Original Research Article

Atherogenic lipid profile of umbilical cord blood of neonates of gestational diabetic mother

Abstract

Background: Gestational diabetes mellitus (GDM) is a metabolic disorder that occurs during pregnancy and affects both the mother and the fetus. GDM can lead to adverse perinatal outcomes such as macrosomia, shoulder dystocia, neonatal hypoglycemia, polycythemia, hyperbilirubinemia, and congenital malformations. Moreover, GDM increases the risk of long-term complications in the offspring, such as obesity, diabetes and cardiovascular diseases. Lipids are essential biomolecules that have various functions in the body, including energy storage, membrane structure and hormone synthesis. The concentration of lipids in the blood can be altered by maternal hyperglycemia and insulin resistance. The use of insulin or oral antidiabetic drugs can improve glycemic control and reduce the incidence of GDM-related complications, but the neonatal mortality rate remains higher than that of normal pregnancies. The aim of this study was to investigate the impact of maternal diabetes on the lipid profile of umbilical cord blood.

Methods:We performed a prospective case-control study on 60 neonates delivered in our hospital. The cases were 30 infants born to mothers with GDM, and the controls were 30 infants born to mothers without GDM. We selected the participants randomly from the labor room.

Results: We observed significant differences between the cases and the controls regarding lipid profile and birth weight. The cases had higher levels of total cholesterol, triglycerides, and LDL-cholesterol in their cord blood than the controls.

Conclusion: Our study demonstrates that maternal diabetes influences the lipid profile of

cord blood in neonates. We also find a significant correlation between lipid profile and birth weight in infants of GDM mothers.

Keywords:GestationalDiabeticmothers,neonates ,CordSerumLipid

Introduction:

Gestational diabetes mellitus (GDM) is a condition of impaired glucose metabolism that occurs during pregnancy. GDM can affect the health and development of the fetus, as well as the long-term health of the mother. One of the main complications of GDM is fetal macrosomia, which is defined as a birth weight above the 90th percentile for gestational age. Macrosomia can result from increased fetal insulin production in response to maternal hyperglycemia, which stimulates fetal growth and adiposity (1). Fetal insulin also influences the growth hormone/insulin-like growth factor-1 axis, which regulates fetal growth and development and has implications for cardiovascular health later in life (2). Moreover, GDM can alter the lipid profile of the mother and the fetus, leading to increased levels of lipoproteins that are associated with atherosclerosis and diabetes in adulthood (3).

Atherosclerosis is a chronic inflammatory disease of the arteries that causes plaque formation and narrowing of the vessels. Atherosclerosis can manifest clinically as coronary heart disease, stroke, peripheral arterial disease, or renal artery stenosis. Atherosclerosis has its origins in early life, as evidenced by the presence of fatty streaks and fibrous plaques in the arteries of children and adolescents (4). The development and progression of atherosclerosis can be influenced by genetic and environmental factors, such as dyslipidemia, hypertension, obesity, smoking, and diabetes. Non-invasive methods, such as ultrasound, can be used to assess vascular changes related to atherosclerosis in peripheral arteries (6).

GDM is a risk factor for adverse maternal and neonatal outcomes, such as preterm delivery, cesarean section, congenital anomalies, preeclampsia, and neonatal hypoglycemia (7-9). The incidence of congenital anomalies in infants of diabetic mothers (IDM) ranges from 6% to 10%, depending on the type and severity of maternal diabetes (10). GDM also increases the risk of future cardiovascular disease and diabetes in both the mother and the offspring (11-14). Therefore, early diagnosis and management of GDM are essential to prevent or reduce these complications.

Lipid metabolism is a key process that affects both maternal and fetal health during pregnancy. In normal pregnancies, lipid metabolism undergoes significant changes to meet the increased energy demands of the mother and the fetus, as well as to support the development of the placenta and the fetal tissues. These changes include increased levels of circulating non-esterified fatty acids (NEFAs), triacylglycerols (TAGs), cholesterol, phospholipids and apolipoproteins (apos) (16).

However, in gestational diabetes mellitus (GDM), lipid metabolism is further disrupted by impaired glucose tolerance and insulin resistance, which can have adverse effects on both maternal and fetal outcomes. GDM is associated with higher levels of serum TAGs and apolipoprotein B (apoB), which are the main components of very low density lipoprotein (VLDL) particles (4, 5). VLDL particles are responsible for transporting lipids from the liver to the peripheral tissues, and their increased production in GDM may lead to excessive lipid accumulation in the fetus, resulting in macrosomia (large birth weight) (17).

The mechanisms underlying the altered lipid metabolism in GDM and macrosomia are not fully understood, but they may involve increased glucose and NEFA availability in the maternal circulation, which stimulate hepatic VLDL synthesis and secretion (18). Moreover, hyperinsulinaemia in GDM may enhance lipid and protein synthesis in the liver and other tissues, as well as increase placental transfer of NEFA to the fetus (19). These factors may

contribute to the elevated TAG and apoB levels observed in GDM mothers and macrosomicneonates, as well as the positive correlation between maternal glycosylated haemoglobin (HbA1c) and TAG levels in late pregnancy (14).

Macrosomic newborns are babies who are born with a higher than average birth weight. They may have some health problems related to their size, such as high cholesterol levels. Cholesterol is a type of fat that circulates in the blood. It comes in different forms, such as very-low-density lipoprotein (VLDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL). VLDL and LDL are considered "bad" cholesterol because they can clog the arteries and increase the risk of heart disease and stroke. HDL is considered "good" cholesterol because it helps remove excess cholesterol from the blood and protects the arteries.

Macrosomic newborns tend to have high levels of VLDL and LDL, which are mainly produced from VLDL by an enzyme called lipoprotein lipase (LPL). This enzyme is also involved in breaking down triglycerides, another type of fat that can be harmful in high amounts. Some studies have shown that macrosomic newborns have higher levels of LPL and another enzyme called hepatic TAG lipase (HTAGL), which may contribute to their high cholesterol levels. These babies may have inherited these traits from their mothers, especially if they have gestational diabetes or type I diabetes.

Macrosomic newborns also tend to have high levels of HDL, which are accompanied by high levels of two proteins called apoA-I and apoA-II. These proteins are important for the structure and function of HDL particles, which carry cholesterol and other fats from the tissues to the liver for disposal. High levels of HDL may reflect the increased need for cholesterol and phospholipids in macrosomic newborns, as these substances are essential for the growth and development of cells, hormones, and surfactants. Surfactants are substances that help the lungs expand and contract during breathing. Macrosomic newborns do not have

abnormal levels of an enzyme called lecithin cholesterol acyltransferase (LCAT), which is responsible for converting free cholesterol into a form that can be carried by HDL.

Cholesterol is a vital component of life, but too much of it can be harmful. Macrosomic newborns may face a higher risk of cardiovascular diseases later in life due to their high cholesterol levels. Therefore, it is important to monitor their cholesterol levels and provide them with appropriate dietary and lifestyle interventions to prevent or reduce the complications associated with high cholesterol.

Methods:

We conducted a prospective (case-control) study in our hospital to compare the lipid profile of umbilical cord blood between infants of gestational diabetes mellitus (GDM) mothers and normal mothers. We collected blood samples from 60 infants (30 GDM and 30 normal) who were born by normal vaginal delivery (NVD) or cesarean section (CS). We clamped or milked the umbilical cord before taking the samples and put them in serum tubes. We included only full-term infants (38 weeks or more) with birth weight between 2.5 and 3.5 kg, without any congenital anomalies, and whose mothers were aged 25 to 37 years and had no other systemic diseases besides GDM. We measured the serum levels of total cholesterol (TC), triglyceride (TG), high-density lipoprotein-cholesterol (HDLC), low-density lipoprotein cholesterol (LDL-C), and very low-density lipoprotein cholesterol (VLDL-C).

We obtained 5 ml of umbilical venous blood from the placental end of the umbilical cord under sterile conditions after the delivery of the placenta and the clamping of the cord. We let the blood stand for a few minutes, then separated the serum from the clot by centrifuging at 3000 rpm for 30 minutes and analyzed it immediately. We used a computerized automated biochemical analyzer and an enzymatic method to measure the serum levels of TC, TG, HDL-C, LDL-C, and VLDL-C with high accuracy.

We used mean values and standard error of mean to describe the data in each group. We compared these values between 30 normal term newborns of GDM mothers and 30 newborns of normal healthy mothers.

Results

Table1	Comparisonbetweentheinfantsof Gestational diabeticandnormalmothers		
Variable	Mean±SD	Mean±SD	*P*-value
Mothers'age	26.86±4.03	30.86±4.24	0.088
Gestationalage	38.93±0.827	37.96±1.017	0.764
Neonatalweight(g)	2454.0.0±191.63	4012.6±481.28	<0.001
Random blood sugar (RBS) ofmother	100.66±15.21	188.23±22.31	<0.001
RBSofinfant	72.50±14.81	47.23±8.05	<0.001

Table2. Lipidprofileinthetwogroups

	Neonates ofnormalmothers	Neonates ofGestational diabeticmothers	
Variable	Mean±SD	Mean±SD	*P*-value
Serumcholesterol(mg/dl)	70.10±22.56	136.23±26.15	<0.001
Serumtriglyceride(mg/dl)	35.4±18.92	72.0±45.02	<0.001
High-density lipoprotein(mg/dl)	39.1 ±11.44	40.50±17.19	0.892
Low-densitylipoprotein (mg/dl)	24.8±3.921	81.5±36.15	<0.001

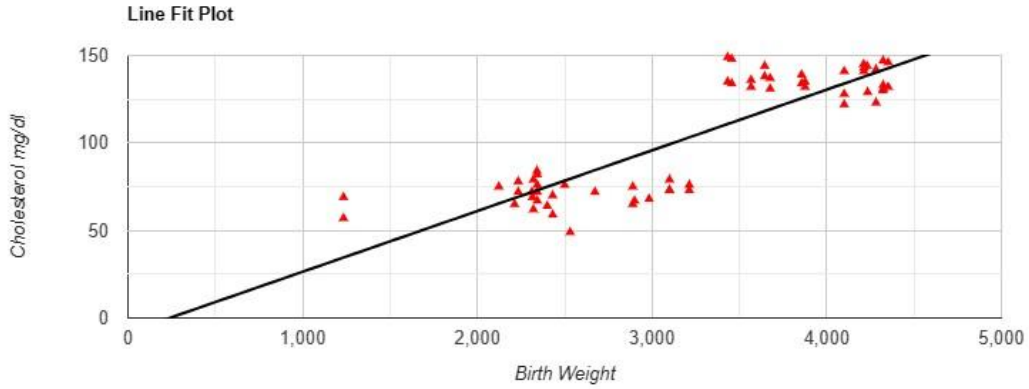

Figure 1. Correlation between serum cholesterol and neonatalweightinboth groups (Newborns of Healthy mother and newborns of gestational diabetic mother)(r=0.8647,P<0.001)

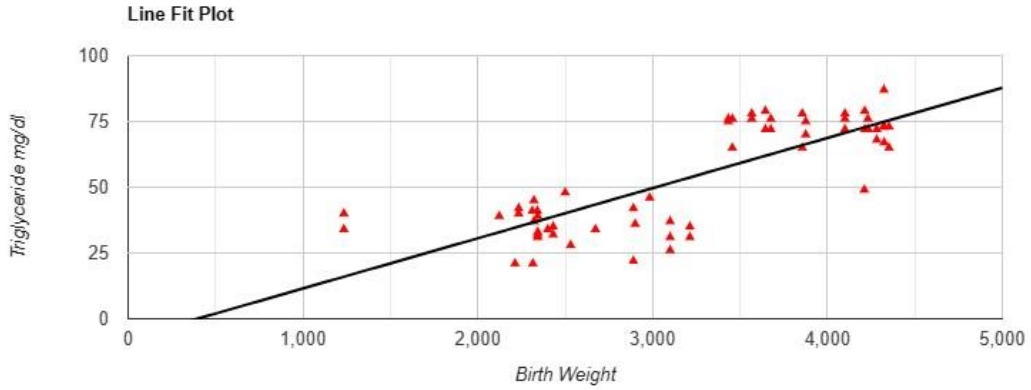

Figure 2. Correlation between triglyceride level and neonatalweightinboth groups(Newborns of Healthy mother and newborns of gestational diabetic mother) (r=0.8039,P<0.001)

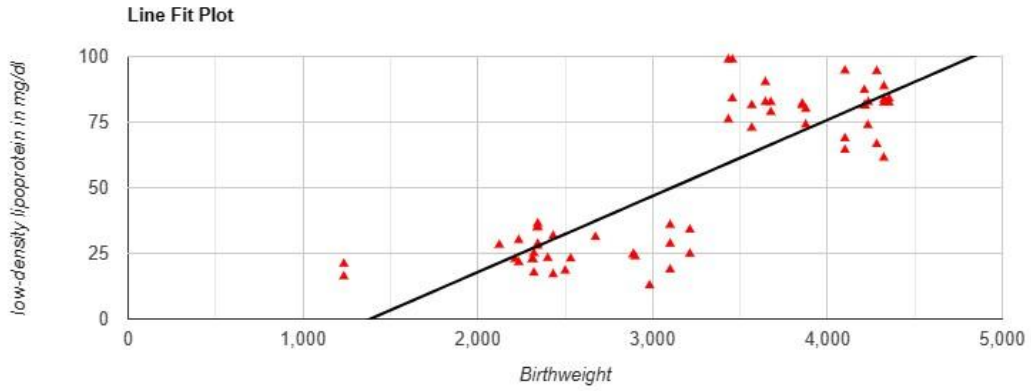

Figure 3. Correlation between low-density lipoprotein levelandneonatalweightinbothgroups(Newborns of Healthy mother and newborns of

gestational diabetic mother)(r=0.8431, P<0.001)

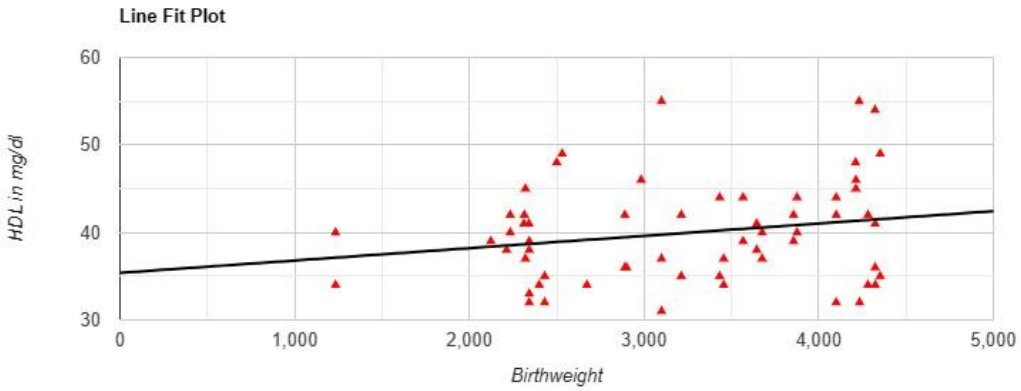

Figure4. Correlationbetweenhigh-densitylipoproteinlevelandneonatalweightinbothgroups (Newborns of Healthy mother and newborns of gestational diabetic mother)(r=-02085, P=0.1099)

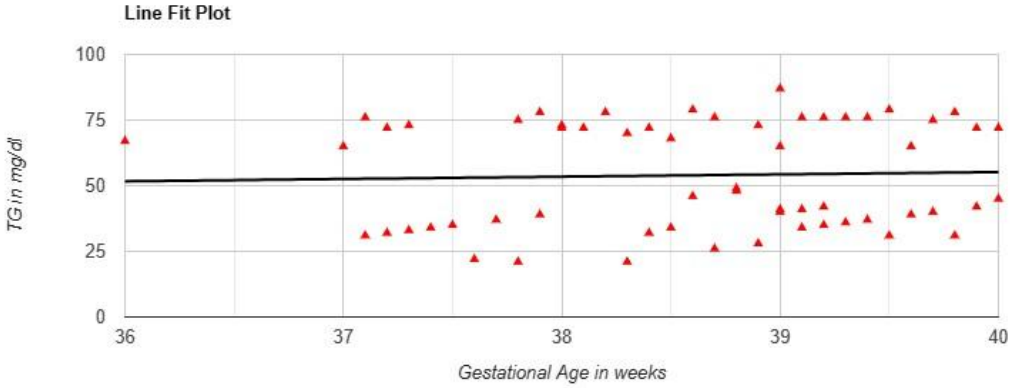

Figure5. Correlationbetweengestationalageandtriglyceride(r=-0.0432, P=0.7597)

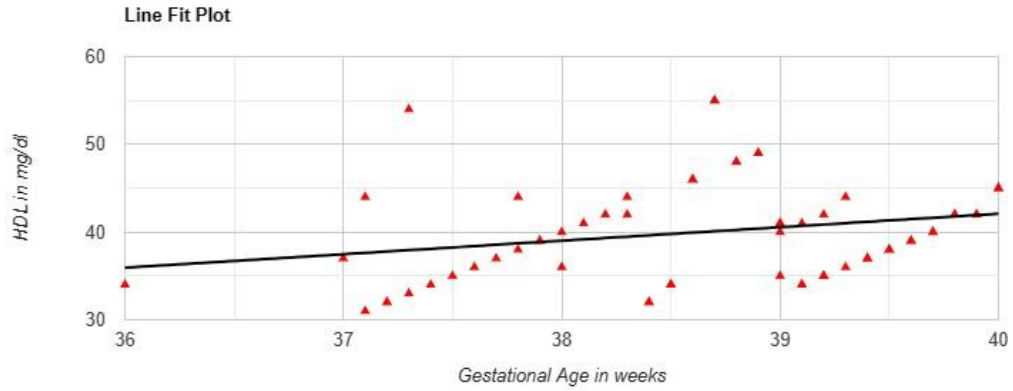

Figure6. Correlationbetweengestationalageandhigh-densitylipoproteininbothgroups(r=0.2476,P=0.357)

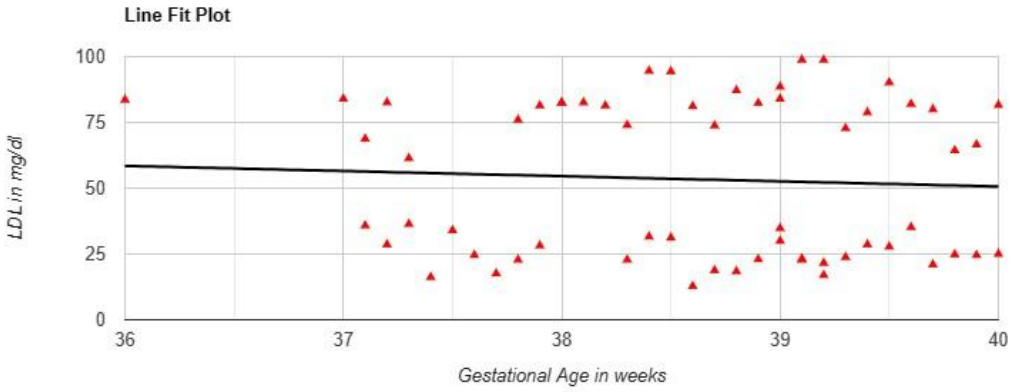

Figure7. Correlation betweengestationalageandlow-densitylipoproteininboth groups (r=-0.619,P=0.6384

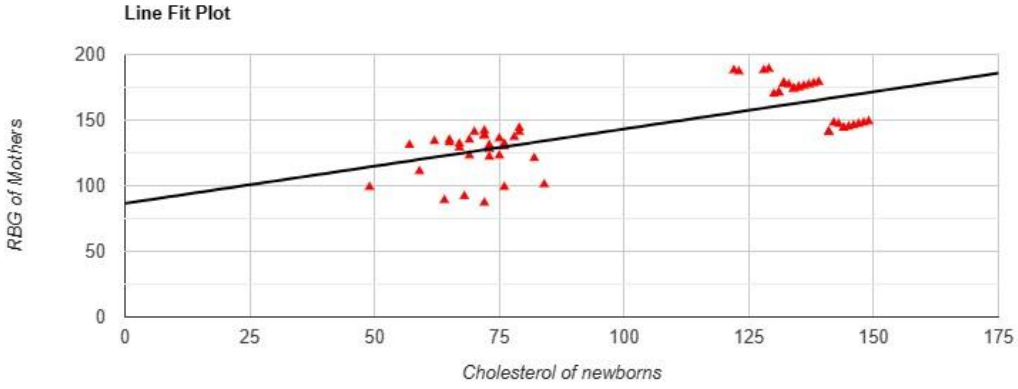

Figure8. Correlationbetweencholesterollevel newbornsandrandombloodsugarofmothers inbothgroups (r=0.722,P=<0.001)Results of the pearson correlation indicated that there is a significant large positive relationship between Cholesterol of newborns and RBG of Mothers, ($r(58) = .722$, $p < .001$)

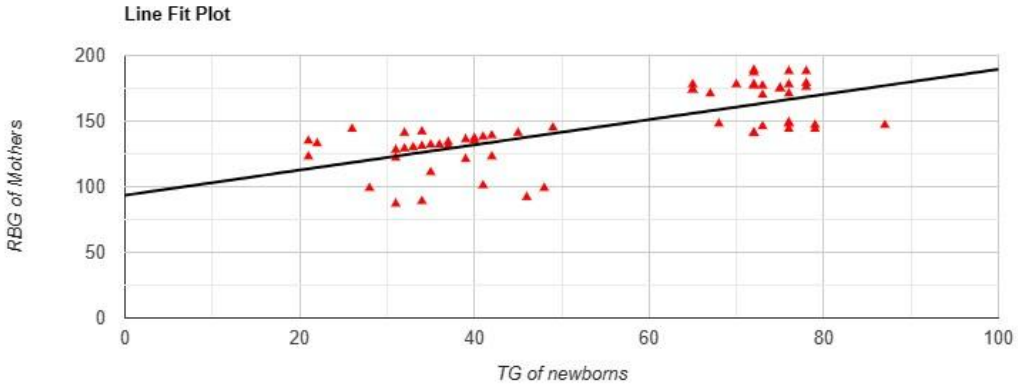

Figure 9. Correlation between triglyceride and random bloodsugarofmothersinbothgroups(r=-0.201,P=0.286).Results of the pearson correlation indicated that there is a significant large positive relationship between TG of newborns and RBG of Mothers, ($r(58) = .723$, $p < .001$).

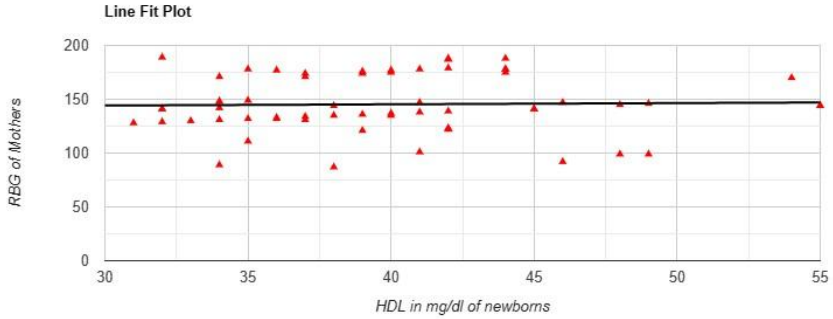

Figure 10. Correlation between high-density lipoprotein andrandombloodsugarofmothersinbothgroups(r=-0.24,P=0.854)

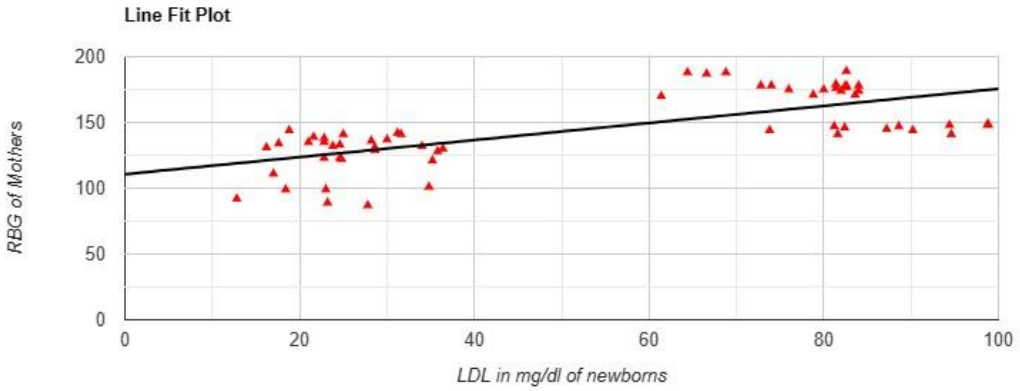

Figure 11. Correlation between low-density lipoprotein andrandombloodsugarofmothersinbothgroups(r=0.709,P< 0.001)

Results of the pearson correlation indicated that there is a significant large positive relationship between LDL in mg/dl of newborns and RBG of Mothers in both groups ($r(58) = .709$, $p < .001$).

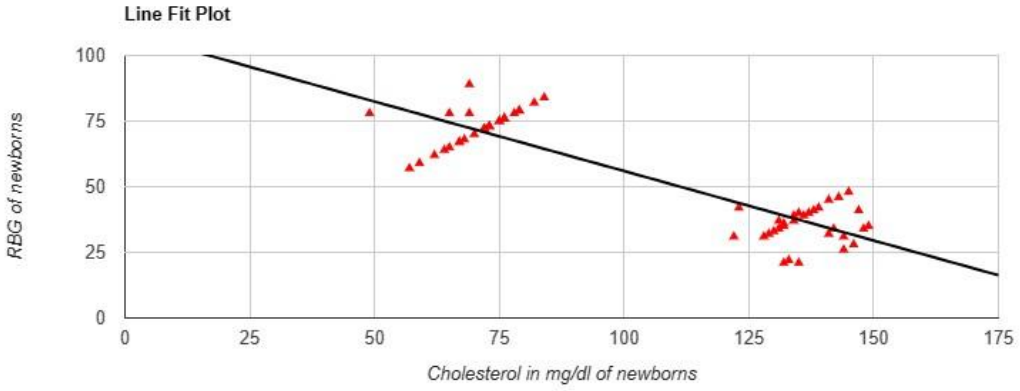

Figure 12. Correlation between cholesterol and random bloodsugarofneonatesinboth groups(r=-0.888,P<0.001)

Results of the pearson correlation indicated that there is a significant large negative relationship between Cholesterol in mg/dl of newborns and RBG of newborns, ($r(58) =$

.888, $p < .001$).

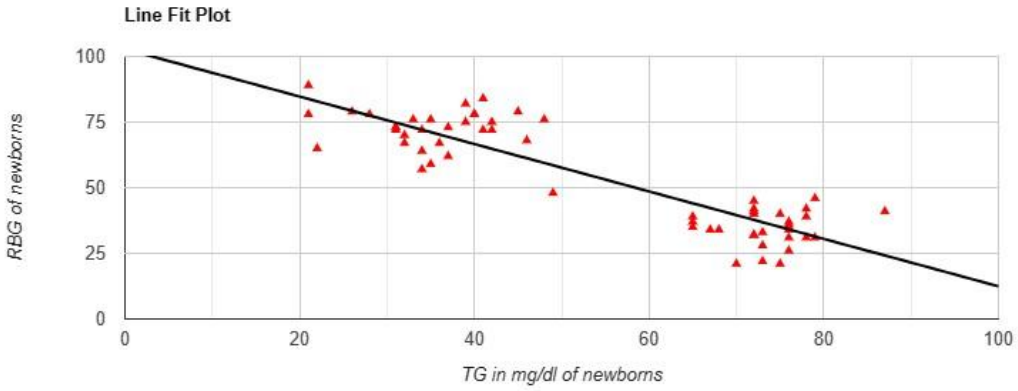

Figure 13. Correlation between triglyceride and random bloodsugarofneonatesinboth groups(r=-0.132,P=0.488)Results of the pearson correlation indicated that there is a significant large negative relationship between TG in mg/dl of newborns and RBG of newborns, ($r(58) = .896$, $p < .001$).

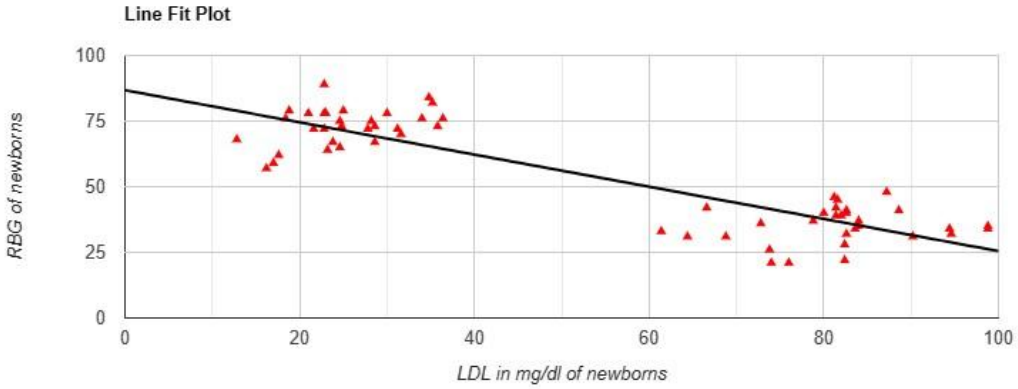

Figure 14. Correlation between low-density lipoprotein andrandombloodsugarofneonatesinbothgroups(r=-0.881,P< .001)

Results of the pearson correlation indicated that there is a significant large negative relationship between LDL in mg/dl of newborns and RBG of newborns, ($r(58) = .881$, $p < .001$).

Discussion

Serum lipid profile in childhood is considered as a predictive factor for serum lipid level later in life. This means that not only diet but also other risk factors affect serum lipid level from birth (22).

This study showed no significant differences between the two groups of infants regarding gestational age (P=0.764) (Table 2). However, as reported by other studies, GDM are at a

higher of preterm birth (low gestational age) (3). The limited number of cases in our study may be the underlying cause of this discrepancy. Moreover, Table 2 demonstrated no significant differences between the two groups regarding mothers' age (P=0.088).

The results of this study reflect a significant difference between the neonates of GDM and of healthy mothers regarding birth weight (P<0001) (the mean birth weight of the IDM was 4012.6 g, while the mean birth weight of the infants of healthy mothers was 2454.0g) (Table 1).

Other studies have reported a decline in the incidence of macrosomia in IDM from 60% to about 20%-35%, which might be secondary to aggressive diagnosis and treatment of GDM (1). In addition, a study carried out in Japan showed that the incidence of preterm labour and low- birth-weight are associated with GDM (23, 24). Whereas, several studies demonstrate that a small (<5%) number of fetuses, usually carried by mothers with advanced diabetic vascular disease, are at risk for fetal growth restriction (birth weight of less than fifth percentile for gestational age) (15, 16), this inconsistencymight be explained by different ways of diabetes management in many studies.

The results of this study showed a significant difference in the mean RBS of diabetic and healthy mothers. The mean RBS of diabetic mothers was 188.2 mg/dl, while the mean RBS of healthy mothers was 100.6 mg/dl (P<0.001) (Table 2). Table 2 also showed a significant difference in the RBS of the infants of diabetic mothers (IDM) and infants of healthy mothers. This finding highlights the importance of HbA1c test for diabetes diagnosis. The IDM had a mean RBS of 47.2 mg/dl, while the infants of healthy mothers had a mean RBS of 72.5 mg/dl (P<0.001). These results are not in agreement with the studies by Rollins et al. and Rooney (25, 26).

Table 2 showed a significant difference in the serum cholesterol levels of IDM and infants of healthy mothers. The IDM had a mean serum cholesterol level of 136.2 mg/dl, while the

infants of healthy mothers had a mean serum cholesterol level of 73.7 mg/dl (P<0.001). Table 2 also showed that the levels of TG and LDL were significantly higher in the IDM with means of 72.0 mg/dl and 81.5 mg/dl, respectively, while the means in healthy mothers were 31.4 mg/dl and 12.8 mg/dl, respectively (P<0.001). These results may be due to decreased LPL activity in adipose and liver tissues (27).

There was no significant difference in the HDL levels between the two groups (P=0.892). These findings are partly consistent with previous studies that reported lower levels of total serum cholesterol, TG, LDL and HDL.

The figures (1 and 2) show the relationship between maternal lipid levels and neonatal weight in the two groups of healthy and diabetic mothers. The results indicate that there is a strong positive correlation between both serum cholesterol and triglyceride levels and neonatal weight in both groups, with a higher correlation coefficient for cholesterol (r=0.8647) than for triglyceride (r=0.8039). The correlation is statistically significant at P<0.001 level, suggesting that maternal lipid levels are an important factor influencing neonatal weight.

The figures show the correlations between different lipid parameters and neonatal outcomes in the two groups of mothers (healthy and gestational diabetic). Figure 3 shows a strong positive correlation between low-density lipoprotein (LDL) level and neonatal weight, indicating that higher LDL levels in mothers are associated with higher birth weight in newborns. This is in line with the studies by Kalra and Mathur, who explained these associations by the placental transport of nutrients and stress factors.

On the other hand, the correlation between neonatal weight and HDL level was weak and negative, but not significant (Figure 4). No significant correlations were found between GA and lipid parameters (TG, HGL and LDL) (P<0.911, =0.357 and =0.07, respectively), as shown in Figures 5-7 for both groups.

We examined the associations between maternal and neonatal blood glucose and lipid levels

using pearson correlation analysis. Figures 8 and 9 show that there were strong positive correlations between maternal and neonatal cholesterol ($r(58) = .722$, $p < .001$) and triglycerides ($r(58) = .723$, $p < .001$), respectively. This suggests that higher maternal blood glucose levels may lead to higher neonatal cholesterol and triglycerides levels. Figure 11 shows that there was also a strong positive correlation between maternal blood glucose and neonatal low-density lipoprotein (LDL) levels ($r(58) = .709$, $p < .001$), indicating that maternal hyperglycemia may increase the risk of neonatal dyslipidemia. On the other hand, Figures 12, 13 and 14 show that there were strong negative correlations between neonatal blood glucose and neonatal cholesterol ($r(58) = .888$, $p < .001$), triglycerides ($r(58) = .896$, $p < .001$) and LDL ($r(58) = .881$, $p < .001$), respectively. This implies that lower neonatal blood glucose levels may be associated with lower neonatal lipid levels.

Conclusion

This study demonstrated that IDM have higher levels of serum cholesterol, triglycerides and LDL than infants of healthy mothers, which may increase their risk of developing cardiovascular diseases later in life. These differences may be attributed to the impaired LPL activity and the placental transport of nutrients and stress factors in IDM. Moreover, this study showed that maternal blood glucose levels are positively correlated with neonatal cholesterol, triglycerides and LDL levels, indicating that maternal glycemic control is important for preventing neonatal dyslipidemia. Further studies are needed to explore the long-term effects of neonatal dyslipidemia and the possible interventions to prevent or treat it. Future research should assess the serum lipid profile of infants born to diabetic mothers to detect any elevation in their lipid levels. Moreover, infants with high lipid levels may require dietary interventions and regular monitoring of their lipid status.

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