Research Article

The Correlation Between Lipid Profiles and Macrosomia in Diabetic Pregnancies

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Abstract

Background: Maternal diabetes is an important risk factor for development of fetal macrosomia. Studies showed that elevated lipid profile levels in third trimester of the diabetic pregnant women may predict the macrosomia of the newborn babies.
Objective: To assess the relationship of elevated lipid profile levels in third trimester with the occurrence of macrosomia in diabetic pregnant women.
Study design: A case control study.
Setting: Carried out at AL- Yarmouk Teaching Hospital/ Department of Obstetrics and Gynecology for one year from March 2011 to March 2012.
Patients and Methods: A hundred pregnant women were enrolled in this study. Fifty women with diabetes mellitus (twenty six women with gestational diabetes mellitus, sixteen women had type 1diabetes mellitus, and eight women had type 2diabetes mellitus) and fifty healthy pregnant women taken as a control. Both groups were in the third trimester. The two groups were comparable for maternal age, gestational age, parity and body mass index. Blood samples were taken for measurement of serum lipid and sugar profile from both groups and correlated with the occurrence of macrosomia.
Results: There were a significant and direct correlation between macrosomia and total cholesterol, triglyceride, low density lipoprotein and very low density lipoprotein cholesterols in diabetic groups (Gestational diabetes , type 1& type 2 DM) in comparison to the control group (p=0.0275, 0.0001, 0.031, 0.0001). There was a significant inverse correlation between macrosomia and high density lipoprotein cholesterol in diabetic group in comparison to the control group (p=0.043).
Conclusion: Macrosomia in newborns of diabetic pregnant women is associated significantly with maternal dyslipidemia during the third trimester of pregnancy.

Keywords: Diabetic pregnancies, Lipid profiles, Macrosomia

INTRODUCTION

Diabetes mellitus (DM) is defined as a carbohydrate disturbance characterized by hyperglycemia and either peripheral insulin resistance or insulin deficiency[1]. Diabetes is one of the most common medical disorders of pregnancy, associated with a high perinatal morbidity and mortality[2]. Gestational diabetes (GDM) is a glucose intolerance first recognized in pregnancy[3]. Macrosomia is defined as a fetus weighing more than 4000 grams [1]. Commonly macrosomia is defined based on mathematical distributions of birth weight. Those infants exceeding the 90th percentile for a given gestational week are usually used as the threshold for macrosomia[4]. Gestational and type 2 DM is one of the risk factors for macrosomia which is most widely recognized[5]. Because there are no current methods to estimate excessive fetal size accurately, the diagnosis of macrosomia cannot be definitively made until delivery. Inaccuracy in clinical estimates of fetal weight by physical examination is often attributable, at least in part, to maternal obesity[4]. Positive correlations between maternal basal free fatty acids and triglycerides

and birth weight have been reported in diabetic pregnancies, suggesting that lipid flux across the fetoplacental unit may contribute to macrosomia[6]. Studies showed that high maternal TG levels in well controlled diabetic pregnancy are associated significantly with macrosomia independently of maternal body mass index (BMI) [7]. The aim of this study was to assess the relationship between 3rd trimester maternal dyslipidemia and delivery of macrosomic baby.

PATIENTS AND METHODS

A case –control study was conducted at AL – Yarmouk Teaching Hospital and the National Institute Of Diabetic Center during the period of one year from march 2011 to the march 2012. The study was approved by the local Medical Research Ethics Committee of College of Medicine, Almustansiryia University, Department of Obstetrics & Gynecology. Informed consent was obtained from all participants before enrolling in the study. A total of hundred women were included in the study and were divided into two groups: Diabetic group: fifty pregnant women with diabetes mellitus. Control group . fifty pregnant women without diabetes mellitus were taken as control. The women were selected while attending the antenatal clinic for assessment or from the inpatient ward . The control group was selected as a healthy pregnant women with normal sugar profile, admitted to the obstetrics ward for caesarean section, in order to know the outcome of the baby weight, with gestational age, maternal age, parity and BMI that were comparable with the case group.

Inclusion criteria: Singleton pregnancy , viable fetus, third trimester 36 to 40 weeks, study group: include pregnancy with all types of diabetes mellitus which include types 1, 2 and GDM.

Exclusion criteria: Women with uncontrolled DM, multiple pregnancies, abnormal fetus, Patients with acute illness or infection at time of study, associated medical diseases which are associated with disordered glucose metabolism, such as Cushing's disease, acromegaly, chronic pancreatitis and pancreatectomy, chronic renal disease, patient who are taking drugs that could affect the lipid profile of the pregnant women e.g. glucocorticosteroid for fetal lung maturation and β-adrenergic agonist. Information's about the age of the patient, gestational age, parity, were taken from all participants. Physical examination was performed to all participants which included general & abdominal examination to assess the fetal lie, fetal presentation, engagement, symphesis fundal height and clinical stimation of the fetal weight .Body mass index was calculated to all patients by dividing the weight of the participant in kilograms over the square of the height in meters. Every patient had under gone the following investigations : plasma glucose, serum lipid profile, glycoslyted haemoglobin (HbA1c) and abdominal ultrasound examination was done to all patients to confirm the normality of pregnancy, to exclude multiple pregnancy and for estimation of fetal weight. Sample collection, processing and storage: The blood was collected after at least 12 hours fasting. A three millilitres of venous blood were collected in plain tube.

The blood samples were transferred to the laboratory and first allowed to clot and then centrifuged at 3000 rpm for 5minutes. All specimens were clearly labeled with names of cases and controls along with the date and the time of collection. The tests were done in biochemistry laboratory at AL- Yarmouk Teaching Hospital. After delivery of the patient, neonatal data were collected including birth weight. Macrosomic infant in our study was considered when the baby weight was more than 4000 grams. The cholesterol (TC) kit and the triglyceride (TG) kit measured by enzymatic colorimetric method. / Linear chemicals company, Spain. The HDL cholesterol (HDL-C) kit measured by enzymatic colorimetric method. HDL-C kit / Randox company, U.K.

The LDL cholesterol (LDL-C) kit measured by enzymatic colorimetric method. LDL-C kit/fortress diagnostics company, U.K. The VLDL cholesterol (VLDL-C) values are most often calculated as the amount of cholesterol not contained in HDL and VLDL.VLDL is estimated by TG/5 because the cholesterol concentration in VLDL particles is usually 1/5 of the total lipid (Friedewald formula).

Statistical Analysis: Data were analyzed using the computer facility with use of SPSS-18 (statistical package for social sciences version 18 "PASW") soft ware package. Data were presented in simple measures of number, frequency percentage, mean, range and standard deviation.

The significance of difference between two quantitative variable was measured using unpaired student's t-test or analysis of variance (ANOVA) for more than two groups. Significance of difference between percentages (for qualitative data) was measured using chi squared test. P value less than 0.05 was considered significant.

RESULTS

Table 1 shows no significant difference in the mean maternal age, parity & BMI between the two groups, P value were 0.065, 486, 0.970 respectively.

Table 1. The demographic characteristics of the diabetic & the control group included in the study , result are presented as mean ± SD.

	Diabetic		Controls		P value
	No.	50	No.	50	
Age (years) mean± SD (Range)	29.84±7.17 (16-41)		28.82±7.74 (16-45)		0.065
Parity Mean± SD(Range)	2.12±1.85 (0-8)		2.26±1.94 (0-8)		0.486
BMI (Kg/m2) Mean± SD (Range)	34.58±1.86 (29-37)		33.16±2.30 (25-35)		0.970
Significant using Pearson Chi-square test for difference between proportions or Student-t-test for two independent means at 0.05 level of significance.					

Table 2 shows no significant difference in the mean gestational age between the two groups p=0.059.No significant difference in the percentage of male & female birth between the two groups as the (p=0.774). Highly significant difference in the mean birth weight of the newborn between the two groups p=0.0001. 58% of the newborn of diabetic mothers had macrosomia in comparison to 8% of the control group, and the difference was highly significant p=0.0001. Table 3 shows highly significant difference in the mean level of total cholesterol (TC), triglycerides (TG) , high density lipoprotein (HDL), low density lipoprotein (LDL), very low density lipoprotein (VLDL) between the two groups p value were 0. 004, 0.0001, 0.002. 0.0001, 0.0001 respectively. No significant difference in the mean level of fasting blood glucose (FBG) , and postprandial blood glucose (PPBG) & the HbA_{1c} between the two groups p value were 0.6, 0.403, 0.420. respectively.

Table 2. The newborn parameters of diabetic& the control groups included in the study.

	Diabetic		Controls		P value
	No.	%	No.	%	
Gestational age (weeks) Mean ±SD (Range)	37.36±0.75 (36-40)		37.80±1.07 (36-40)		0.059
Sex					0.774
Male	19	38.0	21	40.8	
Female	31	62.0	29	59.2	
Macrosomia (BW>4Kg)					0.0001
Yes	29	58.0	4	8.0	
Not	21	42.0	46	92.0	
Birth weight (Kg)Mean ±SD (Range)	3.91±0.48 (2.6-4.5)		3.41±0.34 (3.0-4.2)		0.0001
Significant using Pearson Chi-square test for difference between proportions or Student-t-test for two independent means at 0.05 level of significance.					

Table 3: The level of lipid & glucose & HbA_{1c} in the diabetic & the control groups included in the study

	Diabetic	Controls	P value
	Mean±SD(Range)	Mean±SD(Range)	
TC (mmol/l)	5.96±0.90(4.2-7.1)	5.42±0.96(3.4-6.7)	0.004
TG (mmol/l)	2.77±0.70(1.0-3.6)	2.04±0.77(0.8-3.5)	0.0001
HDL (mmol/l)	1.22±0.28(0.8-1.7)	1.44±0.41(0.9-2.7)	0.002
LDL (mmol/l)	4.18±0.86(2.5-5.6)	3.57±0.78(2.2-4.8)	0.0001
VLDL(mmol/l)	0.55±0.14(0.2-0.7)	0.41±0.15(0.2-0.7)	0.0001
FBG (mmol/l)	5.94±0.67(4.9-6.9)	4.01±0.69(3.9-5.9)	0.6
PPBG (mmol/l)	6.29±0.817(5.9-7.1)	5.14±1.03(5-6.9)	0.403
HbA1c(%)	6±0.96(5-6)	5±0.77(4-6)	0.420
Significant using Student-t-test for two independent means at 0.05 level of significance.			

Table 4shows a direct correlation between the level of TC, TG, LDL& VLDL in diabetic pregnant women and macrosomia in comparison to that of the control group and the relation was significant p value were 0.0275, 0.0001, 0.031, 0.0001 respectively. There was an inverse correlation between the level of HDL in diabetic pregnant women and macrosomia in comparison to that of the control group and the difference was significant p value 0.023.

Table 4: The correlation between serum lipid profile levels & macrosomia in both study groups

Serum Lipid	DM+ Macrosomia	Control+ Macrosomia	P value
	Mean± SD	Mean± SD	
TC(mmol/l)	6.06±0.98	5.50±0.46	0.0275
TG(mmol/l)	3.23±0.28	2.00±0.92	0.0001
HDL-C(mmol/l)	1.20±0.26	1.40±0.58	0.023
LDL-C (mmol/l)	4.21±0.98	3.70±0.07	0.0312
VLDL-C (mmol/l)	0.65±0.06	0.40±0.18	0.0001
Significant using Student-t-test for two independent means at 0.05 level of significance.			

DISCUSSION

DM is considered one of the factors that make pregnancy a high risk, as maternal, fetal or neonatal complications are increased in diabetic pregnancy. One of the recognized fetal complication is macrosomia and because macrosomia have many complications during pregnancy and labour so the diagnosis of big baby is considered very important [8] .

The current study showed that total cholesterol, triglyceride and LDL cholesterol in third trimester of diabetic pregnancy was higher in mother who delivered macrosomic babies in comparison with the control group since the p values were (0.023, 0.0001, 0.031) respectively. A study done by Koukkou et al 1996 had shown an increased level of the total TGs & a decreased level of the LDL cholesterol in women with diabetes. The study suggested that the lipid profile in diabetes is related to the level of insulin resistance, and the insulin sensitivity index is correlated negatively to TG[9].

Increased maternal insulin resistance in diabetes may increase nutrient availability to the fetus, accounting for an increased risk of fetal overgrowth and adiposity[10].While Sobki et al 2010 reported lower levels of TG in diabetic pregnancies when compared to the control pregnancies [11].

Kristof G et al 2008 found that maternal hypertriglyceridemia in diabetic pregnancy is a characteristic feature, and although maternal circulating TGs do not directly cross the placenta, the presence of lipoprotein receptors, fatty acid-binding proteins, and different lipase activities, in the placenta allows the efficient transfer of maternal fatty acids to the fetus [12] . It had been shown that the concentration of TGs in the third trimester is a stronger predictor of birth weight than glucose parameters [13].Kjos et al 2008 reported elevated TG level in GDM women who delivered macrosomic babies[14].

Schaefer et al 2010 agreed with the current study results which found that maternal serum TG levels significantly correlated with abnormal excessive fetal growth in women with diabetes mellitus[15].Current study showed that the level of HDL cholesterol was lower in DM mother who had macrosomic babies in comparison to the control group and the correlation was significantly inverse since the (p=0.023), while, the level of VLDL was higher in DM mother who had macrosomic babies in comparison to the control group and the correlation was positive and highly significant p=0.0001.Watts et al 1996 found that elevated level of TGs and low level of HDL cholesterol at third trimester in diabetic women were significant predictors for macrosomia independent of chronic glycemic control[16], Langer et al 2005 study showed that glucose values were not related to the fetal growth, and good glucose control did not necessarily prevent accelerated growth especially in obese women [17], while Clausen et al 2005 study disagreed with this finding, they found that it is hyperglycemia, not dyslipidemia, that is particularly harmful to embryogenesis and it is glucose, not fat, that is the fetal fuel substrate responsible for fetal hyper insulinaemia and accelerated fetal growth[18].

Knopp et al 2006 reported that neonatal birth weight is positively correlated with concentrations of TGs, which is readily cross the placenta in late pregnancy[19]. Infants of diabetic mothers also showed lipoprotein changes. Some of the lipid abnormalities observed in macrosomic newborns are parallel with those found in their diabetic mothers[20].

So in conclusions the degree of maternal dyslipidemia is more severe in diabetic pregnant women, in comparison to non diabetic pregnant women and is significantly more severe in diabetic pregnant women delivering macrosomic newborns in comparison with those delivering normal baby .

REFERENCES

1. Clare L.T. Diabetes mellitus. David M.L., Philip N.B., Linda C., James O.D., Lucy K., Mark D.L., eds. In: Obstetrics and Gynecology. An evidence- based textbook for MRCOG. ***Arnold Publishing*** 2010 ;7:43-6.
2. Growther G.F., Hiller E.J., Moss R.J., McPhee A.J., Jeffries W.S., RobinsonJ.S., eds. Medical disorder in pregnancy. Justin C.K. In: A comprehensive Guide for MRCOG. ***Hodder Arnold Publishing 2ndedition*** 2009 ;4:64-6.
3. Anne Dornhorst& Catherine Williamson. Diabetes and endocrine disease in pregnancy. D.Keith Edmonds. In: Dewhurst's textbook of Obstetrics &Gynecology. ***Blackwell Publishing. 7th edition*** 2007 ; 27:246-53.
4. Adashech J.A., Akinci B., Albert T.J. eds. Diabetes. Cunningham F.G. ,Bloom S.L., Leveno K.J., Hauth J.C., Rouse D.J., Spong C.Y., et al. In: Williams textbook of Obstetrics.23rdedition. ***MC graw hill Medical Publishing division*** 2010 ; 4:1104-25.
5. Tore H. The macrosomic fetus a challenge in current Obstetrics. ***ACTA*** 2008;87(2):134-45.
6. Lesser K.B., Carpenter M.W. Metabolic changes associated with normal pregnancy and pregnancy complicated by diabetes mellitus. ***Seminin***2000;8:122-5.
7. Ortega H., Schaefer U.M., Meitzner K., et al. Difference in the implication of maternal lipids on fetal metabolism and growth between gestational diabetes mellitus and control pregnancy. ***Diab Med*** 2009;28(9): 1053-59.
8. Talaro K.P. Immunization and immune Assays. Foundations in microbiology basic principles. 5th edition. New York, ***McGraw Hill*** 2005: 490-91.

9. Koukkou E., Watts G.F., Lowey C. Serum lipid, lipoprotein and apolipoprotein changes in gestational diabetes mellitus. A cross sectional prospective study. ***J Clinical Pathology*** 1996;49:634-7.
10. Bartha J.L., Comino R., Martinez P., et al. Insulin sensitivity index and carbohydrate and lipid metabolism in gestational diabetes. ***J Reproductive Med*** 2000;45:185-9.
11. Sobki S.H., Al-Senaidy A.M., Al-Shammari T.A., et al. Impact of gestational diabetes on lipid profiling and indices of oxidative stress in maternal and cord plasma. ***Saudi Med J*** 2010;25(7):876-80.
12. Kristof M.D., Dicianni G., MicooliR., Volpe L., et al. Maternal TG levels and newborn weight in pregnant women with normal glucose tolerance. ***Diabetes Med*** 2008;22:21-5.
13. Herrera E. & Lasuncion M. Maternal lipid metabolism and placental lipid transfer. Hom Res 2006;65:59-64.
14. Kjos S.L., Buchanan T.A., Montoro M., et al. Serum lipids within 36 months of delivery in women with recent gestational diabetes. ***Diabetes*** 2008 ; 40 (2):142-6.
15. Schaefer U.M., Evelyne R., Catherine A., et al. The effect of first trimester diabetes control on the incidence of macrosomia. ***Am J of Obstet & Gyn*** 2010;181(1):202-6.
16. Watts G.F., Jiang Z.Y.& Hunt J.V. Protein glycation and oxidative stress in diabetes mellitus and ageing. ***Free Radical Biology and Medicine*** 1996;10:339-52.
17. Langer O., YogeoY.,Xenakis E.,Brustman L. Overweight and obese in gestational diabetes: the impact on pregnancy outcome. ***Am J Obstet Gyn*** 2005;194:1768-76.
18. Clausen T.D., Mathiesen E., Ekbom P., et al. Poor pregnancy outcome in women with type 2 diabetes. ***Diabetes care*** 2005;28:323-8.
19. Knopp R.H., Chapman M., Bergelin R.O., et al. Relationship of lipoprotein lipids to mild fasting hyperglycemia and diabetes in pregnancy. ***Diabetes care*** 2006; 31:1092-7.
20. Merzouk H., Madani S., Korso N., et al. Maternal and fetal serum lipoprotein concentrations and compositions in type 1 diabetic pregnancy: relationship with maternal glycemic control***. J Lab Clinical Med*** 2000;136: 441-8.