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Original Research Article

OFFSPRING BIRTH WEIGHT AND MATERNAL FASTING LIPIDS IN WOMEN SCREENED FOR GESTATIONAL DIABETES MELLITUS

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Abstract

Introduction: The most common neonatal complication of gestational DM is macrosomia. During early pregnancy, an accumulation of maternal fat depots occurs followed by increased adipose tissue lipolysis and subsequent hyperlipidemia which mainly corresponds to increased triglycerides in all circulating lipoproteins. In GDM women the enhanced insulin resistance and altered estrogen-progesterone ratio are responsible for the reported wide range of dyslipidemic conditions[1]. Association of high maternal glucose levels and fetus macrosomia have been documented.

The prospective Amsterdam Born children and development cohort study, reported that high maternal TG levels in early pregnancy were associated with higher Birth weights and subsequently a higher occurrence of LGA births, whereas low TG levels were associated with accelerated postnatal growth2. Total cholesterol, HDL and lipoprotein concentrations are not significantly different between GDM patients and control subjects3.

Both maternal triglycerides and nonesterified fatty acids levels but not glucose in pregnancies with well-controlled gestational diabetes mellitus has been shown to correlate positively with both neonatal weight and fat mass4.

Significantly elevated triglyceride levels in cord blood of obese GDM patients with macrosomic fetus suggests that TG may be important in the pathogenesis of fetal macrosomia5.

We have undertaken this study to understand the relationship of hyperlipidemia in GDM pregnancy and the relationship between triglyceride levels and fetal macrosomia.

Aims and Objectives: To correlate the relationship between fasting cholesterol and Triglycerides and offspring birthweight in women screened for GDM, To correlate the relationship between fasting maternal cholesterol, Triglycerides and mode of delivery and perinatal outcome.

Materials and Methods: It is a prospective observational study done on patients coming to the department of OBG, Father Mullers Hospital, Mangalore for antenatal checkup over the period of one year and nine months.
All Antenatal mothers are advised to undergo OGCT test as part of universal screening for GDM according to their convenience. Minimum of 100 Patients with positive OGCT (> 140mg/dl) were selected. Detailed clinical evaluation including relevant history and physical examination was undertaken. They are asked to undergo OGTT test. Fasting plasma venous blood glucose value, followed by 1, 2 and 3 hr plasma glucose values following 75 gm glucose intake is calculated. At the time of collection of fasting glucose sample, fasting lipid profile was also done. Those patients with negative OGTT were advised routine antenatal care and were taken as controls. Those patients with positive OGTT were referred to endocrinologist and dietician for multidisciplinary management. They were further classified into those on diet control, insulin, OHA sand both insulin and OHA. When the patient got admitted for delivery, the mode of delivery, Gestational age, gestational weight gain, offspring birth weight and perinatal outcome were analyzed.
Results: Among the total of hundred GCT positive patients studied, 41 patients were GTT positive and 59 were GTT negative. Elevated triglycerides were found in 31(75%) of GTT positive patients. Elevated serum cholesterol levels were seen in 21(51.21%) of GDM mothers. Forty-one (69%) patients in the normal GTT group had elevated triglycerides and 31(52%) among the normal GTT group had elevated cholesterol.
Among the 100 patients studied, there were 25 babies with birth weight more than 3.5 kg. Among these patients,12 (48%) had elevated triglycerides with normal GTT values and 7 (28%) patients had elevated triglycerides along with elevated GTT. Elevated cholesterol with normal GTT was seen in 7 (25%) patients only and elevated cholesterol together with elevated GTT was seen in 5(20%) patients.
Discussion and Conclusion: Various studies have been conducted in different parts of the world to correlate between maternal glucose levels and macrosomia as well as lipid alterations with fetal weight changes in normoglycemic as well as diabetic patients. Our study was also aimed at finding whether any relationship existed between the development of macrosomia in diabetic or nondiabetic patients and relationship with maternal fasting lipids, mainly serum triglycerides.
Our study shows elevated triglycerides and cholesterol both in gestational diabetic patients as well as nondiabetic controls. Significant association with macrosomia was not found in relation to triglyceride and cholesterol levels.
Conclusion: Our study did not find any positive correlation between elevated triglycerides and GDM as well as between elevated total serum cholesterol and GDM. Elevated birthweight more than 3500 g also was not significantly found to be associated with either elevated serum triglyceride levels or serum cholesterol levels. These discrepancies may be due to the fact that lipid alterations in pregnancy are also related to the diet patterns and pre-pregnancy BMI of the patients. Further research is required in this aspect in order to identify the role played by maternal fasting lipids in causing fetal macrosomia and related manifestations.

Keywords: GDM, TG, LIPIDS, MACROSOMIA.

Introduction

Diabetes complicating pregnancy is becoming more common worldwide, but the last 5 years have produced several major advances in the management of diabetic syndromes. The majority of complications seen in fetal development, growth and labor and delivery can be ascribed to relative

maternal hyperglycemia and it follows that optimal maternal diabetic control at all stages from pregnancy planning to the postnatal period is critical to the obstetric outcomes. It is important to note however that - while many of the medical complications of diabetes can affect the success or otherwise of pregnancy such pregnancy itself may contribute to diabetogenic action. This together with the deterioration in the long-term health of the mother.

It is felt that the incidence of this condition is increasing in association with increasing obesity in the population at large and increase in age-specific maximum fertility. Depending on the population sample and diagnostic criteria, the prevalence may range from 1-14% [7].

Fetal complications include macrosomia, neonatal hypoglycemia, perinatal mortality, congenital malformations, hyperbilirubinemia, polycythemia, hypocalcemia and respiratory distress syndrome[8]. Macrosomia defined as birthweight> 4000g occurs in approximately 20-30% infants whose mothers have GDM. Maternal factors thought to be contributing to increased incidence of macrosomia include hyperglycemia, high BMI, older age, and multiparity[9].

Disturbances in maternal lipid metabolism have been associated with an increased risk of GDM, Preeclampsia and fetal macrosomia. The purpose of this study in women selectively screened for GDM is to examine the relationship between maternal fasting triglycerides and cholesterol levels and offspring birth weight.

Gestational Diabetes Mellitus

Gestational diabetes mellitus is defined as carbohydrate intolerance of any degree diagnosed or first recognized during pregnancy[6]. This definition includes women whose glucose tolerance will return to normal after pregnancy and those who will persist with glucose intolerance and type 2 diabetes[6.] Taking into account all pregnancies around the world complicated by diabetes, GDM accounts for approximately 90% [7].

This is a condition caused by high concentrations of steroid hormones such as progesterone, estrogens, prolactin, cortisol and by hormone derived from placenta, human placental lactogen: all of them having decreased sensitivity of insulin receptors within target tissues leads to the diabetogenic state[11]

The insulin resistance plays a role in making sure that the fetus has an adequate supply of glucose. This is done by changing the maternal energy metabolism from carbohydrates to lipids .12. They also have an impaired compensatory increase in insulin secretion, particularly the first phase of insulin secretion. This first phase insulin release decline could be a marker for the deterioration of beta cell function[12].

Risk factors for Gestational Diabetes Mellitus include: High body mass index, excessive weight gain, low physical activity during pregnancy, high dietary intake of PUFA, h/o glucose intolerance or previous h/o large baby or family history of diabetes[13]. H/o GDM is a significant risk factor for serious maternal complications in future including metabolic syndrome, type 2 DM, and cardiovascular diseases. Risk of developing diabetes after pregnancy is up to 3 % in mothers with gestational diabetes.

Maternal complications during pregnancy include hypertension, pre-eclampsia and an elevated risk of need for cesarean delivery. Fetal complications of GDM are macrosomia, neonatal hypoglycemia, perinatal mortality, congenital malformations, hyperbilirubinemia, polycythemia, hypocalcemia and respiratory distress syndrome[12]. There is also increased the incidence of term intrauterine fetal death[8].

Screening between 24-25 weeks of gestation has helped in earlier diagnosis and treatment of Gestational Diabetes Mellitus[10] Controlling maternal glycemia with medical nutrition therapy, close scrutiny of blood glucose levels and treatment with insulin if blood glucose levels are not under control have been effective to decrease fetal and maternal morbidities[14].

Diagnostic Criteria for Gestational Diabetes Mellitus

The recent data on the prevalence of GDM in our country was 16.55% by WHO criteria of 2 hr PG ≥140mg/dl. As such universal screening during pregnancy has become important in our country[15].

Glucose challenge test is used for screening.One hour venous plasma value> 140mg/dl after 50 g glucose ingestion is considered as positive. The Oral Glucose Tolerance Test most commonly used to diagnose GDM. GDM is diagnosed if two or more plasma glucose levels meet or exceed the following thresholds: fasting glucose concentration of 95mg/ dl, 1-hour glucose concentration of 180 mg/dl, 2-hour glucose concentration of 155 mg/ dl, or 3-hour glucose concentration of 140 mg/dl. This is the O Sullivan and Mahan modified by Carpenter and Coustan criteria. This protocol is being followed in our hospital.

Management of Gestational Diabetes Mellitus

A team approach is ideal for managing women with GDM. The team would usually comprise an obstetrician, endocrinologist, a diabetes educator, dietitian, and pediatrician[17].

ACOG recommends insulin therapy for women receiving medical nutritional therapy whose fasting glucose level exceeds 95 mg per dL, whose one-hour postprandial glucose level exceeds 130 to 140 mg per dL, or whose two-hour postprandial glucose level exceeds 120 mg per dl[18]

The ADA describes upper boundary targets of 90 to 99 mg per dL in the fasting state, less than 140 mg per dL one hour after eating, and less than 120 to 127 mg per dL two hours after eating.[19]

A safe and effective oral agent for the treatment of Gestational Diabetes is highly desired. The sulfonylurea glyburide is close to meeting these goals, with prospective and retrospective studies demonstrating its effectiveness and probable safety[20] Metformin may be another option for women with Gestational Diabetes. The Metformin in Gestational Diabetes (MiG) trial randomized 751 women with gestational diabetes to open treatment with metformin and insulin or insulin alone[21]. Although the results of this long-awaited study are encouraging, 46 percent of the women receiving metformin also required insulin therapy.

Fetal Surveillance

Fetal surveillance can be divided into screening for congenital anomalies, monitoring for fetal well-being, and ultrasound assessment for estimated fetal weight and macrosomia. The ADA recommends screening for congenital anomalies in women with gestational diabetes who present with evidence of preexisting hyperglycemia, such as an HB A1C level greater than 7 percent, a fasting glucose level greater than 120 mg per dL, or a diagnosis of gestational diabetes in the first trimester[19.]

Fetal Macrosomia

The incidence of fetal macrosomia is found to be 3-6 times higher in pregnancies complicated with Gestational diabetes mellitus compared to normal pregnancies[22]. It is still under evaluation as to which factors are responsible for the pathogenesis of fetal macrosomia. It is suggested that rather than fetal hyperglycemia alone, metabolic milieu consisting of lipids and amino acids together with glucose is the causative factor.

Mother's age and pre-pregnancy weight, weight gain during pregnancy, a period of gestation, placental dimensions and functions, fetal insulin secretion and substrate concentrations in the maternal plasma have so far been identified as prime factors affecting fetal dimensions[22]. According to Pederson hypothesis, the main substrate affecting fetal macrosomia is glucose. Glucose passes through the placenta by facilitated diffusion and triggers fetal insulin secretion, thus hyperglycemia in mother causes fetal hyperinsulinemia. Insulin which is an anabolizing hormone leads to increase in fetal dimensions and weight which in turn causes fetal macrosomia[23]. Significantly elevated TG levels seen in cord blood of obese Gestational Diabetes patients with macrosomic fetuses suggest that TG might be contributory in the pathogenesis of fetal macrosomia[24] Fetal hyperinsulinemia and increased fetal growth is also associated with a group of abnormalities usually referred to as "diabetic fetopathy" that may be causative factor for serious neonatal complications including hypoglycemia and respiratory distress[25]

Lipid Metabolism in Pregnancy

Insulin resistance occurring in pregnancy has been proved to produce a reduction in lipoprotein lipase activity and this could lead to decreased peripheral catabolism of VLDL TG. This along with increased hepatic TG synthesis and secretion contributes to the increase in circulating plasma and VLDL TG. In a normal pregnancy, the compensatory mechanism by the pancreas makes up for the reduced effectiveness of insulin by increasing secretion of the hormone[26]. Plasma insulin levels are generally insufficient to prevent a certain degree of hyperlipidemia in normal pregnancy[27]. Estrogen has also been proven to increase endogenous production of VLDL TG, decrease adipose tissue lipoprotein lipase activity and hinder hepatic TG lipase activity[28]. Thus estrogenic influence leads to enhanced synthesis and decreased removal and thus increased circulating VLDL TG. Progesterone has a neutral effect. Thus the interaction between estrogen and progesterone would lead to hypertriglyceridemia.

Maternal accumulation of fat becomes maximum in the mid-gestation and reduces in late gestation whereas maternal serum lipid levels increase in mid to late pregnancy. This is regarded as a maternal adaptation in order to maintain constant fuel distribution to the fetus[29]. Cholesterol is an integral component of cell membranes, essential in the synthesis of bile acids and steroid hormones and is also needed for cell proliferation and development of growing body. Consequently, there is high demand for cholesterol in the embryo and the fetus. In early trimester of pregnancy, maternal cholesterol actively contributes to fetal cholesterol and at term, endogenous cholesterol synthesis becomes the principal source[30].

According to a recent study, postprandial triglyceride at mid-pregnancy was found to be significantly associated with birth weight and fetal macrosomia and this was found to be related strongly with impaired serum lipoprotein concentrations and composition [31].

The positive correlation between maternal triglyceride level and birth weight is confusing because maternal triglyceride does not cross the placenta. Explanation by physiologic mechanism states that the hydrolysis of maternal triglyceride by placental lipoprotein lipase to free fatty acids that cross the placenta is increased[32]. Increased insulin resistance seen in late pregnancy would explain the association between maternal TG level and fetal growth. VLDL and HDL Cholesterol levels have not shown many changes throughout the period

of pregnancy[33] Metzger et al has proved that fasting triglyceride concentrations are found to be elevated in all Gestational Diabetes Mellitus patients during second and third trimesters and this is seen more in obese GDM patients and patients where plasma fasting glucose values are high[34] Even in GDM patients with good glycemic control , basal TG levels are elevated and TG elimination rate is decreased whereas other parameters such as free fatty acids show no appreciable difference between normal and GDM [35]

In diabetes, a decreased or ineffective level of circulating insulin results in the inability of the body to use glucose as an energy source and lipolysis is aggravated in order to provide an alternate source of fuel for energy production. Therefore when two physiologic states co-exist which bring about alterations in lipid metabolism: exaggerated hyperlipidemia could be predicted. According to recent evidence, the duration of diabetes, gestational hormone variations and the modality used to treat patients with GDM significantly contribute to the varied effects of GDM on lipid metabolism in pregnancy[36].

Montelongo et al found lower concentrations of gestational hormones and plasma lipoprotein lipids in subjects with GDM compared to others[37].Knopp et al suggested that duration of diabetes in pregnancy causes impaired placental synthesis of gestational hormones and thus decreases the hyperlipidemia[38].These researchers suggested that in women with GDM, who are diagnosed in the third trimester and controlled with diet therapy, the effect of diabetes on lipid metabolism may be more pronounced. It is speculated that in GDM , lipolysis of adipose tissue may be increased above normal in response to the reduced effectiveness of the hormone. Diabetes is thought to induce dyslipoproteinemia and therefore it may be suggested that the emergence of diabetes during pregnancy can cause further alterations in lipoprotein metabolism[39].

Significantly high TG levels found in cord blood of obese GDM patients with macrosomic fetus suggests that TG could be important in the pathogenesis of fetal macrosomia. The HDL subfractions maybe important due to evidence suggesting that approximately 50% of fetal cholesterol is derived from maternal circulation. Both maternal TG and nonesterified fatty acid levels but not glucose levels in pregnancy with well-controlled GDM have found to correlate positively with both neonatal weight and fat mass[40]

Materials and Methods

It is a prospective observational study done on patients coming to the department of OBG, Father Mullers Hospital, Mangalore for antenatal checkups over the period of one year and nine months.

All Antenatal mothers are advised to undergo OGCT test as part of universal screening for GDM according to their convenience. Venous Plasma glucose levels after one hour of intake of 50g glucose were calculated. 115 patients with positive OGCT (> 140mg/dl) were selected.15 patients were excluded from the study as they were lost to follow up.

Inclusion criteria

Antenatal mothers with positive OGCT in any period of gestation.

Exclusion criteria

- Women with pregestational diabetes mellitus
- Women with the hypertensive disorder and pre-eclampsia at the time of registration.
- Women with thyroid disorders, lupus, and APLA
- Subjects with fetal or congenital malformations and multifoetal gestations.

Detailed clinical evaluation including relevant history and physical examination was undertaken. They are asked to undergo OGTT test. Fasting plasma venous blood glucose value, followed by 1, 2 and 3 hr plasma glucose values following 75 gm glucose intake is calculated. At the time of collection of fasting glucose sample, serum total cholesterol and serum triglyceride were also done. Those patients with negative OGTT were advised routine antenatal care. Those patients with positive OGTT were referred to endocrinologist and dietician for multidisciplinary management. They were further classified into those on diet control, insulin, OHA S and both insulin and OHA. When the patient got admitted for delivery, the mode of delivery, Gestational age, gestational weight gain, offspring birth weight and perinatal outcome were analyzed.

All GCT positive patients were taken into the study. Total of 100 patients was studied. Further GTT positive patients were taken as the study group and GTT negative patients were the controls.

Table 1: Normal values of investigations studied

GCT	< 140mg/dl
GTT (Carpenter and Coustan criteria) Any 2 values high considered positive test	Fasting 95mg/dl 1 hour 180mg/dl 2 hour 155mg/dl 3 hour 140mg/dl
Serum total cholesterol	< 200mg/dl Fasting sample
Serum triglyceride	<150mg/dl Fasting sample

The lipid levels used were based on nonpregnant population as there are currently no national guidelines for normal lipids in pregnancy available.

- All biochemical tests were analyzed with COBAS 6000 Rocha analyzer.
- OGCT and OGTT: Plasma venous blood is used and analyzed by the hexokinase method.
- Total cholesterol: Serum sample is taken and analyzed by oxidase/peroxidase method.
- Triglycerides: Serum sample is taken and analyzed by Glycerol phosphate method

Statistical analysis was done by SPSS Software version 23. Collected data were analyzed by mean, frequency, percentage, Fisher`s exact test and by Chi-square test.

Results

Table 2: Age distribution

AGE (in years)	NUMBER OF PATIENTS with GTT POSITIVE n = 41	NORMAL GTT n=59	Elevated triglycerides n=60	Elevated total cholesterol n=40	Both cholesterol and TG elevated n = 12
18-27	18	31	39	17	6
28-37	22	26	20	21	4
>37	01	02	01	02	2

Majority of all our patients fall in the age group of 18-27, with the mean age of 27.52. Most of the GTT positive patients were seen in the age group 28-37. Elevated serum triglycerides were seen more in the age group 18-27 and elevated cholesterol more in the 28-37 age groups.

Among the total of hundred GCT positive patients studied, 41(41%) patients were GTT positive and 59(59%) were GTT negative.

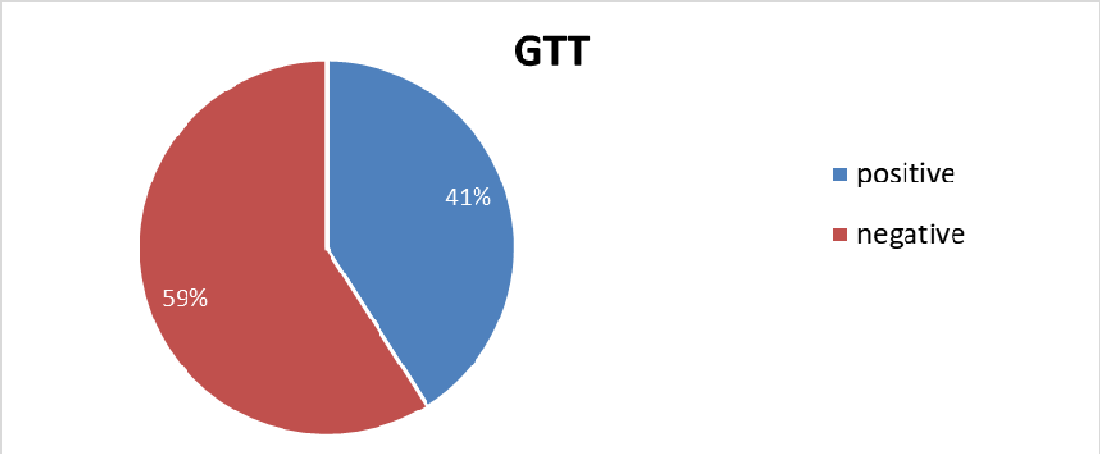

Figure 1:

Table 3: Classification Based on Parity

PARITY	NUMBER OF PATIENTS with GTT POSITIVE n = 41	NORMAL GTT n = 59	Elevated triglycerides n = 60	Elevated total cholesterol n = 40	Both cholesterol and TG elevated n = 12
PRIMI	13	24	24	28	8
MULTI	28	35	36	12	4

Out of the GTT positive patients, 13(31.7 %) patients were primigravida and 28(68.29) patients were multigravida. Majority of patients with elevated triglycerides were in the multiparous group whereas elevated cholesterol was mostly seen in primiparous group.

26 were belonging to normal socioeconomic status and 15 were belonging to low socioeconomic status.

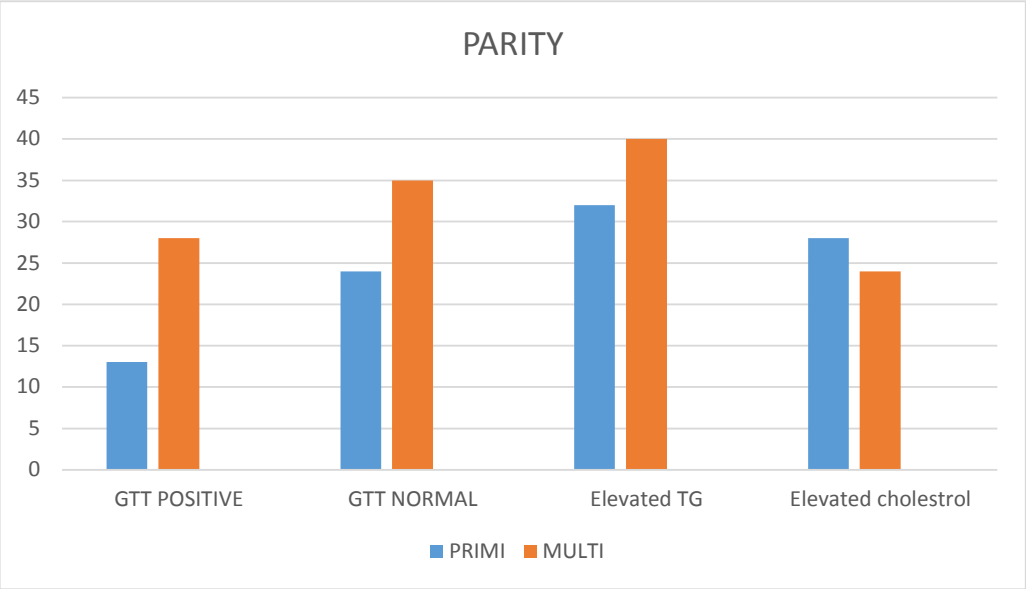

Fig 2: Majority was following the mixed diet. The family history of GDM was found in 4 out of 41 cases.

Classification Based on GTT Values and Lipid Levels

The patients were divided into four groups according to GTT values and lipid levels.

Table 4: Correlation between GTT and Serum TG

GTT POSITIVE ELEVATED TG >150mg/dl	GTT POSITIVE NORMAL TG < 150mg/dl	GTT NORMAL ELEVATED TG >150mg/dl	GTT NORMAL NORMAL TG <150 mg/dl
31	10	41	18
p value : 0.503 ns		p value < 0.005 s	

Elevated triglycerides were found in 31(75%) of GTT positive patients.41 (69%) patients among the normal GTT group also had elevated triglycerides. Hence our study could not correlate with elevated triglycerides and diabetic status.

Table 5: Correlation between GTT and Serum cholesterol

GTT POSITIVE ELEVATED CHOLESTROL >200mg/dl	GTT POSITIVE NORMAL CHOLESTROL <200 mg/dl	GTT NORMAL ELEVATED CHOLESTROL >200mg/dl	GTT NORMAL NORMAL CHOLESTROL <200mg/dl
21	20	31	28
p value :0.896 ns		p value <0.005 s	

Elevated serum cholesterol levels were seen in 21(51.21%) of GDM mothers whereas 31(52%) among the normal GTT group had elevated cholesterol. Therefore cholesterol does not seem to have a strong association with GDM.

Table 6: Mode of treatment of GDM

MODE OF TREATMENT OF GDM	NUMBER OF

	PATIENTS
DIET	10
OHA	12
INSULIN	18
INSULIN + OHA+diet	1

Out of 41 cases detected to be Gestational Diabetes Mellitus, 10 patients were on diet alone, 12 patients were on oral hypoglycemic agents, 18 patients were on insulin and 1 patient was on both oral hypoglycemic agents and insulin. Among these patients, 17 patients had an excessive weight gain of more than 11 kg.

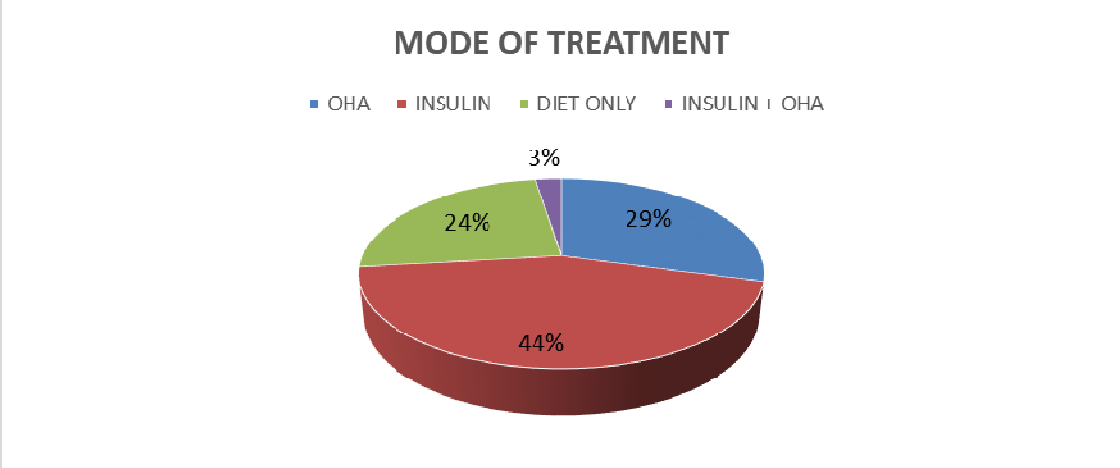

Fig 3:

Table 7: Correlation between mode of delivery and serum triglycerides

MODE OF DELIVERY	GTT POSITIVE ELEVATED TG >150mg/dl n = 31	GTT POSITIVE NORMAL TG <150mg/dl n = 10	GTT NORMAL ELEVATED TG >150mg/dl n = 41	GTT NORMAL NORMAL TG <150mg/dl n = 18
NVD	15	6	11	8
LSCS	16	4	30	10
p value: 0.644 ns			p value :0.182 ns	

Nineteen (46%) patients among the 41 GDM mothers underwent normal vaginal delivery whereas 22 (53%) patients had to undergo cesarean section due to various indications. 34 patients had term deliveries and 7 had term deliveries. Total of 46 patients with elevated triglycerides underwent LSCS.

Table 8: Correlation between mode of delivery and serum cholesterol

MODE OF DELIVERY	GTT POSITIVE ELEVATED CHOLESTEROL n	GTT POSITIVE NORMAL CHOLESTEROL	GTT NORMAL ELEVATED CHOLESTEROL	GTT NORMAL NORMAL CHOLESTEROL
NVD	12	7	20	20
LSCS	9	13	11	8
	p value : 0.155 ns		p value: 0.570 ns	

Majority of patients with elevated cholesterol levels delivered vaginally.

Table 9: Perinatal outcome

APGAR	GTT POSITIVE n = 41	NORMAL GTT N = 59
NORMAL ≥7/8	36	57
LOW < 7/8	5	2
NICU CARE	GTT POSITIVE n = 41	NORMAL GTT n = 59
YES	16	13
NIL	25	46

7 newborn babies had low APGAR scores at one minute and five minutes after delivery. NICU care was needed for 29 babies out of which 6 cases had hypoglycemia.

Table 10: Correlation between birth weight and serum triglyceride levels

BIRTH WEIGHT	GTT POSITIVE ELEVATED TG n = 31	GTT POSITIVE NORMAL TG n = 10	GTT NORMAL ELEVATED TG n = 41	GTT NORMAL NORMAL TG n = 18
≤ 3.5 KG	24	9	29	13
>3.5 KG	7	1	12	5
	p value :0.907 ns		p value : 0.383 ns	

Table 11: Correlation between birth weight and serum cholesterol levels

BIRTH WEIGHT	GTT POSITIVE ELEVATED CHOLESTROL n = 21	GTT POSITIVE NORMAL CHOLESTROL n = 20	GTT NORMAL ELEVATED CHOLESTROL n = 31	GTT NORMAL NORMAL CHOLESTROL n = 28
≤ 3.5 KG	16	17	24	18
>3.5 KG	5	3	7	10
	p value : 0.377 ns		p value: 0.266 ns	

Among 100 patients studied, 25(25%) babies had birth weight more than 3.5 kg. Among these patients, 12 (48%) had elevated triglycerides with normal GTT values and 7 (28%) patients had elevated triglycerides along with elevated GTT. This shows that triglycerides can be considered as an independent parameter contributing to increased birth weight but this requires further studies.

Elevated cholesterol with normal GTT was seen in 7(28%) patients only and elevated cholesterol together with elevated GTT was seen in 5 patients (20%). Hence the cholesterol levels were not found to be significantly contributing to the fetal birth weight.

Discussion

Various studies have been conducted in different parts of the world to correlate between maternal glucose levels and macrosomia as well as lipid alterations with fetal weight changes in normoglycemic as well as diabetic patients. Our study was also aimed at finding whether any relationship existed between the development of macrosomia in diabetic and nondiabetic patients and relationship with maternal fasting lipids, mainly serum triglycerides.

In a study conducted by E. Koukkou et al, women with GDM were found to be having higher serum triglyceride but lower LDL cholesterol concentrations compared to controls. Total cholesterol concentrations were lower in women with GDM[3].

Knopp et al studied 22 women with GDM and 38 controls in the third trimester of pregnancy. They found increased plasma triglycerides and VLDL, but no difference in plasma cholesterol concentrations.[41] Zeynep Ersanli et al also found elevated Triglycerides in GDM group[10]. More recently Montelogo et al did not find any differences in serum lipid, lipoprotein or apolipoprotein concentrations in pregnant women with or without GDM [37]. Our study also shows elevated triglycerides and cholesterol both in gestational diabetic patients as well as nondiabetic controls. Elevated triglycerides were found in 31(75%) of GTT positive patients.41 (69%) patients among the normal GTT group had elevated triglycerides (Table 4).

Table 12: Correlation between triglycerides in GDM mothers

Study	Mean value of TG in GDM patients	p VALUE
Zeynep Ersanli et al [10]	235.28	0.014
Kathy Whyte et al [44]	205.58	0.002
Present study	236.45	0.503
p value <0.005 significant		

Our study failed to detect any significant correlation between serum triglyceride and cholesterol levels in diabetic mothers. Both the parameters were found to be not related to the underlying diabetes status. Both were almost equally elevated in both the group. Many studies are not available for reference to understand physiological changes as well as variation in lipid profile in different pathological conditions of pregnancy at different gestational age as an independent factor.

In the Study conducted by Leila Sekhavat et al in Shaheed Sadoughi University of Medical Sciences and Health Services Iran, found that maternal serum fasting triglycerides at 24-28 weeks were significantly and positively associated with newborn weight at term. The association was independent of weight gain during pregnancy or mid-pregnancy plasma glucose

levels. They suggested that maternal serum triglyceride levels had a more important effect on fetal growth than plasma glucose in nondiabetic women. They also speculated that maternal hypertriglyceridemia in mid-pregnancy reflects increased insulin resistance and consequently is associated with newborn birth weight.

The study by Merzouk et al found that triglyceride levels at 24-28 weeks were significantly associated with adjusted newborn weight independent of maternal obesity [31]. Zeynep Ersanli et al have also suggested that even in well-controlled GDM patients basal TG levels are increased and TG elimination rate is slowed. Changes in Triglyceride metabolism may lead to an increase in the concentration of certain substances which stimulate insulin secretion and thereby promoting fetal macrosomia.

Regarding neonatal birth weight, twenty-five neonates had birth weight more than 3500 grams. Of these, seven were in elevated triglycerides with elevated GTT and twelve patients belonged to elevated triglyceride with normal GTT. We have considered birth weight more than 3500 grams as macrosomia, as the average birthweight of full-term Indian baby is considered to be 2.8 kg[43].

Even though GDM patients have glucose levels under control, they could be developing macrosomia due to the role played by elevated serum triglycerides. Serum cholesterol levels were not found to be significantly associated with birth weight. In a prospective study conducted by K. Whyte et al,- it was proven that in women selectively screened for GDM, increased fasting maternal triglycerides were associated with increased offspring birth weight independent of maternal age, BMI and GDM status.[44] These findings provide further evidence that maternal hypertriglyceridemia may be important in programming intrauterine fetal growth. In a Korean study of 104 women diagnosed with GDM, maternal hypertriglyceridemia at 24-32 weeks gestation was an independent parameter for identifying large for gestational age newborns[45]. Furthermore, the prospective Amsterdam born children and development cohort study reported that high maternal TG levels in early pregnancy were associated with higher birth weights[2]. But many of these studies were confined to white European women, hence these results may show variations with respect to our cases according to ethnic variation.

Table 13: Correlation between maternal triglyceride levels and birthweight>3500g

Study	p-value
Leila Sekhavat et al [42]	.000
K Whyte et al [43]	.004
Present study	.907
p value < 0.005 significant	

Our study did not find any positive correlation between elevated triglycerides and GDM as well as between elevated total serum cholesterol and GDM. Elevated birthweight more than 3500 g also was not significantly found to be associated with either elevated serum triglyceride levels or serum cholesterol levels. These discrepancies may be due to the fact that lipid alterations in pregnancy are also related to the diet patterns and pre-pregnancy BMI of the patients. Pre-pregnancy BMI was not calculated in the study population as many of the patients did not present to us in the pre-pregnancy period and were enrolled when they presented to us for antenatal checkups at varied gestational age. Dietary lipid intake will vary from patient to patient

and it might have affected our study, as dietary lipid intake is not assessed carefully in each patient.

Further research is definitely warranted in this aspect and to determine whether serum triglycerides or cholesterol actually contribute to the development of macrosomia.

Conclusion

Various studies have been conducted to correlate fetal macrosomia with maternal hyperglycemia and fasting hypertriglyceridemia. This study involved similar investigation in 100 patients presented for an antenatal checkup in our hospital. Our study did not find a statistically significant correlation with maternal hyperglycemia, fasting hyperlipidemia and macrosomia. This discrepancy could be the result of false negative tests of the null hypothesis due to the need for a larger population to be studied.

We found that elevated triglyceride levels were seen in diabetic patients to a greater extent than nondiabetics, but it was found to be elevated in both the groups.

Elevated serum total cholesterol was not found to be having an association with diabetic status.

Elevated triglyceride levels could be an independent parameter in determining fetal weight, but there needs to be further research for confirming the association. Elevated cholesterol levels were not seen to be significant in determining fetal weight, Mode of delivery and perinatal outcome were also not found to be significantly associated.

More research is needed in this area, to come to definite conclusions. Early detection of GDM and treatment would also have affected the parameters under study. Elevated birth weight, as well as adverse perinatal outcome, can occur due to the underlying hypertriglyceridemia. Control over the lipid levels as well as tight glycemic control in pregnancy can help to reduce macrosomia and other related complications

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