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Comparison of Serum Lipid Profile between Gestational Diabetes Mellitus and Pregnant Women with Normal Glucose Tolerance

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Abstract

Background: Aberrant lipid metabolism presumed to have important relationship with gestational diabetes mellitus (GDM), though previous studies revealed inconsistent results on this area. **Objectives:** To identify the difference of serum lipid profile between gestational diabetes mellitus (GDM) and pregnant woman with normal glucose tolerance (NGT). **Methods:** This cross sectional study was conducted from January 2017 to December 2017 at Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh with 31 GDM and equal number of NGT pregnant women diagnosed on the basis of WHO criteria-2013, during 24 - 40 weeks of gestation. Glucose was measured by glucose oxidase method and fasting serum lipid profile [Total cholesterol (TC), High Density Lipoprotein-cholesterol (HDL-C) and Triglyceride (TG)] was measured by enzymatic-colorimetric method. Data were analyzed and compared by statistical tests. **Results:** Among total sixty-two (62) study subjects, 31 were GDM (age: 27.52 ± 4.8 years, body mass index (BMI): 27.17 ± 3.3 kg/m^2) and 31 were pregnant women with NGT (age: 24.94 ± 4.2 years, BMI: 25.43 ± 6.5 kg/m^2). Mean age of GDM group was significantly higher than that of NGT group ($p = 0.028$). Women with GDM showed relatively higher BMI than NGT women but that was not statistically significant ($p = 0.194$). Fasting lipid profiles between GDM

and NGT (GDM vs. NGT; total cholesterol: 194.21 ± 42.18 vs. 208.52 ± 42.18 mg/dl, p = 0.187; HDL-C: 47.50 ± 16.17 vs. 47.18 ± 11.71 mg/dl, p = 0.928; LDL-C: 109.25 ± 28.80 vs. 119.30 ± 34.76 mg/dl, p = 0.220 and triglyceride 204.78 ± 58.50 vs. 202.34 ± 79.18 mg/dl, p = 0.891) were not significantly different. The variations in all lipid fraction values were not statistically significant among GDM women when analyzed between BMI groups holding BMI cut-off at 23 kg/m^2. No significant differences of any values of lipid profile were found in GDM women according to various age categories (Age < 25 years vs. ≥25 years). **Conclusions:** Lipid profile does not differ between women with GDM and pregnant woman with NGT.

Keywords

Gestational Diabetes Mellitus (GDM), Normal Glucose Tolerance (NGT), Serum Lipid Profile

1. Introduction

Gestational diabetes mellitus (GDM) is an abnormal glucose tolerance that is the first time detected during pregnancy, and is the most common medical and metabolic complication of pregnancy [1]. The prevalence of GDM is increasing worldwide and 15% to 22% of all pregnancies are affected by GDM; this prevalence may be higher under new diagnostic criteria [2]. GDM could be associated with many consequences, such as fetal macrosomia, preeclampsia and high cesarean section rate [3] [4]. Women with GDM and their offspring are at risk for later development of obesity, type 2 diabetes mellitus and cardiovascular disorders [5] [6]. GDM is a heterogeneous disorder in which age, obesity, and genetic background contribute to the severity of the disease [7]. The hallmark of this condition is increased insulin resistance (IR) [8] [9]. Insulin resistance occurs in pregnant women due to hormonal changes. Maternal hormones interfere with the action of insulin. As a result, glucose level is increased in blood with excess insulin produced in GDM to overcome this resistance in a normal pregnancy [8] [9].

It has been reported that lipid level increases slightly in early pregnancy, but significantly in later pregnancy and maternal dyslipidemia which elevated over a physiologic range is a common phenomenon of pregnancy [10]. Hyperlipidemia is commonly detected in the 2nd half of pregnancy, which is regarded as a physiologically required mechanism to provide metabolic fuel and nutrients for the fetus [11]. However, it still remains obscure to ascertain which level of lipid elevation is physiologic or pathologic.

Lipid profile consists of serum Total cholesterol (TC), High Density Lipoprotein-cholesterol (HDL-C), Low Density Lipoprotein-cholesterol (LDL-C) and Triglyceride (TG). Several factors in the body are responsible for the differences of these components in the body. Lipid profiles differ in people of different gend-

ers, ages, activity levels, overall health, smoking status and glucose levels in the body, which can forecast the presence of various conditions including diabetes mellitus [10]. Therefore serum lipid profile is important in the assessment of blood glucose levels. The abnormalities of carbohydrate metabolism observed in GDM may affect other metabolic pathways especially lipid metabolism [12]. IR which is one of the primary defects in majority of GDM presumed to have important relationship with dyslipidaemia in pregnancy and future cardio-metabolic risk [13].

Early pregnancy dyslipidemia is associated with the risk of developing GDM [13] [14]. GDM is accompanied by alterations in fasting, postprandial, and integrated 24 hours of plasma concentrations of amino acids, glucose, and lipids [15]. GDM is associated with hyperlipidaemia which has evident by the significantly elevated total cholesterol and triglyceride concentrations [5] [16] [17]. Significant increase in serum cholesterol, serum triglyceride and serum very low density lipoprotein (VLDL) levels were found in cases with gestational diabetes when compared to healthy pregnant women [18]. It has been reported that pregnancy and diabetes have additive effect on the development of an atherogenic lipid profile [19].

It has been suggested that abnormal glucose levels, glycosylated hemoglobin (HbA1c), serum cholesterol, and serum triglycerides play an important role in pathophysiology of gestational diabetes [20]. Circulating lipid levels in GDM versus normal pregnancy have been extensively studied, but results were less consistent with most studies focusing on the third trimester [21]. Still there are considerable controversies as to whether lipid patterns differ in women with GDM early in pregnancy and whether these early patterns are potential markers of preexisting insulin resistance [22]. In this study, we were comparing measurements of total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C), in the second and third trimesters of pregnancy in women who developed GDM and those who remain glucose tolerant. Early diagnosis of gestational diabetes and appropriate measures against dislipidemia will decrease adverse neonatal and maternal outcomes.

2. Material and Methods

This prospective cross sectional study was conducted at Department of Endocrinology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from January 2017 to December 2017. The study was approved by the Ethical Review Committee, BSMMU, Dhaka, Bangladesh. According to the statistical calculation, this study comprised of sixty two (62) subjects [31 GDM women, diagnosed by the WHO 2013 criteria as cases and 31 healthy pregnant women (NGT) as control subjects)] [9]. The study population had been recruited from pregnant women attending the antenatal clinic and GDM clinic of Bangabandhu Sheikh Mujib Medical University, following selection criteria. Women

in 24 - 40 weeks of gestation with singleton pregnancy age between 18 to 35 years were screened and enrolled consecutively in this study. Pregnant women with overt diabetes, history of taking oral antidiabetic agents, diabetes mellitus in pregnancy (DIP), patient with other co-morbid diseases (hepatic, renal or thyroid disorders, chronic infections etc.) were excluded from the study. Informed written consent was taken from each participant prior to enrollment in the study. Each pregnant women had been challenged by 75 gm glucose (75 gm in 300 ml of water) following an overnight fast for oral glucose tolerance test (OGTT), as the test fulfilled the diagnostic criteria of GDM as set by WHO, they were enrolled as GDM. Healthy pregnant women with normal OGTT (NGT) were served as control subjects. Demographic, anthropometrics, family history and other related information of each study subject were recorded in a data collection sheet. Measurement of serum fasting total Cholesterol, LDL-cholesterol, HDL-cholesterol and Triglyceride of selected subjects was done from fasting serum samples obtained during OGTT. Glucose was measured by glucose oxidase method and fasting serum lipid profile (Total cholesterol, TG and HDL-c) was measured by enzymatic-colorimetric method. All biochemical tests were performed at the Biochemistry and Molecular Biology Laboratory, Department of Biochemistry and Molecular Biology, BSMMU, Dhaka, Bangladesh. The differences within variables between the groups were analyzed and compared.

2.1. Gestational Diabetes Mellitus

Gestational diabetes mellitus had been diagnosed by the WHO 2013 criteria if any one of the following criteria was met irrespective of gestational age:

- Fasting plasma glucose = 5.1 - 6.9 mmol/l (92 - 125 mg/dl);
- 1-h post 75 g oral glucose load ≥ 10.0 mmol/l (180 mg/dl);
- 2-h post 75 g oral glucose load = 8.5 - 11.0 mmol/l (153 - 199 mg/dl).

2.2. Body Mass Index [BMI (kg/m^2)]

BMI of the subjects was calculated using standard formula, BMI = Weight (kg)/[Height (m)]^2. BMI was classified according to WHO and nutritional status based on "Asian criteria" values [23].

Nutritional Status	WHO criteria (BMI cut-off)	"Asian criteria" (BMI cut-off)
Underweight	<18.5	<18.5
Normal weight	18.5 - 24.9	18.5 - 22.9
Overweight	25 - 29.9	23 - 24.9
Pre-Obese	-	25 - 29.9
Obese	≥30	≥30
Obese Type-1 (obese)	30 - 40	30 - 40
Obese Type-2 (morbid obese)	40.1 - 50	40.1 - 50
Obese Type-3 (super obese)	>50	>50

2.3. Dyslipidemia

Dyslipidemia was defined according to the American Heart Association, if Total cholesterol: >200 mg/dl or HDL-cholesterol: <35 mg/dl or LDL-cholesterol: >130 mg/dl or Triglyceride: >150 mg/dl.

2.4. Statistical Analysis

Data cleaning validation and analysis were performed using the Statistical Package for Social Science (SPSS) software for Windows version-22. Results were described in frequencies or percentages for qualitative values and mean ± SD for quantitative values with normal distribution. Subgroups made on the basis of clinical and biochemical findings were compared by unpaired student's t-test or Chi square test/χ^2-test as applicable. p Value ≤ 0.05 was considered as statistically significant.

3. Results

In an attempt to compare fasting lipid profile between GDM and pregnant women with NGT; 62 pregnant women (age: 26.23 ± 4.70 years, BMI: 26.3 ± 5.20 kg/m^2; mean ± SD) were encompassed in this study. All pregnant women were screened by 3-sample of OGTT following WHO 2013 criterion to include 31 women with GDM (age: 27.52 ± 4.80 years, BMI: 27.17 ± 3.30 kg/m^2; mean ± SD) and equal number of women with NGT (age: 24.94 ± 4.20 years, BMI: 25.43 ± 6.50 kg/m^2; mean ± SD).

3.1. Glucose Profile of the Study Subjects

Table 1 displays the plasma glucose (PG) profile of study subjects. PG values during 75 gm OGTT were significantly higher in GDM at all time points (GDM vs. NGT; 0-h PG: 5.36 ± 0.44 vs. 4.51 ± 0.32; 01-h PG: 9.8 ± 1.42 vs. 7.46 ± 1.2; and 02-h PG: 8.27 ± 1.45 vs. 6.6 ± 1.06 mmol/L, mean ± SD; p < 0.001 for all values).

3.2. Baseline Characteristics of the Study Subjects

Mean (±SD) age of GDM group was significantly higher than the mean (±SD) age of NGT group (GDM vs. NGT; 27.52 ± 4.8 years and 24.94 ± 4.2 years, p = 0.028). Women with GDM showed relatively higher BMI (GDM vs. NGT; 27.17 ± 3.3 kg/m^2 vs. 25.43 ± 6.5 kg/m^2, p = 0.194; mean ± SD) than NGT women but that was not statistically significant. Frequency of GDM was also significantly higher in service holder (GDM vs. NGT; 45.2% vs. 19.4%, p = 0.029). Gestational age (GDM vs. NGT; 29.77 ± 4.09 week vs. 28.81 ± 4.64 week, p = 0.388; mean ± SD), previous history of GDM [GDM vs. NGT; 2 (66.7%) vs. 1 (33.3%), p = 0.554] or family history of DM in 1st degree relative [GDM vs. NGT; 14 (58.3%) vs. 10 (41.7%), p = 0.297] were not significantly different between the groups, however values of these variables were relatively high among GDM women (Table 2).

Table 1. Glucose profile of the study subjects during 75 gm OGTT* (n = 62).

OGTT glucose values (mmol/L)	Plasma glucose of GDM (n = 31) Mean ± SD	Plasma glucose of NGT (n = 31) Mean ± SD	p
0-h plasma glucose	5.36 ± 0.44	4.51 ± 0.32	**<0.001***
01-h plasma glucose	9.8 ± 1.42	7.46 ± 1.2	**<0.001***
02-h plasma glucose	8.27 ± 1.45	6.6 ± 1.06	**<0.001***

p Values obtained by Student's t-test; OGTT: oral glucose tolerance test, [*Glycated hemoglobin (HbA1c) was not used for diagnosing gestational diabetes]; GDM: gestational diabetes mellitus; NGT: normal glucose tolerance; *significant.

Table 2. Baseline characteristics of the study subjects (n = 62).

Variables	GDM	NGT	p
	n = 31	n = 31	
Age (years, mean ± SD)	27.52 ± 4.8	24.94 ± 4.2	0.028*
Occupation			
Housewife	15 (58.1%)	20 (64.5%)	0.200^{ns}
Service	14 (45.2%)	6 (19.4%)	0.029*
Others	2 (6.5%)	5 (16.1%)	0.228^{ns}
BMI kg/m^2, (mean ± SD)	27.17 ± 3.3	25.43 ± 6.5	0.194^{ns}
Gestational weeks at detection (mean ± SD)	29.77 ± 4.09	28.81 ± 4.64	0.388^{ns}
Previous history of GDM	2 (66.7%)	1 (33.3%)	0.554^{ns}
Family history of DM in 1st degree relatives	14 (58.3%)	10 (41.7%)	0.297^{ns}

Significance values stand for comparison between GDM and NGT groups by Student's t-test and χ^2-test; BMI: body mass index; GDM: gestational diabetes mellitus; NGT: normal glucose tolerance; DM: diabetes mellitus; *significant; ns: not significant.

3.3. Fasting Lipid Profile in GDM and NGT

Table 3 shows the mean (±SD) difference of fasting lipid profile between GDM and NGT. It was observed that there was no statistically significant difference between the GDM and NGT groups in concentrations of various lipid fractions (GDM vs. NGT; Total cholesterol: 194.21 ± 42.18 mg/L vs. 208.52 ± 42.18 mg/L, p = 0.187, HDL-C: 47.50 ± 16.17 mg/L vs. 47.18 ± 11.71 mg/L, p = 0.928, LDL-C: 109.25 ± 28.80 mg/L vs. 119.30 ± 34.76 mg/L, p = 0.220 and Triglyceride: 204.78 ± 58.50 mg/L vs. 202.34 ± 79.18 mg/L, p = 0.891).

3.4. Lipid Profile in GDM under BMI at Cut-off 23 kg/m^2

As depicted in Table 4, all lipid fraction values between GDM group with BMI < 23 kg/m^2 and GDM with BMI ≥ 23 kg/m^2 were not significantly different (BMI: <23 kg/m^2 vs. ≥23 kg/m^2; total cholesterol: 210.85 ± 39.52 mg/L vs. 193.06 ± 42.77 mg/L, p = 0.573; HDL-C: 34.24 ± 11.22 mg/L vs. 48.41 ± 16.19 mg/L, p = 0.237; LDL-C: 126.27 ± 1.44 mg/L vs. 108.08 ± 29.43 mg/L, p = 0.397 and triglyceride: 187.46 ± 13.18 mg/L vs. 205.97 ± 60.31 mg/L, p = 0.673). Although total cholesterol, LDL-C levels were relatively high and HDL-C level was compara-

tively low in GDM with BMI < 23 kg/m^2, while triglyceride level was relatively high in GDM with BMI ≥ 23 kg/m^2.

3.5. Lipid Profile in GDM under Age at Cut off 25 Years

A cut-off age was set at 25 years, as age ≥ 25 years considered a risk factor for GDM [24]. GDM women with age < 25 years or ≥25 years had no statistically significant differences of any value of lipid profile (age < 25 years vs. ≥25 years; total cholesterol: 207.38 ± 50.51 mg/L vs. 190.36 ± 39.83 mg/L, p = 0.356; HDL-C: 46.74 ± 13.65 mg/L vs. 47.72 ± 17.09 mg/L, p = 0.890; LDL-C: 113.08 ± 30.88 mg/L vs. 108.13 ± 28.76 mg/L, p = 0.696 and triglyceride: 226.83 ± 70 mg/L vs. 198.35 ± 74.72 mg/L, p = 0.264) (Table 5).

Table 3. Lipid profile in GDM and NGT (n = 62).

Variables (mg/dl)	GDM (n = 31)	NGT (n = 31)	P
Total cholesterol	194.21 ± 42.18	208.52 ± 42.18	0.187^{ns}
HDL-C	47.50 ± 16.17	47.18 ± 11.71	0.928^{ns}
LDL-C	109.25 ± 28.80	119.30 ± 34.76	0.220^{ns}
Triglyceride	204.78 ± 58.50	202.34 ± 79.18	0.891^{ns}

Comparison between groups was done by Student's t test; GDM: gestational diabetes mellitus; NGT: normal glucose tolerance; HDL-C: high density lipoprotein-cholesterol; LDL-C: low density lipoprotein-cholesterol; ns: not significant.

Table 4. Lipid profile in GDM according to BMI categories (cut-off 23 kg/m^2) (n = 31).

Variables	Groups		P
	BMI < 23 (kg/m^2) (n = 2)	BMI ≥ 23 (kg/m^2) (n = 29)	
Total cholesterol	210.85 ± 39.52	193.06 ± 42.77	0.573^{ns}
HDL-C	34.24 ± 11.22	48.41 ± 16.19	0.237^{ns}
LDL-C	126.27 ± 1.44	108.08 ± 29.43	0.397^{ns}
Triglyceride	187.46 ± 13.18	205.97 ± 60.31	0.673^{ns}

Comparison between groups done by Student's t test; ns: not significant; GDM: gestational diabetes mellitus; BMI: body mass index; HDL-C: high density lipoprotein-cholesterol; LDL-C: low density lipoprotein-cholesterol.

Table 5. Lipid profile in GDM according to age categories (cut-off 25 years) (n = 31).

Variables	Groups		P
	Age < 25 years (n = 7)	Age ≥ 25 years (n = 24)	
Total cholesterol	207.38 ± 50.51	190.36 ± 39.83	0.356^{ns}
HDL-C	46.74 ± 13.65	47.72 ± 17.09	0.890^{ns}
LDL-C	113.08 ± 30.88	108.13 ± 28.76	0.696^{ns}
Triglyceride	226.83 ± 70	198.35 ± 74.72	0.264^{ns}

Comparison between groups done by Student's t test; ns: not significant; GDM: gestational diabetes mellitus; HDL-C: high density lipoprotein-cholesterol; LDL-C: low density lipoprotein-cholesterol.

4. Discussions

Although pregnancy is a condition characterized by progressive insulin resistance (IR), GDM develops in only a small proportion of pregnant women [8]. This physiological IR underlies all pregnancies usually start to appear around 24 - 28 weeks of gestation and progressing through the third trimester of pregnancy. Failure of β-cell compensation for pregnancy induced IR results in carbohydrate intolerance by which GDM is diagnosed. Moreover women with GDM are increased risk of developing metabolic dysfunction including hyperlipidaemia after pregnancy. Therefore present study was conducted to observe the changes in lipid profile in GDM and women without glucose aberrance.

Aberrant lipid metabolism in normal pregnancy are characterized by marked elevations of total cholesterol and triglyceride (TG) levels as a result of increased liver synthesis of TG in response to elevated estrogen levels. Reduction of lipoprotein lipase (LPL) activity due to the down regulation of LPL gene expression by estrogen during pregnancy decreases the clearance of lipids [13]. Maternal factors such as BMI, overweight, maternal nutrition, pre-pregnancy lipid levels and various medical complications of pregnancy may also have significant effects on lipid metabolism and plasma lipid levels [13]. In this study it was intended to explore the discrepancy of fasting lipid profile between GDM and pregnancy without glucose abnormality. It was demonstrated that various fractions of lipid profile were not significantly differ between women with GDM and pregnant women with normal glucose tolerance. This finding was consistent with a study where fractions of lipid profile (TG, TC, LDL-C and HDL-C) did not vary between pregnant women with GDM and those without GDM [25]. Lipid parameters were significantly higher in women with GDM than pregnant women with NGT that found in different studies which differ from this current study [9] [26] [27]. Fat storage increases in the second trimester of pregnancy leading to increase plasma TG. LDL-C is formed from VLDL which is principal transport form of TG in the blood. So in GDM when TG concentration increases, LDL-C increases accordingly. In this study, Triglycerides concentration was increased but LDL-C was within normal limit in both GDM and pregnant women with NGT. These results were not consistent with a previous population-based study as reported that LDL-C was significantly higher during normal pregnancy and also in GDM [28]. The results of increased TG level, unchanged HDL-C level and decreased total cholesterol level in GDM compared with pregnant women with NGT obtained from our study were consistent with results of a previous study where similar findings were observed [29]. Besides, increasing maternal age and BMI are classically considered as risk factors for GDM [24] [30] [31]. The present study also noted older age and higher BMI in GDM women compared to NGT women. Previous history of GDM and family history of diabetes was found to be higher among GDM women in this study, these observations were also an agreement with previous studies [24] [30] [31].

Fasting Lipid profile and GDM have been shown to be the important predic-

tors for maternal metabolic disturbances including dyslipidemia, hypertension and cardiovascular disease [12]. Moreover, pre-pregnancy BMI was found to have a far greater effect on IR in pregnancy in Asian women than Caucasians [32]. Besides maternal weight gain, nutrition and pre-pregnancy lipid levels are known to have significant effects on lipid metabolism and plasma lipid levels during pregnancy [13]. Well recognized risk factors for GDM include overweight and obesity [33]. In this study, variables were analyzed among GDM women holding BMI cut-off at 23 kg/m^2. In this series, no significant abnormalities were observed in all values of lipid profile among GDM group under BMI cut off 23 kg/m^2. HDL-cholesterol level was relatively lower in GDM < 23 kg/m^2 than ≥23 kg/m^2. This result was consistent with other studies where HDL-C was found lower in GDM under BMI cut off <25 kg/m^2 [34] [35]. In accordance with some other studies a cut-off of age was set at 25 years; and lipid profile was analyzed in GDM group with age < 25 years and ≥25 years [24]. In our study among GDM women with age < 25 years or ≥25 years, did not shown any statistically significant differences in all values of lipid profile even in its different fractions like total cholesterol, HDL-C, LDL-C and triglyceride. These findings were consistent with previous report where no significant abnormality was found between the maternal age and lipid parameters [9].

To summarize, this study demonstrated that older age and higher BMI in GDM women compared to NGT women, but lipid profile do not differ between women with GDM and pregnancy without glucose aberration. This result is consistent with the previous reports where it was shown that, when BMI and gestational age are taken into account, dyslipidemia is not significantly associated with GDM. Impact of dyslipidemia on pregnancy outcomes and future development of type 2 diabetes in GDM should be addressed in long term prospective studies.

5. Conclusion

This study concluded that lipid profiles do not differ between women with GDM and pregnancy without glucose aberration. Further studies are warranted to elucidate the role of dyslipidemia in the pathogenesis of GDM.

Limitations

It was a single centre study with a relatively small sample size. Lipid profile of study subjects could not be compared in different trimester of pregnancy due to financial and time constrains. Baseline characteristics such as pre-pregnancy BMI and pre-pregnancy lipid profile could not be used for comparison between the study subjects.

Recommendations

Further studies including large sample size and various lipid fractions (free fatty acid, Apo-B: Apo-A ratio etc.) are required to determine dyslipidemia in GDM.

Conflicts of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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