlled	28 (70)	12 (30)	0.565
Uncontrolled	34 (72.9)	11 (24.4)	

Table 6 shows the comparison of LGA and non LGA based on their glycemic control. The 30% of study population delivered LGA babies in spite of well controlled glycemic status. Despite uncontrolled glycemic status, 72.9% of study population delivered non LGA babies. Comparison results of the glycemic control was statistically insignificant.

The age and parity comparison between LGA and Non LGA groups shows statistically insignificant results with p=0.327 and 0.276 respectively. Similarly, FBS and PPBS comparison between non LGA and LGA groups results were statistically insignificant.

DISCUSSION

In normal pregnancies, the incidence of LGA newborn is usually less than 10%. The incidence of macrosomia in GDM is 15-45%. Macrosomia still complicates a significant proportion of diabetic pregnancy. Although diabetic mothers with poor glycemic control during pregnancy are more likely to deliver macrosomia babies than mothers with good glycemic control, strict glycemic control sometimes fails to prevent macrosomia suggesting abnormalities in protein and lipid metabolism in addition to glucose metabolism. Therefore, predicting foetal macrosomia in GDM is important in determining obstetrical outcome.

The findings of our present study indicated that pre-pregnancy BMI, excessive pregnancy weight gain, maternal fasting hypertriglyceridemia are an independent and significant risk factors for delivering a macrosomia in GDM mothers at term.

The normal pregnancy itself a hyperlipdemic state mainly influenced by estrogen hormone. On the other hand, dyslipidemia increases more with insulin resistance like in GDM, obesity, etc. In our study, a positive correlation has been observed between maternal fasting serum TG level and newborn birthweight in GDM mothers. The mean maternal fasting serum triglyceride level noted in our study was 181.75±45 and it is similar with Mossayebi et al (197.5±51) and Wang et al (173±59).[14,15] The observed TG values in LGA and non LGA in our study was 262.35±26.08 and 158.18±13.24 mg/dL respectively. The observed values in the LGA group were significantly higher when compared to the non LGA group. The incidence of foetal macrosomia was also higher among GDM mothers with hypertriglyceridemia. Son et al observed 283.42 and 203.71 mg/dL in LGA and non LGA group respectively.[16] In the study conducted by Gutaj et al the values in LGA and non LGA were 231.16 and 205.48 respectively.[17] There was a significant rise in maternal fasting serum TG level in LGA group than the non LGA group and it was proved to be the most independent risk factor for macrosomia in GDM mothers.

According to the literature it is known that maternal obesity is a major risk factor for delivering a macrosomia especially in GDM mothers. Our study results also confirm this finding. The mean BMI observed in our study was 24.22±2.714 corresponds with the 23.2±4.1 and 22.6±2.3 observed by Son et al and Mossayebi et al respectively.[14,16] Cruz et al reported that overweight and obesity in early pregnancy was associated with foetal macrosomia.[18] The mean BMI comparison among LGA and non LGA are 27.7±1.74 and 22.94±1.6 respectively. Cruz et al and Son et al observed similar finding in their study.[16,18] In contrary to this finding Krstevska et al and Mossayebi et al found no significant association with foetal macrosomia.[14,19] But according to our study, GDM mothers who were overweight and obese according to BMI classification tend to have double the risk of delivering a macrosomia when compared to GDM mothers with normal BMI. Alberico et al and Knopp et al also supports this finding (p<0.001).[20,21]

According to Cruz et al excessive weight gain during pregnancy was associated with fetal macrosomia.[18] 41.5% delivered macrosomic babies and 18.6% delivered non macrosomic babies. The mean weight gain in pregnancy in our study was 15.17±1.82 and 9.60±1.47 in LGA and non LGA respectively. Excessive weight gain is found to be the independent risk factor for foetal macrosomia in the present study. Same observation had been reported by Alberico et al in his study with p<0.001.[20] But in contrary to our finding Gutaj et al and Son et al reported no such association between excessive weight gain and foetal macrosomia.[17,16]

According to Amarasingha et al study the percentage of vaginal delivery was comparatively very less among LGA groups.[22] And clearly the rate of caesarean section was high among the LGA group when compared with the non LGA group. In our study the rate of caesarean section was 73.9% and 27.4% in LGA and non LGA group respectively. Similar finding was observed by Essel and Opai-Tetteh et al in their study with the caesarean rate of 40.54% in LGA group and 21.42% in non LGA group.[23] Three-fold rise of caesarean delivery rate has been observed in LGA group.

In the present study, no significant association found between macrosomia and age, parity, screening OGTT values, FBS, PPBS, Glycemic control and treatment method. Still the association cannot be ruled out completely because of smaller sample size. Causal relation could not be established due to the nature of study design. Fasting hypertriglyceridemia was found to be the most independent risk for foetal macrosomia. Additionally strong association between foetal macrosomia and pre-pregnancy BMI and excessive weight gain in the pregnancy has been observed in our study.

CONCLUSION

Foetal macrosomia is a common morbidity that can result in complications to both mother and the foetus. GDM is a known cause for macrosomia. Therefore, preventive strategies are mainly focused on maintaining a near normal glycemic levels. Despite good glycemic control some patients deliver macrosomic babies. This suggested that macrosomia is associated with abnormalities in protein and lipid metabolism in addition to the glucose metabolism.

It is observed that maternal fasting serum TG may be a strong predictor of foetal size. Our study clearly pointed out the usefulness of measuring serum TG in GDM pregnancy. In addition to maternal hypertriglyceridemia, pre-pregnancy BMI, excessive weight gain in pregnancy is significantly associated with foetal macrosomia in GDM mothers. Thus, suggesting that with a good Regulation body weight before pregnancy, weight gain in pregnancy and lipid profile, we can avoid macrosomia in GDM pregnancies. Achieving an ideal body weight before pregnancy and avoiding excessive weight gain in pregnancy should be the target in this high-risk group.

These results support the evaluation of lipid profile during pregnancy, which may be valuable in identifying and quantifying the metabolic abnormality in GDM and in predicting foetal outcome. This approach correlates well with a secondary analysis of the hyperglycaemia and adverse pregnancy outcome (HAPO) data showing an independent effect of maternal obesity and glucose levels on excessive foetal growth. In view of the studies mentioned above, it is important not only to measure glucose, but also to evaluate the lipid profile during pregnancy with a particular emphasis on TG levels. Both have an impact on foetal growth and outcome. It is especially relevant to advise women to avoid being obese before pregnancy because the presence of a subclinical metabolic dysfunction prior to conception subsequently leads to the development of GDM during pregnancy, and thus to adverse outcomes.

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