Maternal Triglycerides level As Predictor of Fetal Macrosomia in Pregnant Women with Gestational Diabetes Mellitus

Original Article

Khaled Ibrahim Abd Allah[1], Mohamed Samir Sweed[1], Engy Tarek Said Marmoush[2] and Mohamed Adel Ali[1]

[1]Department of Obstetrics and Gynecology, [2]Department of Surgery, Faculty of Medicine, Ain Shams University

ABSTRACT

Background: A diversity of characteristics have been identified in relation to increased risk of macrosomia, such as the high maternal age, height, pre-gestational body mass index (BMI), gravidity, overweight gain in gestation, post-term pregnancy, and male fetal sex.

Objective: This study was carried out to find the relation between high level of maternal serum Triglycerides and fetal macrosomia in women with gestional diabetes.

Materials and Methods: A prospective cohort study.one hunderd seventy pregnant women diagnosed with GDM singleton pregnancies attended to outpatient clinic for glucose control in Ain Shams Maternity Hospital were enrolled in the study; they were randomly divided into two groups: Group A: Diabetic pregnant female with hight levels of serum triglycerides. Group B: Diabetic pregnant female with normal lipid profile. Neonatal characteristics were collected from Both groups. Gestational age was calculated based on the combination of the last menstrual period and the early first-trimester ultrasound. Maternal metabolic parameters were included Serum glucose by oral glucose tolerance test and Blood Serum TG samples.

Results: A highly statistically significant result in group A (*p-value* < 0.001) indicates an increased incidence of fetal macrosomia with increased levels of serum TG.

Conclusion: In women with gestational diabetes mellitus (GDM), higher levels of serum TG were associated with an increased incidence of fetal macrosomia.

Key Words: Fetal macrosomia; gestational diabetes mellitus; maternal triglycerides.

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Corresponding Author: Engy Tarek Said Marmoush, MSc, Department of Surgery, Faculty of Medicine, Ain Shams University, Egypt, **Tel.:** +2 011 3679 4321, **E-mail:** tarekengy97@gmail.com

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INTRODUCTION

Macrosomia is a definition based on neonatal birth weight. The commonly used cutoff value is 4000 g, although some authors have proposed other cutoff values such as 4500 g or 5000 g[1,2].

The risk of extended delivery, cesarean section, post-partum bleeding, and perineal damage among mothers who deliver infants with macrosomia is greater. Neonatal complications are mainly a consequence of shoulder dystocia, brachial plexus injury, direct birth trauma, and birth asphyxia, leading to increased perinatal morbidity and mortality[3].

Genetic, population, and metabolic factors affect fetal growth. Recent research has shown that elevated blood glucose levels are not the primary factor. While macrosomia with maternal blood glucose has been related, prior studies have produced contradictory outcomes. Despite proper glycemic management, macrosomia is nevertheless frequent and is typically associated with undetected maternal hyperglycemia in several pregnant women with GDM[4].

It has been reported that a relationship exists in pregnant females with and without GDM among maternal hypertriglyceridemia and birth weight[5].

In pregnant females with GDM, maternal hypertriglyceridemia was a stronger forecaster of macrosomia than glycemic control. Moreover, the effect of serum triglycerides has been disregarded in developing fetal macrosomia for various subsets of the BMI[4].

Serum lipid levels were increasing progressively over Week 12, including Total Cholesterol (TC), TG, LDL-C (Low-Density Lipoprotein Cholesterol), high-density

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Lipoprotein Cholesterol (HDL-C), and phospholipids, particularly in 2nd and 3rd trimesters. These alterations cannot reveal a pathologic circumstance but constitute an essential adjustment to the mother's physiology for moms and fetuses to fulfill the energy demands and prepare the mother for birth and breastfeeding[6].

However, some researchers have demonstrated that perturbations of maternal lipid metabolism can cause many sorts of unfavorable pregnancy results (e.g., preeclampsia, gestational diabetes mellitus, and premature delivers) in addition, it may endanger fetal health in short or long terms (e.g., macrosomia, LGA, early cardiovascular disease, metabolic syndrome, insulin resistance)[6]. The TG level was connected with the higher risk of more extensive gestational age in the third trimester(LGA)[7].

This research aimed to establish the relationship between maternal TG levels and fetal macrosomia in pregnant women of various BMI sub types with gestational diabetes mellitus (GDM).

The primary purpose was to examine whether hypertriglyceridemia in pregnant women with gestational diabetes Mellitus in specific BMI sub-groups contributed or not to fetus macrosomia.

SUBJECTS, MATERIALS AND METHODS

Type of Study

A prospective cohort study.

Study place

Obstetrics Outpatient clinic, Maternity Hospital, Faculty of Medicine Ain-Shams University.

Study period

The study was conducted from march 2020 till July 2021

Study Population

One hunderd and seventy pregnant women diagnosed with GDM singleton pregnancies attended the outpatient clinic for glucose control in Ain Shams Maternity Hospital was enrolled in the study divided into two groups:

Group A: Diabetic pregnant women with high levels of serum TG.

Group B: Diabetic pregnant women with standard lipid profile.

Study Outcome

The outcome measures in the study were:

1. The difference in birth weight between pregnant diabetic dyslipidemic women and those having normal lipid profiles.
2. The correlation between hypertriglyceridemia and fetal macrosomia.

Selection and Withdrawal of Patients

Inclusion criteria

1. Age:18-40 years old.
2. Live-born singleton pregnancy.
3. Confirmed to have Gestational Diabetes mellitus by oral glucose tolerance test.
4. Controlled GDM according to blood sugar level and HA1C.
5. Controlled GDM on oral hypoglycemic drugs or insulin.
6. BMI ranging from 20-30 kg/m2.
7. PGestional age between 28 and 35 weeks of gestation.
8. Signed informed consent.
9. Normal doppler studies indicating no vasculopathy.
10. Delivery between 37-40weeks.

Exclusion criteria

1. We excluded women suffering from any medical disorder rather than GDM to minimize lipid metabolism and childbirth weight impacts from these conditions.
2. Mothers who delivered before 37weeks of pregnancy.
3. BMI less than 20 kg/m2 or more than 30 kg/m2.
4. Congenital fetal or multifetal gestation cases.
5. Cases of abnormal doppler values denoting underlying vasculopathy.

6. Acute or chronic infections.

Sample size

170 patients (85 in each group).

Sample justification

Using PASS 11 program for sample size calculation and according to (Hashemipour *et al*., 2018), the expected incidence of macrosomia = 20%, sensitivity of maternal triglyceridemia for prediction of macrosomia = 77%, specificity = 62.8%, a sample size of 156 pregnant women can detect these measures with power = 80% and α error 0.05 expecting 10% dropout rate, a sample size of 170 women was involved in the study[4].

Level of significance

The level of significance was $P<0.05$.

Ethical considerations

All participants received written informed permission before screening and registration. Participants actively participated in the study and respected its anonymity. All subjects outlined the advantages of participating in the study, and after clearance by the Committee on Research Ethics, participation was not harmed.

The study protocol was revised and approved by "The ethical research committee of the Obstetrics & Gynecology department - Faculty of medicine, Ain shams University." No. FWA000017585(FMASU MS124/2021)

Patient information sheet

The patient was given enough time to read the document carefully and was had the opportunity to ask any questions to the investigator if necessary.

Study procedure

A) Detailed medical history including

- Personal history
- Menstrual history
- Obstetric history
- Past history

b) physical examination

Clinical examinations, including general abdominal and pelvic assessments, have been performed and fulfill both inclusion and exclusion criteria in the past.

Data collection

According to WHO, which recommend a 100-g OGTT "(Oral Glucose Tolerance Test) between 24~28 weeks of gestation, the diagnosis of GDM can be made when two of the following values are elevated":[8]

- Fasting plasma glucose: >95 mg/dl.
- 1 h post 100g oral glucose load: >180 mg/dl.
- 2 h post 100g oral glucose load: >155mg/dl.
- 3 h post 100 oral glucose load: > 140 mg/dl[8].

The information of neonatal delivery, sex, birth weight (BW) and height, gestational age, mode of delivery, and perinatal outcomes were gathered. Gestational age based on the last menstruation cycle and the early first-trimester ultrasonography was estimated. In gram and centimeters, birth weight and height have been measured respictvely. According to documented birth papers, fetal weight was recorded. Microsomal or above a birth weight of 4,000 g[6].

Maternal metabolic parameters were included Serum glucose by oral glucose tolerance test; Blood Serum TG samples were drawn once between 28 and 35 weeks of pregnancy to measure metabolic parameters after 12 hours of overnight fasting. The amount of blood sample drawn was 5ml. "Hypertriglyceridemia was defined as a TG level greater than the 75th percentile value (>200 mg/dl)"[9].

"Plasma glucose concentration was determined by the hexokinase method on a Hitachi 7600-210 autoanalyzer (Hitachi, Tokyo, Japan). Serum TG concentration was determined by standard enzymatic methods (glycerol phosphate oxidase-peroxidase) on a Hitachi 7600-210 autoanalyzer. Blood samples were collected in serum separation tubes containing a gel separating serum or plasma from blood cells and promptly centrifuged and analyzed using a Hitachi 7600-210 auto-analyzer"[10].

Statistical Analysis

Analysis of data was done using SPSS program version 23. The sample studied by quantitative data was presented as a minimum, maximum, mean, and standard deviation. Qualitative data were presented as count and percentage.

Mann Whitney U test was used to compare between studied groups as regards demographic data. Mann Whitney U test was used to compare between studied groups as regard OGTT and comparison between studied groups as regard TG. Mann Whitney U test was used to compare between studied groups as regard birth weight and Macrosomia. As a predictive factor of Macrosomia, Logistic regression analysis for TG was used. *P value* < 0.05 was considered statistically significant.

RESULTS

No statistically significant difference (*p-value* > 0.05) between studied groups as regard age and gestational age and highly statistically significant difference (*p-value* < 0.001) between studied groups as regard BMI, as shown in (Table 1).

Table 1: comparison between studied groups as regards demographic data.

		Group A (N = 85)	Group B (N = 85)	MW	*P-value*
Age (years)	Median	27	27	3587	0.937 NS
	IQR	23 - 33.5	23 - 34		
G. age (weeks)	Median	30	30	3099	0.104 NS
	IQR	29 - 32	29 - 31		
BMI (kg/m^2)	Median	27.3	25.1	1955.5	< 0.001 HS
	IQR	25.4 - 28.8	23.8 - 26.6		

MW: Mann Whitney U test. **HS:** *p-value* < 0.001 is considered highly significant. **NS:** *p-value* > 0.05 is considered non-significant. **IQR:** Inter quartile range

Regarding OGTT

No statistically significant difference (*p-value* > 0.05) between studied groups as regard OGTT (FBS, 1 hour, 2 hours & 3 hours),as shown in (Table 2).

Table 2: comparison between studied groups as regard OGTT.

		Group A (N = 85)	Group B (N = 85)	MW	*P-value*
FBS (mg/dl)	Median	101	101	3508	0.743 NS
	IQR	97 - 103	96 - 103		
1 hour (mg/dl)	Median	188	188	3380.5	0.468 NS
	IQR	185 - 197	186 - 200.5		
2 hours (mg/dl)	Median	163	164	3417	0.541 NS
	IQR	159 - 176	161 - 176		
3 hours (mg/dl)	Median	149	148	3039.5	0.074 NS
	IQR	144 - 157	143 - 154		

MW: Mann Whitney U test. **NS:** *p-value* > 0.05 is considered non-significant.

Regarding TG

Highly statistical significant difference (*p-value* < 0.001) between studied groups as regard TG as shown in (Table 3)

Table 3: comparison between studied groups as regard TG.

		Group A (N = 85)	Group B (N = 85)	MW	*P-value*
TG (mg/dl)	Median	322	136	0.0	< 0.001 HS
	IQR	277.5 - 411	122 - 149		

MW: Mann Whitney U test. **HS:** *p-value* < 0.001 is considered highly significant.

Regarding birth weight and Macrosomia: Highly statistically significant difference (*p-value* < 0.001) between studied groups regarding birth weight and Macrosomia, as shown in (Table 4).

Table 4: comparison between studied groups as regard birth weight and Macrosomia.

		Group A (N = 85)		Group B (N = 85)		Stat. test	*P-value*
Birth weight (grams)	Median	4180		3000		MW = 1616.5	< 0.001 HS
	IQR	3430 - 4651		2850 - 4025			
Macrosomia	No	30	35.3%	62	72.9%	X^2 = 24.3	< 0.001 HS
	Yes	55	64.7%	23	27.1%		

MW: Mann Whitney U test. **HS:** *p-value* < 0.001 is considered highly significant. **X^2:** Chi-square test.

Using logistic regression analysis, this table demonstrates that TG could be used as a predictive factor for Macrosomia (B = 0.019. SE = 0.005, *p-value* < 0.001, Odds = 1.02 & 95% CL = 1.01 - 1.02) (Tables 5,6).

Table 5: Logistic regression analysis for TG as a predictive factor of Macrosomia.

	B	SE	*p-value*	Odds	95% CL	
(Constant)	- 5.5	1.41	< 0.001	0.004		
TG	0.019	0.005	< 0.001	1.02	1.01	1.02

B: Regression coefficient, **SE:** Standard error, **CL:** Confidence interval.

Table 6: Diagnostic performance of serum TG in discrimination of Macrosomia in group A.

	Cut off	AUC	Sensitivity	Specificity	PPV	NPV	*p-value*
TG	> 303.5	0.84	74.5 %	73.3 %	73.6 %	74.2 %	< 0.001

PPV: positive predictive value. **AUC:** Area under the curve **NPV:** negative predictive value.

Using roc curve, it was shown that serum TG can be used to predict Macrosomia at a cutoff level of > 303.5, with 74.5% sensitivity, 73.3% specificity, 73.6% PPV and 74.2% NPV (AUC = 0.84 & *p-value* < 0.001) (Figure 1).

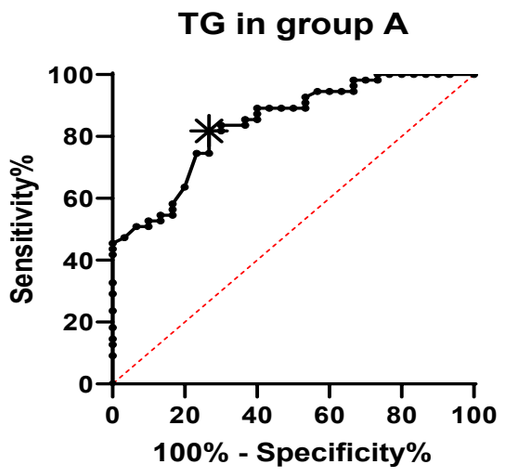

Fig. 1: Diagnostic performance of serum TG in discrimination of Macrosomia in group A.

DISCUSSION

Genetic, demographic, and metabolic factors all influence fetal growth. According to new research, excessive blood glucose levels aren't the main reason for large gestational age (LGA)[11].

Elevated levels of maternal TG have been strongly related to fetal macrosomia in patients with GDM. Moreover, the function of serum triglycerides (TGs) in prenatal macrosomia development in several BMI categories has been neglected[12].

In this prospective cohort trial, the correlation of maternal triglycerides (TG) and fetal macrosomia was determined among pregnant women in various BMI categories with gestational diabetes mellitus (GDM) in Ain Shams University Maternity Hospital. One hundred seventy pregnant women diagnosed with GDM were randomized into two equal groups; group (A): diabetic pregnant female with elevated levels of maternal TG and group (B): Diabetic pregnant female with standard lipid profile.

Regarding basal demographic data and laboratory findings, statistical analysis of current results showed that there was no statistically significant difference (*p-value* > 0.05) between studied groups as regard age and gestational age and OGTT (FBS, 1 hour, 2 hours & 3 hours). At the same time, BMI and serum triglycerides (TGs) were significantly higher in the dyslipidemic group 25.4 - 28.8 vs.23.8 - 26.6 kg/m2 and 277.5 - 411vs.122 – 149 mg/dl respectively (*p-value* < 0.001).

This study agreed with Di Cianni *et al*. (2005), who presented that in women with GDM, the serum TG concentrations (2,47 ± 0,77 mmol/l) were much higher than those of normal glucose tolerance NGT (1,99 ± 0,64 mmol/l) or Impaired glucose tolernce IGT (1,98 ± 0,81 mmol/l) $P < 0.01$. The goal was to assess the prognostic relevance of blood triglyceride (TG) levels in women with positive diabetes but standard glucose tolerance for newborn weight. A hundred and eighty Caucasian pregnant women were admitted with positive diabetes screening. In 36 (20%) women, impaired glucose tolerance (IGT) in 23 (13%), and standard glucose tolerance (NGT) in 121 67%[13].

Findings of this report accord with Schaefer-Graf *et al*. (2008). They intended to assess the intrauterine metabolic environment and the impact of maternal glucose and lipids on fetal growth in gestational diabetic pregnancies (GDM). One hundred fifty pregnancies have been seen in maternal serum and cord blood during the third trimester of serum triglycerides (TGs), cholesterol, free fatty acids (FFAs), glycerol, insulin, and glucose. Measures were conducted simultaneously with the maternal blood and birth weights, and after delivery, fetal abdominal circumference (AC) measurements were taken. They found that maternal FFA levels were more significant in women with LGA infants than in mothers with appropriate for gestational age (AGA) novices (362.8 ± 101.7 vs. 252.4 ± 10.1, P=0.002)[14].

This study came in the same line with Son *et al*. (2010), which indicated that BMI is autonomously connected with the LGA infants on a term basis. The LGA group showed considerably higher maternal TG levels than those of the non-LGA group [3.2 (2.4–3.6) vs. 2.3, p=0.001], while the LGA group showed a significantly higher level of BMI pregnancy (26.0 ± 4.7 VS 22.3 ± 3.5, $p<0.0001$). They sought to assess the significance of mother lipids to predict neonates born to mothers with gestational diabetes mellitus (GDM) for large-gestational age (LGA). A total of 104 women with GDM diagnoses were diagnosed in

this retrospective research. Women who had sound effects on the 50 g oral glucose challenge test (24 to 28 weeks of gestation) and were referred to patients suspected of GDM had a 3 hours 100 g oral glucose tolerance test diagnosed GDM. Maternal blood fasting Triglycerides were measured at 24–32 weeks of pregnancy, together with total high-density lipoprotein (HDL) and low-density lipoprotein levels of cholesterol[10].

Olmos *et al*. (2014) conducted a study on Two-hundred and seventy-nine singleton GDM pregnancies divided them into three groups according to pre pregnancy BMI: normal weight (BMI520–24.9; n5128), overweight (BMI525–29.9; n5105), and obese (BMI_30; n546). Individual z-scores (ZS) of maternal triglycerides and newborn weight (NWZS) were calculated as deviations from published 50th percentiles. They were designed to detect the connection between maternal obesity and macrosomia in pregnancy. They have concurred with the current findings and indicated a statistical similarity of standard, overweight, and obese women concerning gestational age. There was a tangible link between normal to overweight and obese moms between birth weight and newborn macrosomia[15].

Regarding fetal outcomes, statistical analysis of current results showed that birth weight and macrosomia were significantly higher in dyslipidemic group 3430 – 4651 vs.2850 – 4025 g and 55(64.7%) vs. 23 (27.1%) (*p-value* < 0.001) respectively.

Di Cianni *et al*. (2005) agreed with the current study. They stated that macrosomia and LGA newborns were more often seen in IGT than in GDM or NGT ($P < 0.01$ The incidence of LGA infantile was considerably greater in 83 women with positive diabetically screening but a standard glucose tolerance than in males with normal TG (4.5%) ($P < 0.05$) compared with those having 75th percentiles (> 2.30 mmol/l) in TG[13].

This study has been carried out in agreement with Schaefer-Graf *et al*. (2008), which reports that TGs and FFAs in maternal cases which are associated with fetal AC size (28 weeks: triglycerides, P = 0.001; FFAs, P = 0.02), and when delivered, all neonatal anthropometric measurements are related. (FFA: birth weight, P= 0.002; BMI, P= 0.001; fat mass, P= 0.01). The only parameters for newborns large for the gestational age (LGA), P= 0. 008 and P= 0.04, persisted after confusing variables after delivery[14].

Results of the present study were corroborated by Son *et al*. (2010), who found that the occurrence of LGA infants in females with hypertriglyceridemia was substantially more significant than in females with regular TG (12/26, [46%] vs. 13/78, [4%]; p= 0.02).). Conversely, they were not in agreement with this study. They said that TGs of mothers were generally related to the weight of newborn births but were not statistically significant (r=0.17, p=0.07) because of various populations, samples, and GDM methodology screening compared to the present study[10].

It also agrees with Olmos *et al*. (2014), who revealed that the association between the mean maternal TG and the birth weight of Z scores was significant. Overweight (r50.42; $P<0.001$; n5105) and obese (r50.47; $P<0.001$; n546) were significant but not normal mothers were significantly affected by the correlation (r50.12; P50.158; n5128)[15].

In addition, this study was agreed by Jin *et al*. (2016). They were designed to study the relationship amongst the Chinese population between maternal dyslipidemia and bad pregnancy results. It was reported that every unit elevation in the third trimester TG was related with an increased risk of large for gestational age (OR = 1,13, 95 percent CI: 1,02-1,26) and fetal macrosomia after adjustment of covariates (OR = 1.19, 95 percent CI: 1.02-1,39), respectively[7].

These findings are consistent with results of recently conducted research by Hashemipour *et al*. (2018), which showed that the increased risk of macrosomia in women averaged in weight ($P < 0.01$) and overweight ($P < 0.01$), respectively, is 4.2 and 1.9 times the increase in the level of TG. They were intended to examine the relationship between maternal and fetal macrosomic levels in Iranian pregnant women with gestational diabetes mellitus of various BMI groups[4].

The findings of this study was in agreement with Wang and al. (2018). They showed the association between the late gestation of maternal lipid profiles and the chance that women without diabetes mellitus will develop macrosomia (DM). They reported that the macrosomal levels for mother serums triglyceride (TG) and high-density lipoprotein cholesterol (HDL-C), each with one mmol/L TG increased macrosomal hazard by 27 percent, while each increase for one mmol/L for the level of HDL-C reduced macrosomal threat by 37 percent, even when adjusted for potential macrosomal risk. In addition to increased maternal TG-serum levels and declining HDL-C values, the risk of macrosomia is steadily growing[5].

Pazhohan *et al*. (2019) measured the frequency of large gestational age (LGA) in neonates with pre-gestational and gestational diabetes women is caused by maternal hyperlipidemia. The study was conducted on women with PGDM and GDM with a single center (35th to 38th weeks); data was collected. Maternal TG and cholesterol levels were significantly higher in the group of LGA than in the AGA group. They agreed with the current study and stated that the preponderance of LGA newborns was considerably higher in women with hypertriglyceridemia[16].

Using logistic regression analysis; statistical analysis of current results showed that TG could be used as a predictive factor for macrosomia (B = 0.019. SE = 0.005, *p-value* < 0.001, Odds = 1.02 & 95% CL = 1.01 - 1.02). Also, using roc curve, it was shown that serum TG can be used to predict macrosomia at a cutoff level of >303.5 mg/dl, with 74.5% sensitivity, 73.3% specificity, 73.6% PPV and 74.2% NPV (AUC = 0.84 & *p-value* < 0.001).

These results correspond to Di Cianni *et al*. (2005). In several regression analyses, it was found that only birth weight, but also lower cutoff (<2,30 mmol/l) levels, were separately linked with the pregnancy B MI (F-test = 7.26, *P* <0.01) and fasting serum TG (F-test = 4.07, *P* < 0.01)[13].

Son *et al*. (2010) agreed with the current study and indicated that hypertriglyceridemia is independently linked with infant LGA in 24-32 weeks of gestation, pregnancy, and multiple pregnancies. In the LGA infants predictions, the area below the ROC curve was 0,702 for the maternal serum TG. The ROC analysis for serum TG showed an appropriate cutoff value of 3.33mmol/l. TG used that cutoff value, with sensitivity and specificities of 48.0 and 83.5 percent, respectively, to indicate LGA infants (95 percent CI, 0.59–0.81; p=0.002)[10].

This observation agrees with Jin *et al*. (2016), who showed that the ideal cutoff values for the TG prediction of 3.534mmol/L for the third-trimester of LGA were separate. For third trimester HDL-C, the best cutoff points were 1,817 mmol/L[7].

These results are in line with the results of Hashemipour *et al*.(2018) recent research. The area below the TG level curve for macrosomia was reported to have been 0.828 (95% CI:0.712-0.911, *P*<0.001) and 0.711 (95% CI: 0.639-0.775), respectively, for women who were averaging in weight and overweight[4].

The current work was confirmed by Wang *et al*. (2018). They said women with TG levels of more than 3.92 mmol/L exhibited an approximately 2.8-fold increase in macrosomal risk compared with women with serum TG levels of < 2.5 mmol/L. Moreover, the risk of macrosomia in women with concurrent hypertriglyceridemia and low serum HDL-C levels was higher compared with the levels of hypertriglyceridemia and low serum HDL-C (OR 2,074, 95% confidence interval [IC]: 1,760%–3,273) in comparison to those of hypertriglyceridemia and low serum HDL-C levels alone (OR, 2,074, 95% CI, 1,60%–2,67, OR 1,36, 95% CI, respectively: 1,028–1,80). The present study, however, has not evaluated HDL-C serum[5].

In addition, it comes in agreement with Pazhohan *et al*. (2019), who reported that maternal triglycerides levels tended to be correlated with a newborn birth weight with sensitivity 86.7%, specificity 70.1%, and cut off value >345mg/dl, respectively[16].

The strengths of the current study were due to:

- It was a prospective cohort trial with minimal percent of bias.
- Every effort was made to ascertain that all follow-up data were correct, and only complete information was included in data analysis.
- All clinical assessments, sonographic measurements, deliveries, and assessment of study outcomes were done by the same team.

The limitations of the current study were due to:

- COVID 19 pandemic.
- Relatively small sample size.

CONCLUSION

In women with gestational diabetes mellitus (GDM), higher levels of serum TG were associated with an increased incidence of fetal macrosomia.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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