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ORIGINAL ARTICLE

IMPACT OF GESTATIONAL DIABETES MELLITUS ON MATERNAL LIPIDS.

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ABSTRACT

Introduction: Gestational diabetes mellitus (GDM) according to ACOG is any degree of glucose intolerance that either commences or is first diagnosed in pregnancy. The prevalence of GDM ranges from 1 to 14% of all pregnancies, however it depends on the diagnostic criteria used and the ethnic background of the population being tested. The trend towards older maternal age, modern lifestyle, eating habits and reduced physical activity contribute towards increasing prevalence of GDM. Lipid levels during normal pregnancy and in women with gestational diabetes mellitus (GDM) have been extensively studied with varying results. However it remains unclear whether dyslipidemia is a potential marker of coexisting insulin resistance. **Objective:** The aim is to analyse the impact of gestational diabetes mellitus (GDM) on maternal lipid profile. **Methods:** Study group included 30 GDM women and control group included 30 equal cohort normal pregnant women. Fasting lipid profile which includes serum cholesterol, serum triglycerides, serum low density lipoprotein and serum high density lipoprotein were estimated along with HbA1c on post natal day 1. **Results:** There was a significantly higher value of total cholesterol (215.4 vs 170.7., $t=5.454$, $p=0.001$) low density lipoprotein (91.1 vs 72.23., $t=2.817$, $p=0.001$) triglycerides (200.2 vs 92.03., $t=18.632$, $p=0.001$) and high density lipoprotein (65.27 vs 47.93., $t=3.296$, $p=0.001$) in GDM women compared to normal pregnant women. **Conclusion:** Women with GDM had higher levels of total cholesterol, triglycerides, HDL and LDL compared to normal pregnant women.

Keywords: Gestational diabetes mellitus (GDM), high density lipoprotein (HDL), low density lipoprotein (LDL), Triglycerides (TG), total cholesterol (TC).

1. INTRODUCTION

Diabetes mellitus is a disorder of carbohydrate metabolism. It is caused by a combination of hereditary and environmental factors and is characterised by either inadequate secretion or inadequate action of insulin. The world prevalence of diabetes among adults was 6.4% in 2010 affecting 285 million adults and has been estimated to increase upto 7.7% and 439 million adults by 2030 (Wild et al., 2004). Gestational diabetes mellitus (GDM) according to ACOG is any degree of glucose intolerance that either commences or is first diagnosed in pregnancy (Committee Opinion, 2014). This is a growing concern as women with GDM are at increased risk of developing diabetes post pregnancy, in addition to hypertension, hyperlipidemia and coronary heart disease.

Physiological insulin resistance underlies all pregnancies beginning around 24-28 weeks of gestation and progresses through third trimester. Early in pregnancy, the fetus does not produce its own cholesterol but rather dependent upon the transport of maternal cholesterol across the placenta (Mudd, 2010). Maternal cholesterol levels may rise during the first two trimesters of pregnancy to address the needs of the fetus. As the fetus begins to produce its own cholesterol in late second trimester, the demand for maternal cholesterol reduces thereby resulting in a decrease in the maternal cholesterol. However GDM enhances this already existing metabolism and has been proposed as a possible risk factor for elevated maternal lipids (4). In human endothelial cells L-arginine is metabolised to nitric oxide (NO) and L-citrulline by endothelial NO synthase (Woollett, 2005). In GDM there is an increase in the elements of L-arginine NO pathway but decreased bioavailability leading to endothelial dysfunction.

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All these explain the hyperglycemia associated hyperlipidemia in GDM women.

2.METHODS

In accordance with the ethical principles and with the approval by the institutional ethical review board, this comparative cross sectional study was conducted in the department of Obstetrics and Gynaecology at Rajah Muthiah Medical College and Hospital from December 2014 till August 2016. 30 GDM women and 30 normal pregnant women who came for delivery to RMMCH were taken up for the study. Detailed history was elicited and thorough clinical examination done. Fasting lipid profile which includes serum total cholesterol, serum triglycerides, serum LDL and serum HDL along with HbA1c were measured on postpartum day1. Known hyperlipidemia patients on drugs, known hypertensive patients, history of heart disease, insulin resistant Diabetes mellitus, overt diabetic patients, hyper/hypothyroidism, chronic renal diseases, currently on medications thought to adversely influence glucose tolerance, multiple pregnancy, <16 yrs or >40 years of age were excluded from the study. Women were scrutinised according to their age, parity, BMI, previous history of GDM or family history of diabetes and HbA1c levels.

3.RESULTS

The study group included 30 GDM women and control group included 30 normal pregnant women. Both the study and control group were age matched. Gestational age was similar for the two groups and any preterm and post dated pregnancy were excluded from the study.

12 women (40%) in study group reported a positive family history of diabetes and 10 women(33%) had a positive first degree relative with dyslipidemia, myocardial infarction, hypertension or stroke. Further 4 women had GDM in previous pregnancy.

Out of the 30 GDM women in my study group 20 of them received insulin, 9 were on meal plan and one was on oral hypoglycaemic agent Tablet metformin.

It was rather striking to notice that 17 women (56.6%) from the study group had to undergo Lower Segment Caesarean Section (LSCS). Among those who delivered vaginally 5 women had instrumental delivery. Control group women had 33% women who underwent LSCS.

Table 1 -BMI Between Study And Control Group

BMI (kg/m ²)	Study Group	Control Group
<25	21	25
>25	9	5
Total	30	30

Study group had 21 women and control group had 25 women with BMI <25 kg/m². 9 in the study group and 5 in the control group had BMI > 25 kg/m². The mean BMI was 24.5 vs 22.59 kg/m² between the two groups

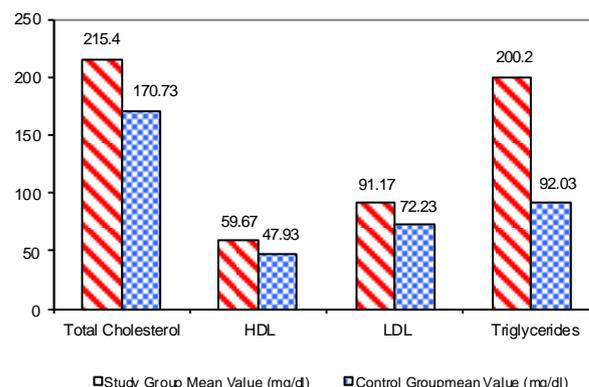
Table 2- Glycaemic Control and Antenatal treatment

HbA1c	On insulin	Meal plan	Oral hypoglycaemic agent
5-6%	6	7	0
6-7%	13	1	1
>7%	1	1	0
Total	20	9	1

Out of the 15 women in the HbA1c range of 6-7% 13 women were already on insulin, one on meal plan and one woman on oral hypoglycaemic drug. In the range of 5-6% 6 women were on insulin and 7 were on meal plan. HbA1c above 7% one woman was on insulin and another one was on meal plan.

Table 3. Comparison of maternal lipids between the study and control group.

Lipid Parameter	Study Group Mean Value (mg/dl)	Control Group mean Value (mg/dl)	t value	Statistical Significance
Total Cholesterol	215.40 ± 39.64	170.73 ± 17.80	5.454	Significant P=0.001
HDL	59.67 ± 13.17	47.93 ± 8.12	4.591	Significant P=0.001
LDL	91.17 ± 29.40	72.23 ± 23.74	2.817	Significant P=0.001
Triglycerides	200.20 ± 30.57	92.03 ± 12.25	18.632	Significant P=0.001



4.DISCUSSION

It was found that study group had high total cholesterol than the control group (215.40 mg/dl vs 170.43mg/dl). Out of the 19 women in study group who had elevated total cholesterol values 15 were on insulin, and 4 on meal plan. Study group had higher HDL than the control group (65.27mg/dl vs 47.93mg/dl). Among women treated with insulin 10 had higher HDL values (>60 mg/dl) and 10 had lower HDL values(<60 mg/dl) Among women on meal plan 3 had higher HDL and 6 had lower HDL. One woman on OHA also had higher HDL. Study group had higher LDL than the control group (91.17 mg/dl vs 72.23 mg/dl). 9 women on insulin had normal LDL whereas 7 had increased LDL. Among the women on mealplan 8 had elevated LDL and 5 had normal LDL. 1 woman on OHA also had normal LDL. Study group had higher Triglyceride than the control group (200.20 mg/dl vs 92.03 mg/dl). All women on insulin, 8 on meal plan and 1 on OHA had increased triglycerides. Only one woman on meal plan had normal triglycerides. Our results were

consistent with the study conducted by Akinçi et al (2011) and Meyers-seifer et al(1996). Both of their studies showed increased TC, HDL, LDL, TG in GDM women compared to normal pregnant women.

Studies	TC variation Study vs control (mg/dl)	HDL variation Study vs control (mg/dl)	LDL variation Study vs control(mg/dl)	TG variation Study vs control (mg/dl)
Akinçi et al	199 vs 175	61 vs 51	123 vs 96	122 vs 87
Meyers-Seifer et al	189 vs 165	49 vs 44	121 vs 105	131 vs 85
Our study	215 vs 170	59 vs 47	91 vs 72	200 vs 92

Senaidy et al(2012) also found higher values of lipid profile in insulin treated women compared to women on meal plan and normal pregnant women. Compared to Akinçi et al., (2011) and Meyers seifer and Vohr ,(1996) our study had the advantage of evaluating HbA1c and insulin treatment and its possible association in increasing the lipid levels.

our study results were conflicting to the results of Sokup et al(2012) and Marsille tremblay,(2008) et al as far as HDL was considered. Both these studies revealed slightly lower values for HDL.

Studies	HDL Variation Study vs control (mg/dl)
Sokup et al	59.17 vs 66.90
Marseille-Tremblay et al	63.03 vs 69.99
Present study	59.67 vs 47.93

On the other hand both Sokup and Marseille-tremblay also found an increase in total cholesterol, LDL and triglycerides which was coinciding with our study.

This increase in lipid values could possibly be due to changes in the expression of multiple genes involved in lipid and cholesterol metabolism in placental tissues of pregnancies coursing with GDM. These genes include the fatty acid coA ligase, long chain 2,3 and 4 involved in the novo synthesis of cholesterol. In human endothelial cells L-arginine is metabolised to nitric oxide (NO) and L-citrulline by endothelial NO synthase (Woollett, 2005). In GDM there is an increase in the elements of L-arginine NO pathway but decreased bio availability leading to endothelial dysfunction. This clearly explains the hyperglycemia associated hyperlipidemia affecting the fetal metabolism.

5.CONCLUSION:

In the present study total cholesterol, serum triglycerides, HDL, LDL were significantly elevated in GDM women. This alteration could be harmful both to the mother and the fetus. Extended studies are required to study the effect of these alterations. Early diagnosis and treatment of diabetic pregnancy will reduce the severity of complications associated with this condition.

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