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Research Article

Lipid Profile in Pregnant Women With and Without Gestational Diabetes Mellitus: A Case-Control Study

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Abstract

Background: Gestational diabetes mellitus (GDM), the most common metabolic disorder of pregnancy, is associated with alterations in circulating lipids.

Objectives: The aim of this study was to compare lipid profiles in women with and without GDM.

Methods: This study was performed on 84 pregnant women at 26-30 weeks of gestation (42 pregnant women with GDM as cases and 42 healthy pregnant women as controls). After obtaining informed consent and gathering demographic data, subjects underwent a 75-g oral glucose tolerance test and lipid profile was also measured in all subjects.

Results: We found that high-density lipoprotein (HDL) levels were significantly higher in the GDM group (53.10 ± 1.72 vs 46.64 ± 1.70 mg/dL, $P = 0.008$). Total cholesterol (228.96 ± 52.03 vs 211.59 ± 41.83 mg/dL) and triglyceride (TG) levels (225.58 ± 89.84 vs 208.38 ± 80.66 mg/dL) were also higher in the GDM group; however, the differences were not statistically significant ($P = 0.770$ and $P = 0.327$, respectively). On the contrary, low-density lipoprotein was found to be non-significantly higher in the healthy group (144.54 ± 26.01 vs 122.41 ± 4.82 mg/dL, $P = 0.709$). Besides, there was a significant association between HDL levels and GDM (OR: 1.049; 95% CI: 1.009-1.090, $P = 0.015$). This association remained significant when adjusted for age, body mass index (BMI), and gestational age (OR: 1.010; 95% CI: 1.002-1.017, $P = 0.009$). No significant association was found between GDM and TG, cholesterol, and LDL levels.

Conclusion: HDL levels are significantly higher in pregnant women with GDM compared to pregnant women without GDM. HDL level is significantly associated with GDM even after adjustment for age, BMI, and gestational age.

Keywords: Dyslipidemia, Gestational diabetes mellitus, Lipid profile, Pregnancy

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Background

First occurrence of glucose intolerance during pregnancy is defined as gestational diabetes mellitus (GDM) (1). It is the most common metabolic disorder during pregnancy which can be diagnosed via an oral glucose tolerance test at 24-28 weeks of gestation (2). Approximately 1% to 20% of pregnancies are affected by GDM worldwide and its incidence continues to increase (3,4). Obesity, ethnicity, and older maternal age are risk factors for GDM, among which obesity is the strongest (5). GDM is associated with unfavorable maternal and neonatal outcomes (6-13).

Some physiologic alterations occur during pregnancy to meet the nutritional needs of the fetus, namely accumulation of adipose tissue, insulin resistance, increase in insulin secretion with unchanged, decreased, or increased sensitivity to insulin in early pregnancy, and accelerated lipolysis, shrinkage of adipose tissue, increased levels of free fatty acids, decreased ability of insulin to inhibit lipolysis in late pregnancy (14-16). It has been demonstrated that these alterations are at least in part due to changes in human placental lactogen, estrogen, progesterone, cortisol, chorionic gonadotrophin, serum adiponectin, and prolactin (17,18). All the aforementioned processes are exaggerated in GDM leading to a greater increase in free fatty acid levels, more severe insulin resistance and increased glucose production in the liver (1,14,19,20). Put differently, there may be an underlying metabolic dysfunction in some women before pregnancy that transiently manifests itself as GDM during pregnancy (21).

Several researchers have studied the different lipid patterns in healthy pregnant women in comparison

with pregnant women with GDM and there is almost a consensus that triglyceride (TG) levels are higher in GDM; however, the same agreement does not exist regarding other circulating lipids (22). In a meta-analysis of 60 studies to evaluate the relationship between lipid measures throughout pregnancy and GDM, TG levels were significantly elevated in women with GDM compared to those without GDM and this finding was consistent across all the three trimesters of pregnancy. On the other hand, high-density lipoprotein (HDL) levels were significantly lower in women with GDM in the second and third trimesters of pregnancy. However, there was no difference between women with and without GDM regarding total cholesterol or low-density lipoprotein (LDL) levels (23).

Pregnancy dyslipidemia can worsen insulin resistance in GDM, and vice versa. Hypertriglyceridemia in pregnant women can adversely affect maternal outcomes; moreover, it can have a long-term effect on the development of metabolic syndrome in the offsprings (24). In addition, maternal hypercholesterolemia is associated with altered fetal development, susceptibility to atherosclerosis, obesity, and type 2 diabetes later in life (25-27).

Objectives

To the best of our knowledge, there have been fewer studies on the lipid profile of pregnant women with or without GDM in Iran compared to other parts of the world. Therefore, in this study, we aimed to compare the lipid profile of pregnant women with and without GDM in Iranian population.

Methods

Participants

This case-control study was conducted in the endocrinology clinic of Shahid Mohammadi hospital in Bandar Abbas, in 2015. Inclusion criteria were women of childbearing age with 26 to 30 weeks of gestation and single-fetus pregnancy. Exclusion criteria were a history of diabetes mellitus, dyslipidemia, and chronic diseases. According to suggested formula for sample size calculating in order to comparison of means between two independent groups, considering type I error of 5% ($\alpha = 0.05$) and type II error of 20% ($\beta = 0.20$, power = 80%), and based on the mean and standard deviation of LDL-C concentration in case and control groups reported in a same previous study (28), forty subjects for each group were calculated. Subjects were selected from those who had been diagnosed as having GDM by a gynecologist and were referred to the Diabetes Clinic of Hormozgan University of Medical science for further investigation, treatment, or intervention. No previous treatment or lifestyle alteration had been made prior to referral.

Study Design

After obtaining written informed consent from the subjects, in general, 84 pregnant women were evaluated; 42 cases previously diagnosed with GDM according to an impaired GTT (Glucose Tolerance Test) who attended the endocrinology clinic to receive treatment, and 42 healthy pregnant women (with normal GTT) in the control group. A 75-g GTT test and a lipid profile test were performed for cases (before initiation of insulin therapy) and controls.

In order to measure lipid profile, after at least 12 hours of fasting and 5 minutes of rest, an 8 mL venous blood sample was collected from the cases and controls using a Venoject syringe containing anticoagulant. The samples then underwent plasma centrifugation and cholesterol, TG, LDL, and HDL were measured using an enzymatic assay using commercial kits (Pars Azmun Inc, Iran). Reference ranges for cholesterol, LDL, HDL, and TG were based on NCEP-ATP III (National Cholesterol Education Program-Adult Treatment Panel III) (29).

In order to perform the GTT test, a fasting sample was first taken from the subjects. Then they received a solution of 75 mg glucose in 300 mL water and two more 2-mL blood samples were subsequently collected at 1 hour and 2 hours after taking the solution. Plasma glucose levels were determined in all the three samples after plasma centrifugation using gluco-oxidase method using a commercial kit (Pars Azmun Inc, Iran). According to the American Diabetes Association (ADA) statement, pregnant women meeting at least one of the following criteria are considered to have GDM: 1) fasting plasma glucose (FPG) ≥92 mg/dL; 2) one-hour plasma glucose (1h-PG) ≥180 mg/dL; and 3) two-hour plasma glucose (2h-PG) ≥153 mg/dL (30).

A urine sample was also collected from the participants to determine proteinuria by a dipstick. The results of urine dipstick for proteinuria were negative, trace, or positive.

In addition, demographic data was gathered from all the subjects using a check-list consisting of age, gravidity, parity, live births, gestational age, family history of dyslipidemia, pre-pregnancy body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), weight gain during the first and second trimesters, history of high blood pressure in previous pregnancies, and history of abortion or still birth.

Data Analysis

Statistical analysis of data was performed using SPSS software, version 24 (SPSS Inc., Chicago, IL, USA). The normality of data distribution was assessed using Kolmogorov-Smirnov. Descriptive statistics were used to describe the mean, standard deviation, frequency and percentage of variables. Independent *t* test (for normally distributed data) and Mann-Whitney test (for non-normally distributed data) were used to compare quantitative variables between the two groups. Chi-square test was performed to compare qualitative variables between groups. *P* value <0.05 was considered statistically significant.

Results

This study was performed on 84 pregnant women at 26 to 30 weeks of gestation (42 pregnant women with GDM as cases and 42 healthy pregnant women as controls). Tables 1 and 2 show the general and clinical characteristics of participants. The mean ages of the cases and controls were 29.62 ± 0.80 and 27.54 ± 0.95 years, respectively. We found that gestational age, gravidity, parity, live births, SBP, FPG, and 1h-PG and 2h-PG were significantly higher in the GDM group ($P < 0.05$). Other measured variables were not different between groups (Table 1).

Significantly more women in the GDM group had GDM in previous pregnancies compared to the healthy group (15.5% vs 0%, $P = 0.007$), while no differences were observed regarding hypertension in previous pregnancies, family history of dyslipidemia, and proteinuria between two groups (Table 2).

By comparing the lipid profiles, we found significantly higher HDL levels in the GDM group compared to the healthy group ($P = 0.008$). TG and cholesterol levels were also higher in the GDM group; however, the differences were not statistically significant ($P = 0.327$, $P = 0.770$, respectively). Conversely, LDL levels were higher in the healthy group with no statistical significance ($P = 0.709$) (Table 3).

We found a significant association between HDL levels and GDM (OR: 1.049, 95% CI: 1.009-1.090, $P = 0.015$). This association remained significant when adjusted for age, BMI, and gestational age (OR: 1.010, 95% CI 1.002-1.017, $P = 0.009$). No significant association was found between GDM and TG, cholesterol, and LDL levels ($P > 0.05$) (Table 4).

Discussion

The main purpose of this study was to compare lipid profiles of pregnant women with and without GDM. All components of the lipid profile were higher in pregnant women with GDM, except for LDL; however, only the differences regarding HDL were statistically significant between groups. HDL was also significantly associated with GDM in pregnant women, even after adjustment for age, BMI, and gestational age. On the contrary, there was no significant association between GDM and TG, LDL, and cholesterol.

Abnormal lipid profile in pregnant women with GDM has been reported (23,30). Koukkou et al found that total cholesterol concentration was not significantly different between pregnant women with GDM and normal pregnant women, while lower LDL-c concentration was reported in the third trimester of pregnancy in GDM group compared to controls (30). Moreover, Schaefer-Graf et al (31), Sobki et al (32), and Grissa et al (33) showed that maternal serum cholesterol and LDL-C levels did not differ between control pregnancies and those with GDM. Total cholesterol and LDL-C levels did not differ between pregnant women with and without GDM in our study, which was consistent with the results of the aforementioned studies. In contrast, Asif et al (34),

Table 1. Comparison of General and Clinical Characteristics Between Pregnant Women With GDM and Healthy Pregnant Women

Variables	Groups		*P* Value[a]
	GDM Group (n=42) Mean ± SD	Healthy Group (n=42) Mean ± SD	
Age (y)	29.62 ± 0.80	27.54 ± 0.95	0.073
Gestational age (wk)	26.87 ± 0.89	27.69 ± 0.24	0.039
BMI (kg/m^2)[b]	23.51 ± 3.37	22.80 ± 3.18	0.287
Weight gain in the 1st trimester (kg)	0.68 ± 0.84	0.82 ± 0.99	0.272
Weight gain in the 2nd trimester (kg)	5.54 ± 0.12	5.38 ± 0.304	0.441
Gravidity	2.24 ± 0.17	1.71 ± 0.13	0.048
Parity	1.06 ± 0.14	0.5 ± 0.09	0.006
Live births	1 ± 0.14	0.5 ± 0.09	0.020
Abortion	0.18 ± 0.67	0.21 ± 0.08	0.714
Death	0.069 ± 0.033	0	0.084
FPG[b] (mg/dL)	93.36 ± 11.32	78.88 ± 7.52	<0.001
1h-PG[b] (mg/dL)	190.48 ± 28.89	129.69 ± 23.56	<0.001
2h-PG (mg/dL)	159.39 ± 3.206	110.5 ± 2.81	<0.001
SBP (mm Hg)	112.5 ± 0.85	110 ± 1.32	0.045
DBP (mm Hg)	70.94 ± 0.92	68.69 ± 1.13	0.101

Abbreviations: BMI, body mass index; GDM, gestational diabetes mellitus; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; 1h-PG, one-hour plasma glucose; 2h-PG, two-hour plasma glucose.

[a] *P* value ≤ 0.05 was considered statistically significant.

[b] Analyzed by independent *t* test. Other variables were analyzed by the Mann-Whitney test.

Table 2. Comparison of Some Clinical Features Between Pregnant Women With GDM and Healthy Pregnant Women

Variables		Groups		*P* Value[a]
		GDM Group (n = 42) No. (%)	Healthy Ggroup (n = 42) No. (%)	
Family history of dyslipidemia	Yes	7 (16.66)	8 (19)	0.479
	No	35 (83.33)	34 (81)	
GDM in previous pregnancies	Yes	7 (16.66)	0 (0)	0.007
	No	35 (83.33)	42 (100)	
HTN in previous pregnancies	Yes	2 (4.76)	1 (2.4)	0.757
	No	40 (95.23)	41 (97.6)	
Proteinuria	Negative	38 (90.47)	37 (88.1)	0.500
	Trace	4 (9.52)	4 (9.5)	
	Positive	0 (0)	1 (2.4)	

Abbreviations: BMI, body mass index; GDM; HTN, hypertension.
[a] *P* value ≤ 0.05 was considered statistically significant.

Table 3. Comparison of Lipid Profile Between Pregnant Women With GDM and Healthy Pregnant Women

Variables[b]	Groups		*P* Value[a]
	GDM Group (n=42) Mean ± SD	Healthy Group (n=42) Mean ± SD	
Triglyceride (mg/dL)	225.58±89.84	208.38±80.66	0.327
Cholesterol (mg/dL)	228.96±52.03	211.59±41.83	0.770
LDL (mg/dL)	122.41±4.82	144.54±26.01	0.709
HDL (mg/dL)	53.10±1.72	46.64±1.70	0.008

Abbreviations: GDM, gestational diabetes mellitus; HDL, high-density lipoprotein; LDL, low-density lipoprotein.
[a] *P* value ≤ 0.05 was considered statistically significant.
[b] Triglyceride and cholesterol were analyzed by independent *t* test. LDL and HDL were analyzed by the Mann-Whitney test.

Table 4. Association Between Lipid Profile and GDM in Pregnant Women

Variables	Odds Ratio (95% CI)	*P* Value[a]	Adjusted Odds Ratio[b] (95% CI)	*P* Value[a]
Triglyceride	1.002 (0.998-1.007)	0.324	1.000 (0.999-1.002)	0.469
Cholesterol	1.008 (0.999-1.017)	0.082	1.002 (1.000-1.004)	0.074
LDL	0.988 (0.993-1.003)	0.406	1.000 (0.999-1.000)	0.390
HDL	1.049 (1.009-1.090)	0.015	1.010 (1.002-1.017)	0.009

Abbreviations: GDM, gestational diabetes mellitus; HDL, high-density lipoprotein; LDL, low-density lipoprotein.
[a] *P* value ≤ 0.05 was considered statistically significant.
[b] Adjusted for BMI, age and gestational age

McGrowder et al (35), and Khan et al (36) found that higher proportion pregnant women with GDM had high levels of total cholesterol compared to controls.

With regard to TG level, Koukkou et al (30), Di Cianni et al (37), Sánchez-Vera et al (38), and Aslan et al (39) found that women with GDM had significantly higher serum TG concentrations compared to controls; these results were in contract with findings of Grissa et al study (33). Similar to other studies, we found higher TG levels in pregnant women with GDM, although the difference between groups was not statistically significant.

In addition, Koukkou et al (30), Sobki et al (32), McGrowder et al (35) and Khan et al (36) did not find a significant difference in HDL-C levels between groups. While, Di Cianni et al (37), Khosrowbeygi et al (28) and Ryckman et al (23) found lower levels of HDL in GDM subjects compared to healthy pregnant subjects. We found significantly higher HDL levels in women with GDM; in this regard, the results of our study were opposed to the aforementioned studies.

It has proved that metabolic disorders such as GDM are associated with a lower level of HDL, although in this study, a higher level of HDL was observed in women with GDM. It should be noted that we did not assay the various components of HDL ((A-I) HDL and (A-2) HDL). So, merely based on HDL quantity, it should not be concluded that higher level of HDL in the GDM group is in contrary with the component of metabolic disorders (40). Furthermore, we did not assay dietary intake and physical activity level of subjects in our study; therefore, the contrast between our study and other studies may be due to differences regarding nutrition and physical

activity in the study populations. Additionally, different quality of enzymatic assays which results in heterogeneous results should be taken into consideration. Besides, some studies had evaluated lipid profiles of pregnant women with GDM across all the three trimesters of pregnancy, while in our study the evaluation of lipid profile was limited to the third trimester; thus, some results were not comparable.

Conclusions

Mean values of TG, cholesterol, and HDL levels were higher in women with GDM compared to healthy pregnant women with only significant differences regarding HDL. LDL levels were non-significantly higher in the healthy group. Because of inconsistent Data in this context, further study with the large sample size and strong design are recommended.

Authors' Contribution

Study concept and design: LH. Acquisition of data: ZF. Analysis and interpretation of data: MM. Drafting of the manuscript: GZ. Critical revision of the manuscript for important intellectual content: MKhe. Statistical analysis: SZ. Administrative, technical, and material support: MKha. Study supervision: RS.

Conflict of interests

The authors declare that they have no conflicts of interests.

Ethical Approval

The study received ethics approval from the Ethics Committee of Hormozgan University of Medical Sciences.

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