VOLUME - 11, ISSUE - 07, JULY - 2022 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper | Obstetrics & Gynaecology

ASSOCIATION OF SERUM LIPID PROFILE IN SECOND TRIMESTER OF PREGNANCY WITH ADVERSE PREGNANCY OUTCOMES

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ABSTRACT Pregnancy is a state of metabolic stress associated with high lipid levels , the highest concentration observed during third trimester. The imbalance in the amount of lipids has been related to maternal-perinatal pathologies such as preeclampsia (PE), gestational diabetes mellitus(GDM) and preterm birth . A cohort of 150 antenatal mothers were recruited and were evaluated for serum lipid profile during the second trimester. They were followed up till delivery and adverse pregnancy outcome , if any , was recorded .Our study was aimed at studying the association of serum lipid profile during second trimester with the various adverse pregnancy outcomes .

KEYWORDS : Perinatal,Pre eclampsia (PE),Gestational diabetes mellitus (GDM),Preterm birth (PTB)

INTRODUCTION

Pregnancy in healthy women is associated with changes in lipid metabolism that are essential for fetal growth and development[1] .Multiple physiologic changes occur that contribute to alteration in lipid profile including an anabolic phase with an increase in lipid synthesis and fat storage in preparation for fetal development and subsequently in third trimester, a phase where lipid physiologically transitions to a net catabolic phase with breakdown of fat deposits[2] . Pregnancy is a state of insulin resistance reflected by the lipid and lipoprotein profiles of the mother. Within 6 weeks of gestation, lipid levels drop slightly, followed by an increase during each trimester of pregnancy. Triglyceride levels increase sharply during pregnancy, as do cholesterol levels. LDL increases in a similar pattern as that of total cholesterol . On an average, cholesterol and triglyceride levels do not exceed 250 mg/dL. However, when abnormal pregnancies are included, levels can exceed 300 mg/dL.[3] .

Maternal hyperlipidemia for the most part has been considered physiological and has not been routinely screened. However, there are direct implications of dyslipidemia on maternal and fetal health, and therefore it is prudent to screen for lipid disorders[4]. The imbalance in the amount of lipids-either before or during pregnancy - has been related to maternal-perinatal pathologies such as preeclampsia (PE), gestational diabetes mellitus(GDM), preterm birth. Identification of early markers of metabolic conditions that may adversely affect pregnancy outcome is imperative. The identification can potentially lead to expeditious implementation of risk reduction intervention, ultimately improving maternal, fetal and neonatal health and resulting in effects that extent into adulthood and future generation.

MATERIAL AND METHODS

A prospective cohort study in which 150 pregnant females attending the antenatal clinic in outpatient department ,satisfying the inclusion criteria were enrolled for the study .In all these antenatal mothers, a detailed history with special reference to dietary habits followed by a complete obstetric and general physical examination was done . The purpose of investigation and interrogation was explained to every patient and their informed consent was taken.

All antenatal mothers included in the study were subjected to serum lipid profile estimation between 16-20 weeks. A 3 ml non fasting blood sample was taken and serum lipid profile was estimated .These women were followed up till delivery to determine the association between serum lipid profile measured during second trimester of pregnancy and adverse pregnancy outcomes(PE,GDM,Preterm birth).

RESULTS

In short, lipid profile is variable during each trimester of a normal pregnancy . The findings of our study have been mentioned in the Table 1.

Table 1 : Reference Values For Serum Lipid Profile In Second Trimester Of Pregnancy

Lipid profile		%
TC	176-299 mg/dl >300 mg/dl MEAN+_SD MEDIAN(IQR)	86.7% 13.3% 235.31+_ 53.08 225(189-278.25)
TG	75-382mg/dl >383 mg/dl MEAN+- SD MEDIAN (IQR)	94% 6% 232.39+-54 210(173-300)
LDL	77-184mg/dl >184 mg/dl MEAN +-SD	86% 14% 112.78+- 12.15
VLDL	13-23 mg/dl >23 mg/dl MEAN+- SD	86.7% 13.3% 20.23+-4.72
HDL	52-87 mg/dl >87 mg/dl MEAN +_ SD MEDIAN (IQR)	89.3% 10.7% 68.39+- 10.94 66(60-76)

The association of lipid profile with various adverse pregnancy outcomes has been mentioned in following tables

Table 2:association Of Serum Lipid Profile With Preeclampsia

SERUM LIPID PROFILE	OUR STUDY (p value)	Singh et al (2018)	Ghodke et al (2017)	Jin et al (2016)
TC	<0.001	<0.001	0.38	0.979
TG	<0.001	<0.001	0.00	0.002
LDL	<0.001	<0.001	0.94	0.65
VLDL	<0.001	<0.001	0.01	-
HDL	0.69	-	0.26	0.352

Table 3:association Of Serum Lipid Profile With Gdm

SERUM LIPID PROFILE	OUR STUDY (p value)	Jin et al(2016)	Ghodke et al(2017)	Li et al (2021)
TC	<0.001	0.109	0.24	0.05
TG	O.O2	0.000	0.00	<0.001
LDL	<0.001	0.000	0.02	0.159
VLDL	<0.001	-	0.73	-
HDL	1	0.27	0.04	0.511

Table4: association Of Serum Lipid Profile With Preterm Birth

SERUM LIPID PROFILE	OUR STUDY (p value)	Sharami et al(2018)	Ghodke et al (2017)	Jin et al (2016)
TC	<0.01	0.002	0.86	0.180
TG	0.01	0.02	0.00	0.818
LDL	0.001	0.007	0.94	0.430
VLDL	0.09	-	0.41	-
HDL	0.43	-	0.95	0.93

ROC curve analysis was conducted to determine the optimal cut off points for TC,TG and HDL for predicting adverse pregnancy outcomes. Each optimal cut off point was assessed via searching for the maximal value of sensitivity+specificity-1(Youden Index). Area under the curve (AUC) was calculated to evaluate the predictive powers .

Table 5: Diagnostic performance of lipid profile to predict GDM

	TC	TG	HDL
AUC	.91	0.86	0.68
95% CI	0.85-0.97	0.77-0.94	0.56-0.81
Youden Index	0.714	0.67	0.406
Cut off value	277	276	62
Sensitivity	91.7%	91.7%	100%
Specificity	79.7%	75.4%	40.6%

The optimal cut off points by ROC curve analysis in predicting GDM was found to be 277 mg/dl for TC,276 mg/dl for TG and 62 mg/dl for HDL. TC predicting GDM owned the strongest predictive power with largest AUC[0.91(95% CI: 0.85-0.97)] followed by TG with AUC [0.86(95% CI:0.77-0.94)]. HDL had the least predictive power with AUC[0.68(95% CI-0.56-0.81)].

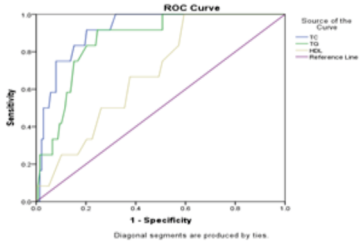

Image 1:roc Curve Usinf Tc,tg And Hdl To Predict Gdm

Table 6: Diagnostic performance of lipid profile to predict preeclampsia

	TC	TG	HDL
AUC	0.82	0.86	0.59
95% CI	0.71-0.93	0.76-0.96	0.44-0.74
Youden Index	0.597	0.681	0.232
Cut off value	255	276	87
Sensitivity	89.5%	89.5%	31.6%
Specificity	70.2%	78.6%	91.6%

The optimal cut off points by ROC curve analysis in predicting PE was found to be 255mg/dl for TC, 276 mg/dl for TG and 87 mg/dl for HDL. TG predicting PE owned the strongest predictive power with largest AUC[0.86(95% CI: 0.76-0.96)] followed by TC with AUC [0.82(95% CI:0.71-0.93)]. HDL had the least predictive power with AUC[0.59(95% CI-0.44-0.74)].

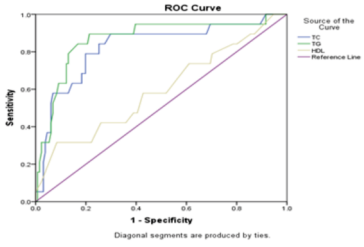

Image 2:roc Curve Usibf Tc,tg And Hdl To Predict Pe

Table 7: Diagnostic performance of lipid profile to predict preterm birth

	TC	TG	HDL
AUC	0.67	0.68	0.62
95% CI	0.53-0.81	0.55-0.81	0.50-0.75
Youden Index	0.389	0.34	0.21
Cut off value	286	204	60
Sensitivity	52.6%	84.2%	89.5%
Specificity	83.3%	49.6%	31.3%

The optimal cut off points by ROC curve analysis in predicting PTB was found to be 286 mg/dl for TC, 204 mg/dl for TG and 60 mg/dl for HDL. TG predicting GDM owned the strongest predictive power with largest AUC[0.68(95% CI: 0.55-0.81)] followed by TC with AUC [0.67(95% CI:0.53-0.81)]. HDL had the least predictive power with AUC[0.62(95% CI-0.50-0.75)].

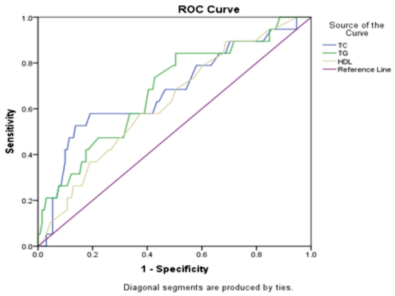

Image 3:roc Curve Using Tc ,tg And Hdl To Predict Preterm Birth

DISCUSSION

Physiological insulin resistance underlies all pregnancies beginning around 24-28 weeks of gestation.

Altered maternal lipid metabolism is also common in pregnancy with modest increases in lipid early in pregnancy and significant elevation in lipids later in pregnancy .

In women with GDM, the physiological changes in insulin and lipids are exaggerated and may indicate underlying metabolic dysfunction that transiently manifests during pregnancy. Dyslipidemia also impairs trophoblastic invasion contributing to cascade of events responsible for PE,like endothelial dysfuntion secondary to oxidative stress , decreased release of prostacyclin, leading to PE . Hyperlipidemia is regarded as an instigator of inflammation and oxidative stress which is risk factor for PTB.

It can be concluded from our study that LDL,TC and VLDL were significantly associated with GDM,TC,TG,LDL and VLDL were significantly associated with PE and TC,TG and LDL were associated with preterm birth.

Jin et al (2016) conducted a study in which 934 mothers were assayed for lipid profile and adverse outcomes were recorded.It was found that only TG and LDL were significantly associated with GDM,TG was significantly associated with PE whereas lipid profile was not found to be associated with Preterm birth 5.

Ghodke et al (2017) conducted a study on 200 subjects between 13-28 weeks and was found that GDM was significantly associated with TG and LDL,PE was significantly associated with TG and VLDL and preterm birth was significantly associated with Tg6. Singh et al (2018) evaluated the association of lipid profile with development of feto-maternal compication and showed significant association between PE and LDL, TG,TC and VLDL7.

Sharami et al (2018) did a cross sectional study with and without hyperlipidemia and showed significant association

between Preterm birth and TC,TG and LDL8. Li et al (2021) evaluated maternal mid trimester lipid profile in relation to GDM . He concluded that women with GDM had higher levels of TG than controls.9

CONCLUSION

Normal gestation is characterized by increase in lipid production to foster the healthy fetal development . Human gestation is associated with an " atherogenic " lipid profile which could act as a risk factor for adverse pregnancy outcomes. It can be concluded from this study that there are direct implications of dyslipidemia on maternal and perinatal outcomes.Increase in maternal TG , TC ,LDL and VLDL concentrations were the most important changes affecting maternal outcomes and had significant association with GDM ,PE and PTB.. HDL did not have any association with any adverse maternal or neonatal outcome.

Thus, it may be concluded that the estimation of lipid profile in early second trimester will bring about early recognition of patient at risk of having adverse pregnancy outcomes before the onset of clinical symptoms and their complications. Thereby enabling timely intervention in preventing pregnancy complications and adverse birth outcomes . Close monitoring and lifestyle management should be carried to prevents pregnancy complications as much as possible.

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