Lipid Profile In Ghanaian Women With Gestational Diabetes Mellitus

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Abstract: - Lipid profile has been a useful tool for the efficient screening and management of patients with diabetes mellitus. Lipid profile changes associated with gestational diabetes mellitus (GDM) are well documented in other parts of the world but not in Ghana. The role of plasma lipids in the pathogenesis of GDM in Ghanaian women was investigated. Ante-natal patients were selected as a case control study including 100 patients with GDM (cases) and 100 pregnant women without GDM (control). Mean values (GDMs vs controls in mmol/L) of TG (2.29± 0.07 vs 1.75±0.08, p<0.001), TCHOL (7.26±0.16 vs 5.85±1.65, p<0.001), LDL (4.71 ± 0.17 vs 3.83±0.16 p<0.001), and VLDL (1.12±0.03 vs 0.80±0.04 p<0.001), respectively were significantly higher in GDMs than the controls. Mean HDL for the GDMs was significantly lower in GDMs compared to controls (1.2±0.07 vs 1.46±0.08 p=0.023). Mean cortisol concentration for GDMs (509±12.02ng/ml) was significantly higher than controls (402.70±13.12ng/ml) (p<0.05). Also, mean progesterone was significantly higher in GDMs (46.41±2.75ng/ml) than controls (33.06±1.66ng/ml) (p<0.05). These study showed that generally, lipid parameters [LDL, total cholesterol, VLDL) were significantly higher in GDMs compared with controls. However, HDL was significantly higher in controls compared with GDM.

KEY WORDS: - Cholesterol, Cortisol, Gestational Diabetes Mellitus, Impaired Fasting Glycaemia, Insulin Resistance, Preeclampsia, Progesterone, Very Low Density Lipoprotein-

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy [1]. Risk factors for developing GDM include a previous diagnosis of gestational or pre-diabetes, impaired fasting glycaemia, a family history revealing a first degree relative with type 2 diabetes, maternal age, ethnic background, being overweight and a history of previous pregnancy which resulted in a child with a high birth weight>4gk [2].

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Insulin resistance emerges in the second trimester of pregnancy, and may progresses thereafter to levels seen in non-pregnant patients with Type 2 diabetes [3]. Hormonal changes during pregnancy such as increased levels of progesterone, cortisol, oestrodiol and human chorionic somatomammotropin (hCS) mediate insulin resistance [3]. In normal women, high maternal insulin in early pregnancy promotes gestational weight gain and weight retention postpartum increasing the risk of GDM and later development of Type 2 DM [4] Obesity has been identified among others, as a risk factor for GDM [2]. Obesity among Ghanaian adults is common particularly among the elderly, females and urban dwellers [5]. Maternal obesity increases the risk of pregnancy complications, including preeclampsia, GDM, and caesarean delivery [6]. The worldwide prevalence of obesity has increased substantially over the past few decades as a result of economic, technologic and lifestyle changes that have created an abundance of cheap, high-calorie food coupled with decreased physical activity [6]. About 10% of patients develop Type 2 diabetes mellitus soon after delivery [7], whiles about 70% develop Type 2 diabetes mellitus 5 to 15 years later [8]. The risk is higher in women who required insulin for treatment [9,10]. There is also a 10% risk of polyhydramnios that may increase the risk of abruption placentae and preterm labour as well as postpartum uterine atony [11]. Women with GDM experience twice the number of urinary tract infections than women who do not have GDM. This increased infection incidence is thought to be as a result of increased amount of glucose in the urine beyond the normal glycosuria that is present in pregnancy [11]. There is also an increased risk of pyelonephritis and asymptomatic bacteriuria [11]. Therefore, it is recommended to check glucose tolerance in all women who have had GDM at six weeks post-partum and every three years afterwards [12]. Pregnancy and diabetes have additive effect on the development of an atherogenic lipid profile. Lipid abnormalities associated with insulin resistance affect all lipid fractions [13], leading to elevated triglycerides and LDL cholesterol with low HDL cholesterol. Although this pattern correlates strongly with cardiovascular risk, treatment decreases the risk [14]. Low HDL cholesterol levels are independent risk factor for cardiovascular

disease relates to a reduced HDL particle size. Various studies in different parts of the world have strongly indicated that lipid metabolism during pregnancy may have a role to play in the aetiology and pathogenesis of GDM. The major objective of this study was to examine lipid profile pattern in women with GDM in Ghana as well as progesterone and cortisol and how the result would provide useful information in the management of women with GDM.

STUDY DESIGN AND METHODS

Study participants

This was a case control study involving a total of 100 GDMs cases and 100 healthy controls. Selection of GDMs was based on the criteria of the American Diabetes Association.

Study site.

The study was carried out at the Maternity Department and the National Diabetes Management and Research Center (NDMRC), Korle-Bu Teaching Hospital Accra, Ghana. The hospital serves as a referral hospital for the country.

SInclusion criteria

Pregnant women who satisfied the following criteria were included in the study:

- Had GDM
- Glycated haemogolobin of less than 6.5%
- Maternal age between 24 and 44 years
- Gestational age of between 24 and 28 weeks

Exclusion criteria

Individuals who satisfied the following criteria were excluded from the study:

- Known diabetics
- Glycated haemoglobin greater than 6.5%
- Post-partum women and patients with history or clinical features suggesting chronic liver disease
- Polycystic ovarian syndrome.

Sample collection

The University of Ghana Medical School Ethical Committee reviewed the consenting process. Patients' overnight fasting blood (5) samples were drawn into vacutainer tube between 7.00am and 8.00 a.m. for all assays. Ten (10) patient samples were taken daily. The samples were kept on ice for 1 hour for sera to separate. The samples were then centrifuged at 3000 rpm for 5 minutes at 4^0C. Sera were aliquoted and stored at -21^0C until ready to use.

Analysis of samples

Samples were brought to room temperature and allowed to thaw before analysis. Analysis of lipid profile was done using VITROS dry-Chemistry analyzer. Cortisol and progesterone were estimated using the NoviWell-cortisol microtiter method and mini VIDAS automated Enzyme Linked Fluorescent Assay (ELFA) technique respectively.

Data analysis

Data was analyzed using statistical software package, SPSS version 18 and Excel. Data were presented as mean±SD, mean±SEM. For comparisons of means, student t-test was used to determine the significance between GDM and controls. p –values <0.05 were considered statistically significant.

RESULTS

Table 1. Demographic characteristics of the study subjects (cases and controls)

	GDM (n=100)			CONTROLS (n=100)		
	Min	Max	Mean	Min	Max	Mean
Age (Years)	24	44	33 ± 5.07	24	42	32± 4.79
Weight (kg)	38	122	92.81± 15.90	55	122	88.37±15.15
Height (cm)	150	175	161.11± 6.39	146	173	159.11 ±6.63

Table 1 shows the demographic characteristics of GDMs and Controls. The mean values for age (years), weight (Kg) and height (cm) for the GDMs were 33, 92.81, and 161.11 respectively and were 32, 88.37, and 159.11 for controls respectively. Data are presented as mean ± standard deviation (SD).

Serum triglycerides and total cholesterol levels of GDMs and Controls

The results showed that the mean serum triglycerides concentration for the GDM (2.29±0.074mmol/L) was statistically significantly higher ($p<0.001$) than controls (1.75±0.083mmol/L) (Fig 1). Also, total cholesterol was significantly higher ($p<0.05$) in GDMs (7.26±0.016mmol/L) than controls (5.85±1.06mmol/L) (Fig. 2).

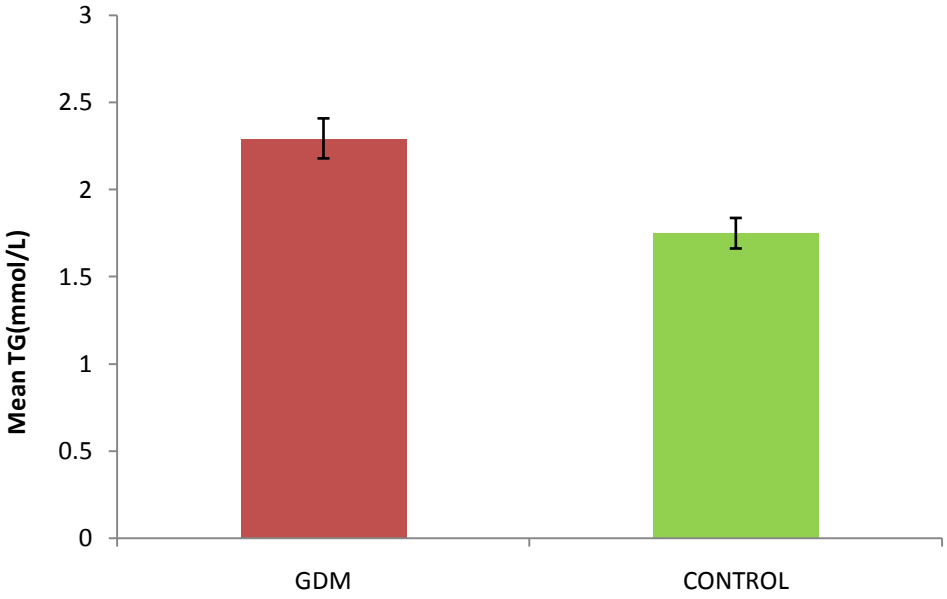

FIG. 1 Triglycerides levels in GDM and controls. Fig 1 shows that the mean triglycerides level in the GDM was higher than the controls (P<0.001). Data are presented as means ± SEM.

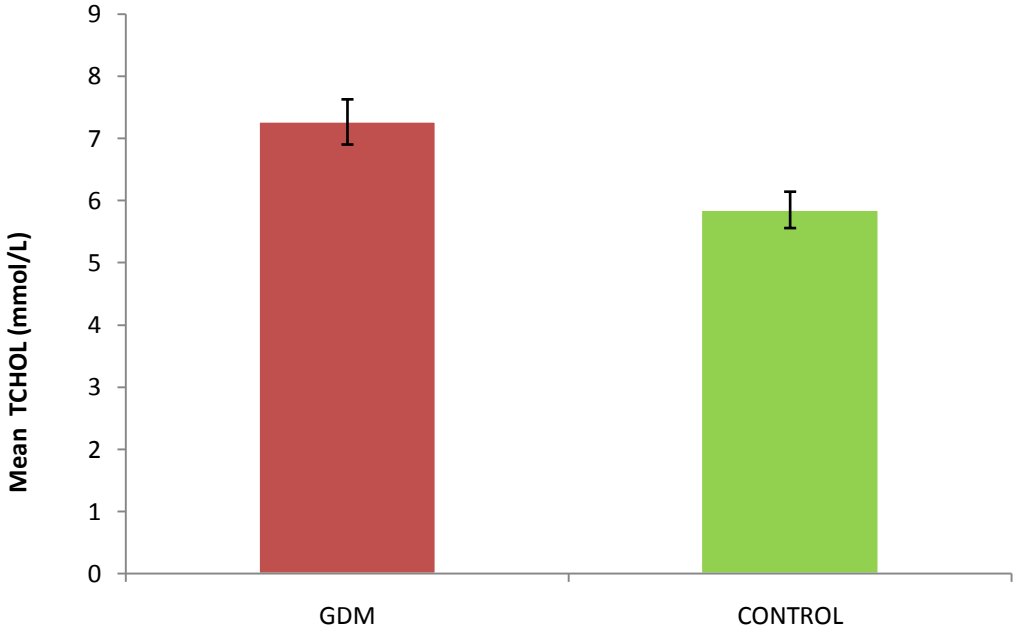

FIG. 2 Total cholesterol levels in GDMs and controls. Fig. 2 shows that the mean total cholesterol levels in GDM was significantly higher than the controls (p<0.001). Data are means ± SEM.

Serum Lipoprotein levels of GDMs and the Controls

The results showed that the mean HDL cholesterol concentration for the GDMs (1.21±0.071mmol/L) was significantly lower (p=0.023) than controls (1.46±0.084mmol/L) (Fig. 3). However, mean LDL cholesterol for GDMs (4.71±0.173mmol/L) was significantly higher (p<0.001) than controls (3.83±0.162mmol/L) (Fig. 4). The results further showed that mean VLDL cholesterol for GDMs (1.12±0.033mmol/L) was significantly higher (p<0.001) than controls (0.93±0.037mmol/L) (Fig.5). Statistically, there was significant difference between the means of the GDMs and the controls

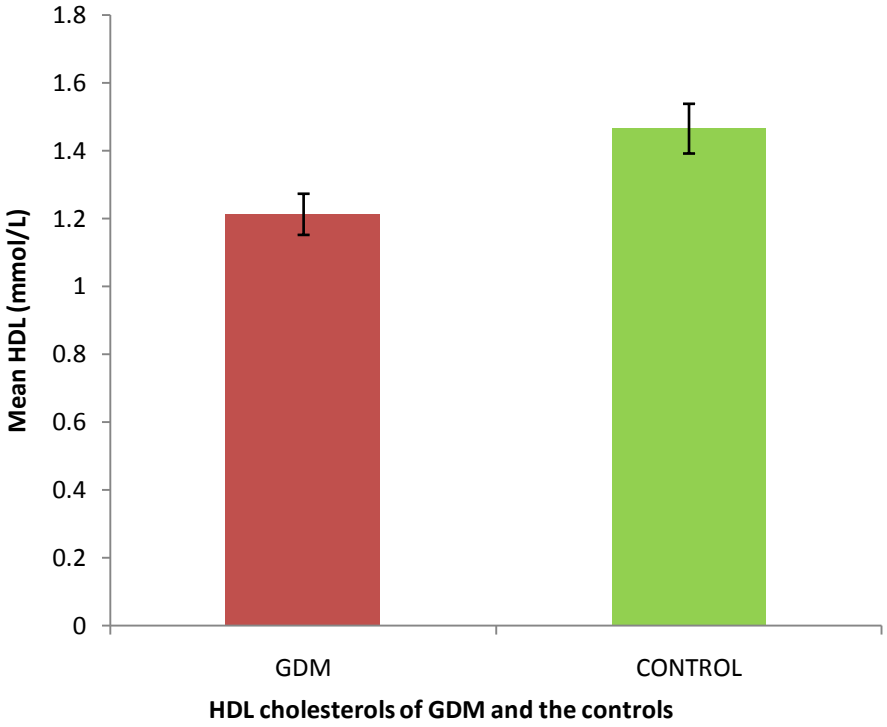

FIG.3. HDL cholesterol levels of GDM and controls. Fig. 3 shows that the mean HDL cholesterol level of the GDMs was lower than the controls (P=0.023). Data are means ± SEM.

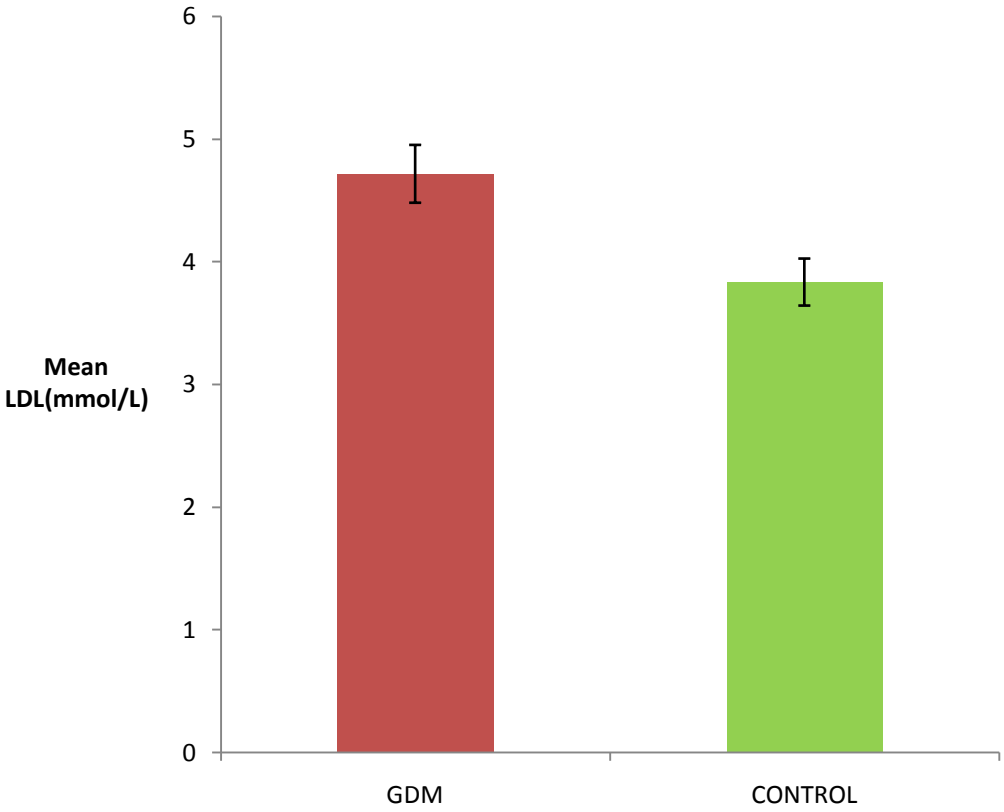

FIG.4. LDL cholesterol of GDMs and the controls. Fig. 4 shows that the mean cholesterol level of the GDMs was higher than the controls (p<0.001). Data are means ± SEM.

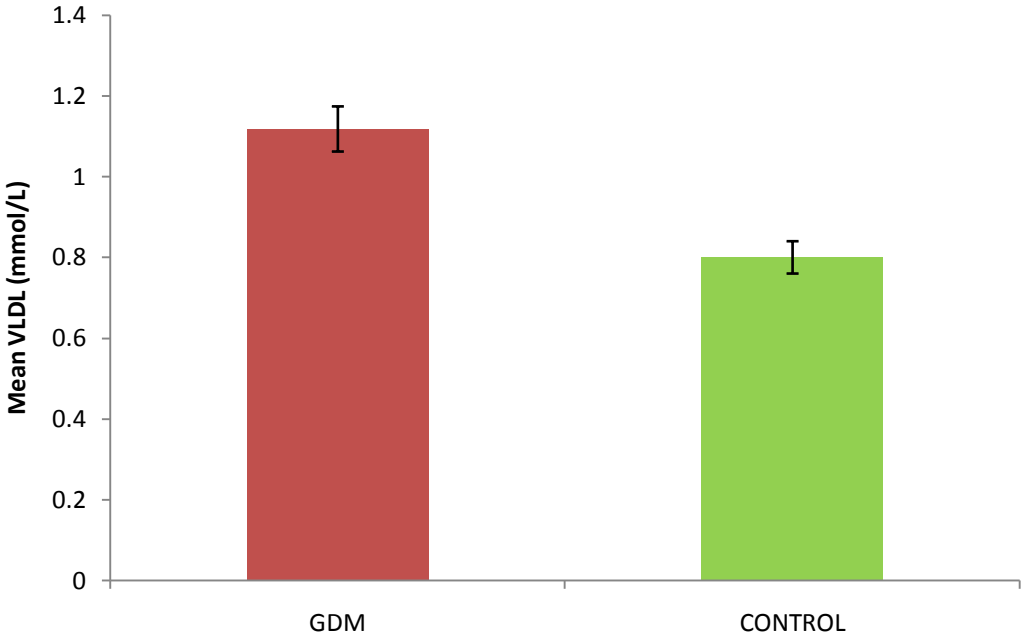

FIG.5. VLDL cholesterol levels of GDM and controls. Fig. 5 shows that the mean VLDL cholesterol for the GDM was higher than the controls ($p<0.001$). Data are means ± SEM.

Serum Cortisol and progesterone levels of GDMs and Controls

The results showed a mean cortisol concentration of 509.5±12.02ng/ml for the GDMs and 402.70±13.12ng/ml for the controls (Fig. 6). Statistically, there was significant difference between the GDMs and the controls ($p < 0.05$).

For progesterone, the results showed mean concentrations of 46.4098±2.753ng/ml for the GDMs and 33.06±1.659ng/ml for controls (Fig.7). Statistically, there was significant difference between the GDMs and the controls ($p < 0.05$).

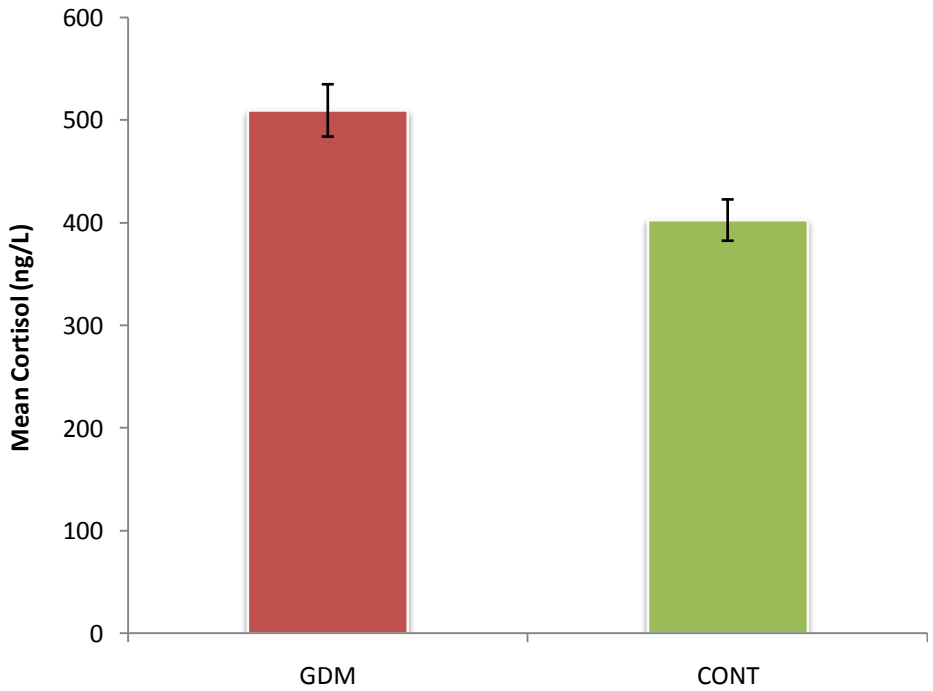

FIG.6. Cortisol levels of GDM and the controls. Fig. 6 shows that the mean cortisol level of GDMs was higher than the controls ($p < 0.05$). Data are means ± SEM.

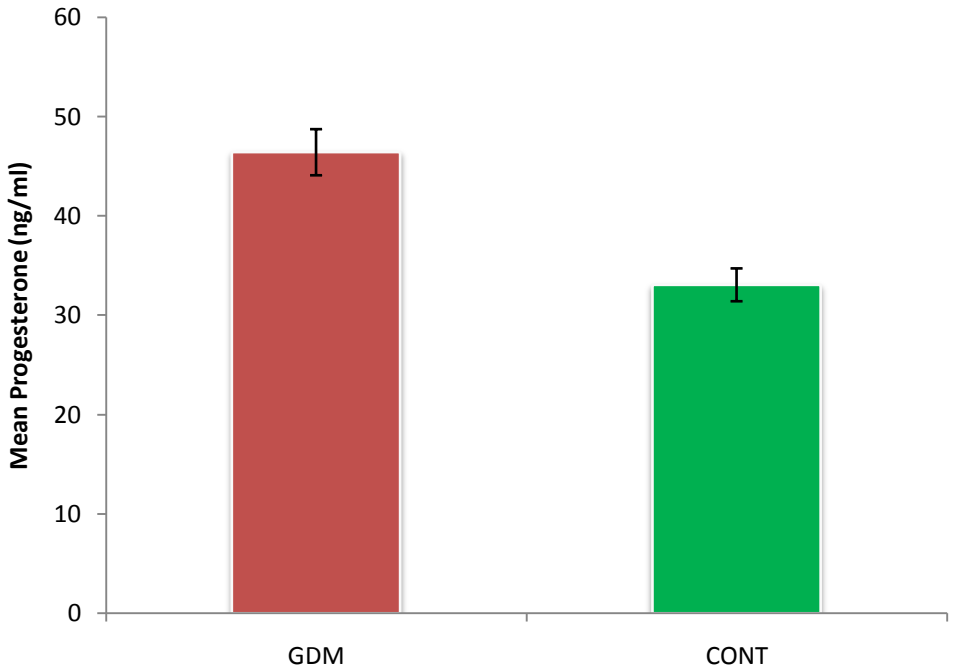

FIG.7. Progesterone levels of GDM and the controls. Fig. 7 shows that the mean progesterone level of the GDM was higher than the mean progesterone value for the controls ($p < 0.05$). Data are means ± SEM.

Discussions

Lipid profile changes in normal pregnancy are characterized by marked elevations of total plasma cholesterol and triglyceride levels as a result of increased liver synthesis of triglycerides (TG) and Very Low Density Lipoprotein-Cholesterol (VLDL-C) in response to elevated oestrogen levels [15]. Reduction in Lipoprotein lipase (LPL) activity due to the down regulation of LPL gene expression by oestrogen during pregnancy decreases the clearance of VLDL-C [16]. Maternal gestational diabetes mellitus increases the offspring's cardiometabolic risk and in utero hyperinsulinaemia is an independent predictor of abnormal glucose tolerance in childhood [17]. Maternal factors such as BMI (body mass index), maternal weight gain, maternal nutrition, pre-pregnancy lipid levels and various medical complications of pregnancy may also have significant effects on lipid metabolism and plasma lipid levels [18]. In this study, it was observed that lipid profiles (TG, TCHOL, LDL and VLDL cholesterols) were significantly elevated in gestational diabetes mellitus. HDL, even though show significant difference between the gestational diabetics and controls, it was not as highly elevated as the rest of the lipid components. Triglycerides concentrations for GDM were significantly higher than controls for all the age groups. This agreed with a study by Amraei and Azemati [19] who reported a significant increase in the concentration of triglycerides levels in pregnancy complicated by glucose intolerance as compared to normal pregnancy. [20, 21] however, did not find significant difference in triglycerides concentration between women with previous GDM cases and controls. The discrepancies could be as a result of differences in the method of selection of subjects for the study. In part, the GDM group of the subjects studied by Koivumen and colleagues [21], involved women with previous gestational diabetes mellitus, some of whom were treated with insulin and others with diet and it is possible that the treatment as well as the time period between the time they had the GDM and the time of the study, could affect the lipid profile patterns. The significant increase in total cholesterol concentrations in GDM compared with controls in this study is as a result of the fact that GDM significantly alters cholesterol metabolism leading to dyslipidaemia. These findings are consistent with reports by Amraei and Azemati [19], who reported significant difference in total cholesterol levels between pregnancy complicated by GDM and normal pregnancy. In a study done in Pakistan on the lipid profile and serum insulin levels in gestational diabetes mellitus, [20] reported significantly higher total cholesterol levels in women with GDM than the controls. Fat storage increases in the second trimester of pregnancy leading to increase plasma triglyceride concentration [22]. LDL is formed from VLDL which is the principal transport form of triglyceride in the blood and so in GDM, when triglyceride concentration increases, LDL increases accordingly. In this study, LDL cholesterols were significantly higher in GDMs than the controls. These results are in agreement with previous reports that indicated that LDL cholesterol increases significantly during pregnancy and more especially pregnancy complicated by GDM [19, 20, 23]. However, [24] reported lower LDL levels in GDM compared with the controls. VLDL cholesterol levels for the GDMs were significantly higher than in controls. This could be as a result of the high triglycerides levels observed in this study. VLDL is formed from triglycerides synthesized in the liver de novo or by re-esterification of free fatty acids. Therefore, VLDL level increases when triglyceride level increases. The results of this study are in agreement with reports by Amraei and Azemati ; Aziz and Mahboob [19, 20]. The increased levels of triglycerides, total cholesterol and LDL cholesterols observed in GDMs is as a result of increase fat storage [22] and progesterone [23] in the second trimester of pregnancy, that act in a way to reset the

lipostat in the hypothalamus leading to increase in the lipids concentration. HDL cholesterol levels for the GDM case were significantly lower than the controls. This is contrary to the report by Koukkou et al., and Wiznitzer et al., [25, 26] who did not find significant difference in HDL levels between GDM and normal pregnant women. The results of this study, is however consistent with a report by Aziz and Mahboob [20], who reported significantly lower HDL levels in GDM compared with normal pregnant control women. Amraei and Azemati [19] and Koivunen et al., [21] also reported significantly lower HDL levels in pregnant women with impaired glucose tolerance than the controls There have been reports that cortisol and progesterone are among the hormones responsible for insulin resistance during pregnancy and are implicated in GDM [3, 11]. In this study, the mean cortisol and progesterone values for the GDMs were significantly higher than the controls. The results of this study are in agreement with reports by Ahmed and Shalayel; Koivunen et al., [21, 27], found significantly higher serum cortisol levels in women with previous GDM. The cortisol levels for both GDM and the control groups were generally high. However, mean cortisol and progesterone values were significantly higher in GDM than the controls suggesting that in pregnancy complicated by glucose intolerance, there is a further increase in the levels of placental hormones leading to insulin resistance and eventually gestational diabetes mellitus.

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