



PLAN TO WORK ON LIPID PROFILE STUDY IN PREGNANCY AS A MATERNAL AND PERINATAL OUTCOME

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ABSTRACT

Background Pregnancy induced hypertension or gestational hypertension is defined by the presence of newly diagnosed hypertension in pregnant women after 20 weeks of gestation with no proteinuria. There should be at least two occasions six hours apart where the blood pressure was more than 140/90 mm of Hg. Hypertensive disorders are second most common medical disorder in pregnancy. It is a significant contributor of maternal mortality and morbidity in liaison with infection and haemorrhage. **Aim and Objective** To study the strength of association lipid profile in pregnant women with associated Hypertension To test hypothesis that woman with lipid profile in early second trimester have risk of developing GHT **Material and Methods** The study was undertaken in 100 pregnant women. Data for the study was collected from 100 normotensive pregnant women with more than 20 weeks of gestational age (control group) and 100 Pregnancy Associated Hypertension patients (study group) admitted in the antenatal ward in Department of Obstetrics and Gynaecology in Government Dharmapuri medical college hospital. Cases and controls were matched. Serum lipid profile in early trimester were estimated. **Results** A Study of lipid profile in a early second trimester is a predictor of GHT. This study was done at Govt. Dharmapuri Medical College. In total 100 women, lipid profile evaluation was done in early second trimester. Those who have elevated value taken as cases and others included in Control population. Elevated values in cases were compared with GHT population, showed statistically significant ($p < 0.01$) The present study showed elevated lipid profile in GHT, suggesting the role of abnormal placentation and endothelial dysfunction due to lipoprotein lipase in the etiology of GHT, though the exact mechanism remains to be elucidated. The strength of association between these factors and GHT are very much significant. So it can be used as a predictor of GHT. These factors are very useful in the earlier period of gestation in the screening of GHT. In this study there is no maternal mortality, CVA, severe acute renal failure, HELLP syndrome. With the regular monitoring I had 2 cases of severe preeclampsia and one eclampsia. Regarding the perinatal outcome incidence of IUGR and RDS are more common in GHT. **Conclusion** This study concludes that regular monitoring of patients for these biomarkers will aid in early diagnosis and management. Thus, monitoring serum lipid profile levels can be effective in preventing maternal morbidity and mortality and help to reach a favorable outcome in pregnancy.

KEYWORDS : Blood Pressure, GDM, Low birth weight, Pre-Term Labour, IUGR.

INTRODUCTION

Pregnancy is a physiological state with increased alteration in biochemical and mechanical processes. The biochemical changes are reversible after delivery^{Ref.1}. Hypertension and proteinuria are the important complications of pregnancy which are associated with high maternal mortality and morbidity^{Ref.2}

Gestational hypertension is defined as systolic blood pressure more than 140mm Hg and diastolic blood pressure more than 90mm Hg after 20 wks of gestation without proteinuria

Preeclampsia is defined as presence of systolic blood pressure above 140mmhg and diastolic blood pressure above 90mmhg, associated with proteinuria. If GHT mother develops generalised tonic clonic type of seizure is termed as eclampsia. It may occur before, during or after delivery.

Sometimes these changes occur earlier when there is multiple pregnancy (or) extensive hydatid form changes in chorionic villi^{Ref.3}

Eclampsia usually occurs in 5- 10 percentage of pregnancies. It is specific to pregnancy and usually associated with high maternal and perinatal morbidity and mortality.

Severe Preeclampsia with imminent signs is associated with headache, visual disturbances, oliguria, epigastric pain, vomiting..^{Ref.4} High blood pressure is the most important tool for identification of pregnancy induced hypertension.

Recording of blood pressure and urine albumin level is essential for monitoring the complications of PIH.

The pathophysiological mechanism is characterised by absent Trophoblastic invasion of spiral arteries, leading to maladaptation of the spiral arterioles, so there is increased vascular resistance of the uterine artery and decreased perfusion of the placenta..

The spiral arterioles have a prime role in pre eclampsia. The structural and physiological changes in the spiral arterioles lead to the development of gestational hypertension.. Development of GHT is usually associated with change in lipid profile..

Vascular endothelial dysfunction also plays an important role in development of pregnancy induced hypertension. The change in serum and lipid profile play a vital role in the early detection of GHT in second trimester.

Most important feature in GHT is due to vasospastic phenomenon in kidney, uterus, placenta and brain. Altered lipid synthesis leading to decrease in PGI2: TXA2 ratio which plays an important role in the pathogenesis of GHT.

Measurement of serum lipid parameters will be of good predictive Value in GHT
Maternal complications include:

1. Abruptio placenta
2. Acute Kidney injury
3. HELLP syndrome

4. Eclampsia
5. Pulmonary edema
6. Possible complication of caesarean section

Fetal complications include:

1. Prematurity
2. Fetal growth retardation
3. Intrauterine death
4. Fetal distress

These complications of gestational hypertension could be prevented by prompt diagnosis, proper antenatal care and with timely intervention. When the GHT sets in very early trimester, close monitoring of the patient is necessary. If GHT women are on regular follow up and prompt medications, adverse outcomes are greatly reduced.

Uteroplacental insufficiency is also reduced by controlling the blood pressure. Decrease in platelet count may be associated with GHT which leads to severe bleeding tendencies which happens due to alteration in coagulation factors and fibrinogen. Regular monitoring of platelets and hepatic enzyme is essential.

Termination of pregnancy is the treatment for severe preeclampsia/eclampsia. The risk for both mother and fetus is more with continuation of pregnancy.

GHT may progress to severe preeclampsia/ eclampsia with uncontrolled hypertension. This is usually preventable by early detection of GHT using change in biochemical markers in maternal serum and prompt treatment of hypertension.^{Ref.7,8} Known GHT cases should be kept under regular follow up.

They are advised to check blood pressure regularly, routine blood analysis and urine albumin monitoring. There are several methods to identify GHT which include isometric hand grip test, roll over test, angiotensin II presser response, mean arterial response test.

However these tests have some limitation for screening in view of false positive results and subjective nature of interpretation. GHT complicates 5-10% of all pregnancies^{Ref.9}. In the developed countries 16% maternal mortality is due to hypertensive disorders. Early detection of GHT and appropriate management is mandatory to decrease both maternal and perinatal morbidity and mortality.

AIMS AND OBJECTIVES

1. To test the hypothesis that women with lipid profile in early second trimester have risk of developing hypertensive disorder of pregnancy^{Ref.10}
2. To identify the "at risk" women earlier may help in taking timely prevention and curative management and to prevent complications associated with GHT.
3. To study the strength of association between the elevated lipid profile with GHT

Abnormal Lipid levels in early pregnancy can be a good predictor of development of preeclampsia in patients. Dyslipidemia in early pregnancy leads to more oxidative stress by the formation of lipid

Aim Of The Study:

This study is aimed to evaluate the association of lipid profile in maternal and perinatal outcomes

Objective Of The Study:

Our objective is to evaluate whether fasting maternal total cholesterol and triglyceride levels during early pregnancy are associated with major adverse pregnancy outcomes.

MATERIALS AND METHODS

This was a prospective study, conducted in OP population at Govt. Dharmapuri Medical College, Dharmapuri. Total number of 100 pregnant women who attended antenatal clinic of department of O&G Govt. Dharmapuri Medical College were included. All the patient were screened for serum lipid profile in early second trimester between (14-20 wks), to be followed up till their delivery. The study groups involved both primi & multi gravida. They were selected on the basis of simple random sampling.

A study of lipid profile performed between those who remain normotensive and those who develop GHT. GHT was defined as systolic blood pressure more than 140mmhg and diastolic blood pressure more than 90mmhg occurring on two (or) more occasions after 20 wks of gestation recorded 6 hours apart. Preeclampsia is defined as gestational hypertension and proteinuria of at least (2+) / 1g/dl on dip stick (or) 24 hrs urinary protein excretion > 0.3g. Fasting venous blood sample (3ml) was collected and tests were carried out on the same day.

Serum lipid profile estimation was done by enzymatic calorimetric test with lipid clearing factor (LCF) using kits. LDL cholesterol & VLDL cholesterol values in mg/dl are indirectly measured. The cases were followed up regularly in the antenatal OPD till delivery. All the detailed data were collected from the delivery log book. Data was analysed statistically. The study group participated voluntarily in this study and each of them gave an informed consent. This study was approved by ethical and research committee of Dharmapuri medical college.

Inclusion Criteria:

- 100 antenatal mothers admitted to the OG Department
- Singleton pregnancy
- Gestational age < 24wks
- Reliable dates and first trimester scans

Exclusion Criteria:

- Patient not giving informed consent
- Multiple gestation
- Gestational Age > 24wks
- Wrong dates
- Family and Personal History of Dyslipidemia
- Known case of PCOS, Obese

Source Of Data :

Patients admitted to Antenatal ward and Labour ward of OBSTETRICS & GYNAECOLOGY Department, Govt Dharmapuri Medical College Hospital, DHARMAPURI.

Methodology

- Study Population Divided Into Two Groups:
- GROUP 1: who are all testing abnormal lipid profile in first and second trimester
- GROUP 2: who are all with normal lipid profile in first and second trimester

Method Of Study

- Patient history
- Baseline Investigations, including GDM specific investigation (OGCT)
- General examination
- Obstretic examination
- Expert USG Abd (Obstetrics)

Cut Off Values

	NORMAL	ABNORMAL
TG mg/dl	< 200	>200
VLDL mg/dl	< 40	>40
TC mg/dl	<200	>200
LDL mg/dl	< 130	>130

HDL mg/dl	>65	<65
BP mmofHg	110-138/72-88	140/90

Statistical Analysis

Data was expressed in terms of mean +/- SD. Chi square test was applied to estimate the difference between positive groups. Unpaired 't' test was used to study the changes in the lipid profile values.

- P value > 0.05 was taken as non significant
- P value < 0.05 was taken as significant
- P value < 0.01 was taken as highly significant
- P value < 0.001 was taken as very highly significant

RESULTS

Table - 1

GA in weeks	Abnormal	Normal
<12	12	14
12 - 24	38	36
Total	50	50
p value	0.82	Not sig

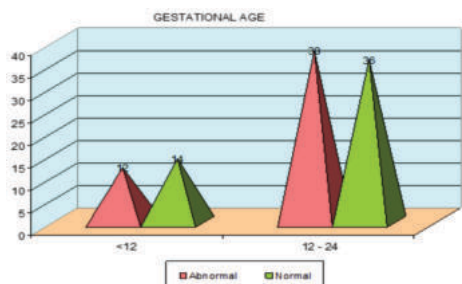


Table - 2

Past H/O	Abnormal	Normal
GDM	1	3
PIH	3	1
CVT	0	1
GHT	0	1
IUD	0	1
Nil	46	42
Total	50	49
p value	0.403	Not sig

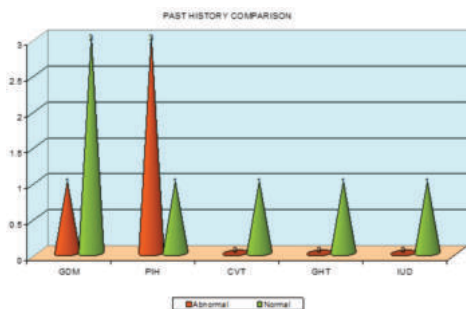


Table - 3

TG >200	Abnormal	Normal
Mean	233.36	177.1
SD	29.31	10.634
Pvalue	<0.001 Sig	

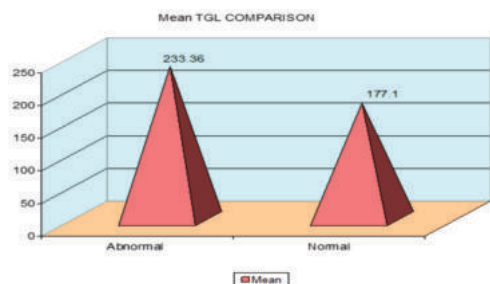


Table - 4

VLDL > 40	Abnormal	Normal
Mean	46.62	29.18
SD	4.462	4.104
Pvalue	<0.001 Sig	

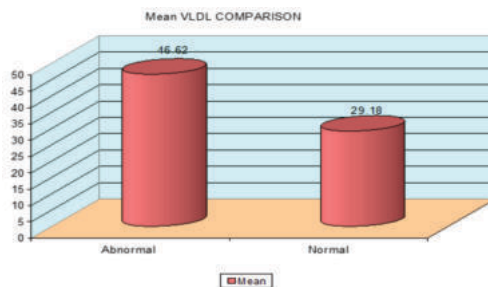


Table - 5

TC >200	Abnormal	Normal
Mean	260.3	169.52
SD	50.552	22.276
Pvalue	<0.001 Sig	

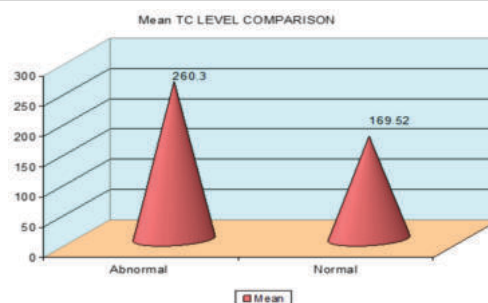


Table - 6

HDL	Abnormal	Normal
Mean	50.48	70.04
SD	4.367	2.672
Pvalue	<0.001 Sig	

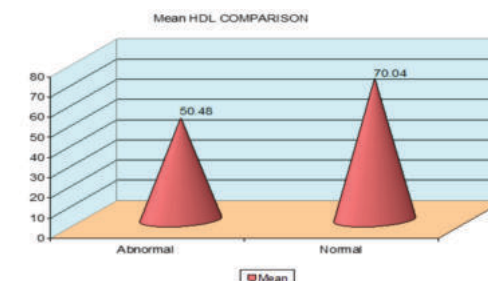


Table - 7

LDL	Abnormal	Normal
Mean	156.74	105.64
SD	17.724	17.694
Pvalue	<0.001 Sig	

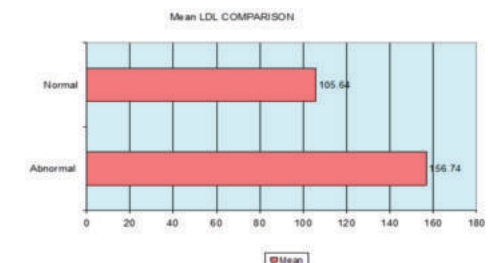


Table - 8

BP	Abnormal	Normal
<140/90	2	49

> 140/90	48	1
Total	50	50
p value	<0.001 Sig	

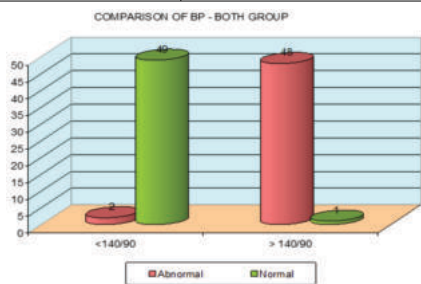


Table – 9

Maternal complications	Abnormal	Normal
Precelampsia	8	1
Eclampsia	1	1
HELLP syndrome	5	2
Total	14	4
p value	0.428	

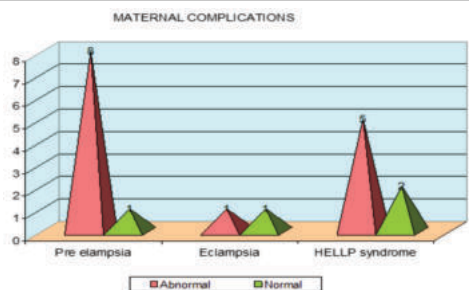


Table – 10

Fetal complications	Abnormal	Normal
IUGR	6	2
Preterm	5	1
RDS	3	1
Total	14	4
p value	0.923	

DISCUSSION

Pregnancy is the most important period in women's life, but it can be dangerous also. Hypertension and proteinuria are the important complications of pregnancy. Abnormal placentation is the one of the important pathology for the development of GHT. Because of abnormal placentation there may be increased synthesis of lipid profile. (Table-1)(figure-1)

There may be a dysregulation of lipoprotein lipase in GHT prone women, that causes elevated plasma lipid and lipoprotein levels, may induce endothelial dysfunction secondary to oxidative stress. Endothelial dysfunction is the prominent pathology, usually occurs in early trimester (8-18weeks) but signs and symptoms occur in late trimester.

In this study lipid profile estimated in early second trimester, women with elevated levels, categorized under high risk group (Table-2)(Figure-2). So it is easy to identify the high risk women and kept under regular follow up. It is help in preventing development of complication inGHT.

Study conducted in OP population in Govt. Dharmapuri Medical College Dharmapuri. It is a prospective study, conducted on 100 pregnant women who attended the antenatal OPD. All the patients screened for lipid profile in early second trimester between (14-20 weeks) and followed up till their delivery.

Normally GHT is more common in teenage pregnancies. In our study most of the GHT patient within the age group

between 26-30 years with standard deviation of 24.48 ± 2.08 years.

Other factors less strongly associated with preeclampsia include, but are not limited to:

Advanced maternal age,Family history of preeclampsia. Short duration of sexual relationship (<6 months) before the pregnancy.

Normally GHT more common in primi gravida, in our study also more number of GHT cases were primi gravida Blood pressure (140/90 mm of Hg) was used as a cut off for GHT. (Table 8)(figure-8) 58% had less than that above value, 42% had blood pressure more than 140/90 mm of Hg. GHT cases had mean SBP with SD of about 143.76 ± 5.84 and mean DBP with SD was 90.28 ± 5.53.

In our study among 100 women, 48 of them had elevated lipid profile value, among them 32 of them developed GHT. Development of GHT with p value<0.01.

In our study lipid profile showed 80% specificity & 86% positive predicting value. Similar results were obtained in Yaron et al. They shown that lipid profile had high positive predictive value of about 88%.

They concluded with that predictive value, can be used as a predictor for GHT. In our study strength of association between lipid profile and GHT is about 3.2%. In our study among 100 women, 34 of them had elevated triglycerides value, among them 22 of them developed GHT. 66 of them had triglycerides less than 200, among them only 15 women developed GHT. With that value statistical significant relationship exist between elevated triglycerides and development of GHT with p value<0.01. (Table-3)(Figure-3)

In our study elevated triglycerides value had 98% high specificity 0 & 97% positive predictive value. In Poutaet al (2000) found that significant correlation between the elevated triglycerides and development of GHT with 96% specificity. Clausen et al concluded that hypertri glycedemic dyslipidemia before 20 weeks of gestation had increased relationship with early onset GHT . They had a significant p value of about <0.01 and high positive predictive value(92%) In our study strength of association between triglycerides and GHT is about 1.8%. In our study among 100 women, 35 of them had reduced HDL value, among them 32 of them developed GHT. 65 of them had HDL more than 65, among them only 10 women developed GHT. With that value statistical significant relationship exist between reduced HDL and development of GHT with p value<0.01.

In our study HDL had 90% specificity & 86% positive predictive value. Similar results were obtained by Lima et al (1999) with 92% specificity & 88% positive predictive value.

In our study strength of association between increased HDL and preventing GHT is about 3.2%. In our study among 100 women, 37 of them had elevated VLDL value, in which 32 of them developed GHT. 63 of them had VLDL less than 40, among them only 10 women developed GHT. With that value statistical significant relationship exist between elevated triglycerides and development of GHT with p value <0.01.

In 1998 Taitalmikic researchers they foundthat there is a significant rise in VLDL value in GHT women. They did Meta analysis study in 2004; they concluded that elevated VLDL is a common finding in GHT women, in all study. They had a statistical significant value between elevated VLDL and GHT women (p<0.001). (Table-4) (Figure-4) In our study VLDL had 92% specificity, this is supported by FranZ H, Wender D (2002), they

proven that elevated VLDL had 90% specificity & positive predictive value, with that they agreed that VLDL is the one of good predictor for GHT.

In our study among 100 women, 39 of them had elevated LDL value, among them 36 of them developed GHT. 61 of them had LDL less than 130, among them only 6 women developed GHT. With that value statistical significant relationship exist between elevated triglycerides and development of GHT with p value <0.01.

In study in 150 pregnant women. In that 96 of them had elevated LDL more than 130mg/dl, among them 78 developed GHT. 54 of them had normal LDL value. In this only 10 developed GHT. With this result they proved very highly significant relationship between LDL and GHT ^{(Table-7)(Figure-7)}

In our study strength of association between LDL & VLDL with GHT was 6% & 3.2% respectively, it had proven that similar association between the LDL & VLDL with GHT. For every one unit increase in LDL & VLDL 6.8% & 4.5% there is increase risk of developing GHT in pregnant women respectively.

Induction of labour is more common in GHT. This also happened in our study, but there is no statistical significance was obtained in our study. This may be due to small sample size, variation in the gravida in total study population.

In our study 2 of them had severe pre eclampsia & 1 of them had eclampsia. Women with severe preeclampsia had high levels lipid profile particularly TGs. This study with lipid changes in pregnant women associated with the development of gestational hypertension. They concluded that women with elevated triglycerides level (> 3.0 MoM) had increased chances (17%) of developing GHT and early onset severe preeclampsia.

In our study fetal complications like IUGR and RDS are more common in GHT patients. This supported by Gonen et al & Valient et al, they found that there is increase risk of development of IUGR & RDS more common in GHT than control groups. The lipid profile was a marker of high risk for GHT & associated with small for gestational age. They did a study in 192 pregnant women. They also found that women with elevated lipid profile were associated with increased risk of IUGR baby with statistical significance value (p <0.01).

Hypertensive disorders during pregnancy affect around 8-10% of all pregnant women and can be associated with substantial complications for the woman and the baby ^{(Table-8)(Figure-8)}

Women with hypertension in pregnancy are also at increased risk of cardiovascular disease later in life. NICE guideline 133 on the management of hypertension in pregnancy aims to reduce the risks of preterm birth for the baby, ^{(Table-10)(Figure-10)} and describes treatments to prevent or delay early labour and birth ^{(Table-9)(Figure-9)}

CONCLUSION

Even in this era of advanced medical knowledge what we don't know far outweighs what we know. The case is no different with GHT, a leading killer of mothers worldwide. Despite one of the top causes for maternal mortality and morbidity very little is known about its etiology. Many studies were conducted to determine to exact sequence of events behind its presentation. Recent studies have found out that the clinical manifestation of GHT is proceeded way back by biochemical and pathological changes in the body. This is the reason why all modes of treatment except delivery are only palliative.

If we can detect these changes before hand a major share of

Maternal Mortality can be prevented. The level of lipid profile are two factors strongly associated with development of GHT. These can be used as "POWERFUL PREDICTIVE TOOL" for obstetrician for early identification and expert management. Then close monitoring of maternal and fetal status of identified cases can be done in tertiary care center like our institution resulting in a good maternal and perinatal care

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