A dissertation on

STUDY OF SERUM LIPID PROFILE IN GESTATIONAL HYPERTENSION AND PREECLAMPSIA

Dissertation submitted in partial fulfillment of

regulation for the award of

M.S. DEGREE IN OBSTETRICS AND GYNAECOLOGY

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

Chennai – 600 032.

APRIL-2014

DECLARATION

I solemnly declare that this dissertation entitled **" STUDY OF SERUM LIPID PROFILE IN GESTATIONAL HYPERTENSION AND PREECLAMPSIA"** is a bonafide and genuine research work carried out by me under the guidance of **Prof. Dr. Vathsala Devi M.D., DGO**., Associate Professor of Department of Obstetrics and Gynaecology, Coimbatore Medical College, Coimbatore.

Date: **Signature of the Candidate**

Place: Coimbatore

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This is to certify that the dissertation entitled **" STUDY OF SERUM LIPID PROFILE IN GESTATIONAL HYPERTENSION AND PREECLAMPSIA"** is a bonafide research work done by **Dr. MENAKA.V** in partial fulfillment of the requirement for the degree of **M.S. Obstetrics and Gynaecology.,** under the guidance of **Prof. Dr. Vathsala Devi,** Associate Professor of Department of Obstetrics and Gynaecology, Coimbatore Medical College, Coimbatore.

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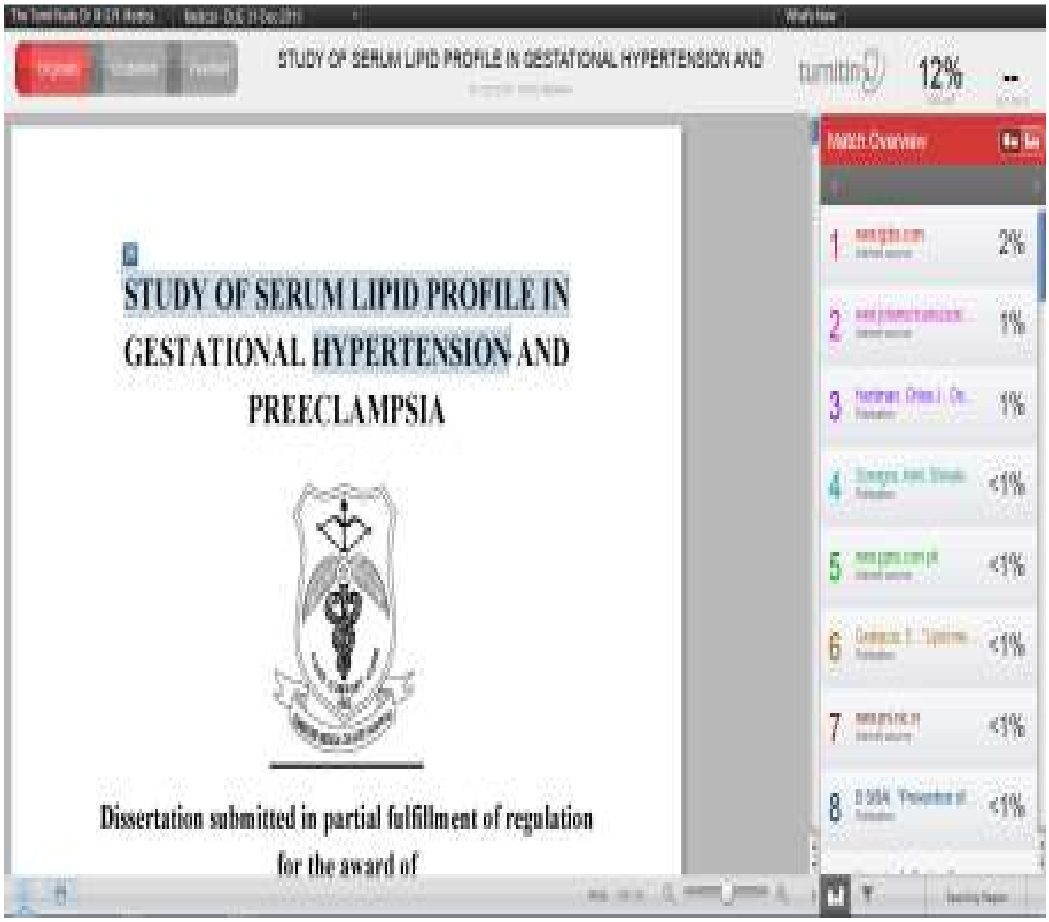
STUDY OF SERUM LIPID PROFILE IN GESTATIONAL HYPERTENSION AND PREECLAMPSIA Dissertation submitted in partial fulfillment of regulation for the award of M.S. DEGREE IN OBSTETRICS AND GYNAECOLOGY The Tamilnadu DR. M.G.R. Medical University APRIL-2014 INTRODUCTION Pregnancy is a state associated with changes in anatomy , physiology , biochemistry1 .The characteristic of normal pregnancy is developing well tolerated allograft i.e fetus , developed placenta ,increase in circulating steroids2 . As a result of this changes serial alteration in lipid profile ,mainly increase in serum triglycerides , cholesterol occurs in pregnant women. Preeclampsia is specific2,3,4 to pregnancy, multi system...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I am grateful to my family who are a constant source of inspiration and support

LIST OF ABBREVIATIONS USED

ALT	–	Alanine aminotransferase
ANOVA	–	Analysis of variance
Apo	–	Apolipoprotein
AST	–	Aspartate aminotransferase
ATP	–	Adenosine triphosphate
BMI	–	Body mass index
BP	–	Blood pressure
CETP	–	Cholesterol ester transport protein
CRH	–	Corticotropin releasing hormone
Da	–	Dalton
DIC	–	Disseminated intravascular coagulation
DNA	–	Deoxy ribonucleic acid
ECF	–	Extracellular fluid
EDTA	–	Ethylene Diamine tetra acetic acid
et al	–	and others
Flt	–	fms like tyrosine kinase
GFR	–	Glomerular filtration rate
GH	–	Growth hormone
GHT	-	gestational hypertension
H & E	–	Haematoxylin & Eosin
hCG	–	Human chorionic gonadotropin

HDL	–	High density lipoprotein
HELLP	–	Haemolysis, elevated liver enzymes and low platelet count
HMG CoA	–	3-Hydroxy-3-methyl glutaryl-coenzyme A
XI		
IL	–	Interleukin
IU	–	International unit
lb	–	Pound
LCAT	–	Lecithin cholesterol acyl transferase
LDH	–	Lactate dehydrogenase
LDL	–	Low density lipoprotein
mm of Hg	–	millimeter of mercury
PAI	–	Plasminogen activation inhibitor
PIH	–	Pregnancy induced hypertension
ROS	–	Reactive oxygen species
SD	–	Standard deviation
sFlt	–	Soluble fms like tyrosine kinase
SHBG	–	Sex hormone binding globulin
TC	–	Total cholesterol
TG	–	Triglycerides
Th	–	T helper cell
TNF-α	–	Tumour necrosis factor – alpha
TSH	–	Thyroid stimulating hormone
VLDL	–	Very low density lipoprotein

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INTRODUCTION

Pregnancy is a state associated with changes in anatomy , physiology, biochemistry[1]. The characteristic of normal pregnancy is developing well tolerated allograft i.e fetus, developed placenta ,increase in circulating steroids[2]. As a result of this changes serial alteration in lipid profile, mainly increase in serum triglycerides, cholesterol occurs in pregnant women.

Preeclampsia is specific[2,3,4] to pregnancy, multi system involvement[5,6]. It is hypertensive disorder includes new onset hypertension and proteinuria after 20weeks of gestation and resolves after delivery[2,7].

Preeclampsia is a common medical complication in pregnancy in developing countries[3,8]. It is one of the most common cause that lead to maternal and fetal morbidity and mortality[5,6,9,10]. Incidence of Preeclampsia in world is 3-5%[3]. In India preeclampsia complicates 5-15% of pregnancies[11].

Eventhough etiopathogenesis of preeclampsia remain obscure and poorly understood[13], genetic component may play a major role[12]. It includes complex pathophysiological state in which regulatory

systems of inflammation and endothelial function are altered beyond the normal physiological limits of pregnancy[14].

Endothelial dysfunction may be due to the changes in metabolism of lipoproteins[8,10]. The mechanism that lead to endothelial dysfunction is not well defined. The spectrum of endothelial changes are provoked by multiple circulating factors including altered lipoproteins .Endothelial dysfunction explains many of symptoms of preeclampsia including proteinuria[5,10].

Even in normal pregnancy there is increase in plasma lipid seen, but in normal pregnancy it is not atherogenic, may be physiological, due to hormonal control[5,8]. Whenever this mechanism of adjusting physiologic hyperlipidemia is altered that lead to complications in pregnancy[2,6,15,16]. So, In pregnancy if serum lipid profiles are estimated it helps to identify high risk cases prone for preeclampsia. Even before, some studies evaluated lipid profile in preeclampsia and relationship between lipid concentration(serumtriglycerides) and severity of preeclampsia is evaluated .In my study I included serum cholesterol, LDL-C, HDL-C also with Triglycerides.

This study was conducted in the Department of Obstetrics with the help of Biochemistry Department, Coimbatore during the period of November 2012 to October 2013.

AIMS & OBJECTIVES

AIM

1) To compare the serum lipid parameters (triglycerides, total cholesterol, LDL, HDL) of normal pregnant women with gestational hypertension and preeclampsia.

OBJECTIVES

1. To measure serum lipid profile in gestational hypertension, preeclampsia and normal pregnant women.
2. To compare serum lipid profile levels in three groups.
3. To know the role of altered lipid profile in the pathophysiology of preeclampsia.
4. To establish the relationship between serum lipid profile and preeclampsia
5. To correlate the lipid profile levels with the severity of preeclampsia.

REVIEW OF LITERATURE

The major cause of maternal , fetal morbidity and mortality is Preeclampsia. In pathogenesis of Preeclampsia, altered lipid metabolism seems important.

DEFINITION[17]

National High Blood Pressure Education Program (**NHBPEP**) 2000 & **ACOG** (2002) defines Gestational Hypertension as,

Systolic pressure of more than equal to 140 mmHg, Diastolic pressure of more than equal to 90mmHg after 20 weeks of gestation,measured 4 to 6 hours apart in a previously normotensive women.

Severe Hypertension in pregnancy is defined as,

a) Systolic BP greater than or equal to 160 mmHg or

b) Diastolic BP greater than or equal to 110 mmHg

This represents a cut off level of BP beyond which cerebral autoregulation stops functioning , because of which complications like cerebral hemorrhage and hypertensive encephalopathy may happen.

CLASSIFICATION OF HYPERTENSIVE DISORDERS IN PREGNANCY[17,18]

NHBPEP classifies as,

1. Gestational Hypertension
2. Preeclampsia
3. Eclampsia
4. Super imposed Preeclampsia on Chronic Hypertension
5. Chronic Hypertension

1.GESTATIONAL HYPERTENSION

Systolic BP of greater than or equal to 140mmHg or Diastolic BP of greater than or equal to 90mmHg without proteinuria and other imminent symptoms &signs and BP returns to normal before 12 weeks post partum.

2. PREECLAMPSIA

Systolic BP of greater than or equal to 140mmHg or Diastolic BP of greater than or equal to 90mmHg with proteinuria of more than 300mg in 24 hours i.e more than 1+ in dipstick test.

3.ECLAMPSIA

Generalised tonic clonic seizures with preeclampsia ,which cannot be contributed by other causes.

4. **SUPER IMPOSED PREECLAMPSIA ON CHRONIC HYPERTENSION**

It is diagnosed by

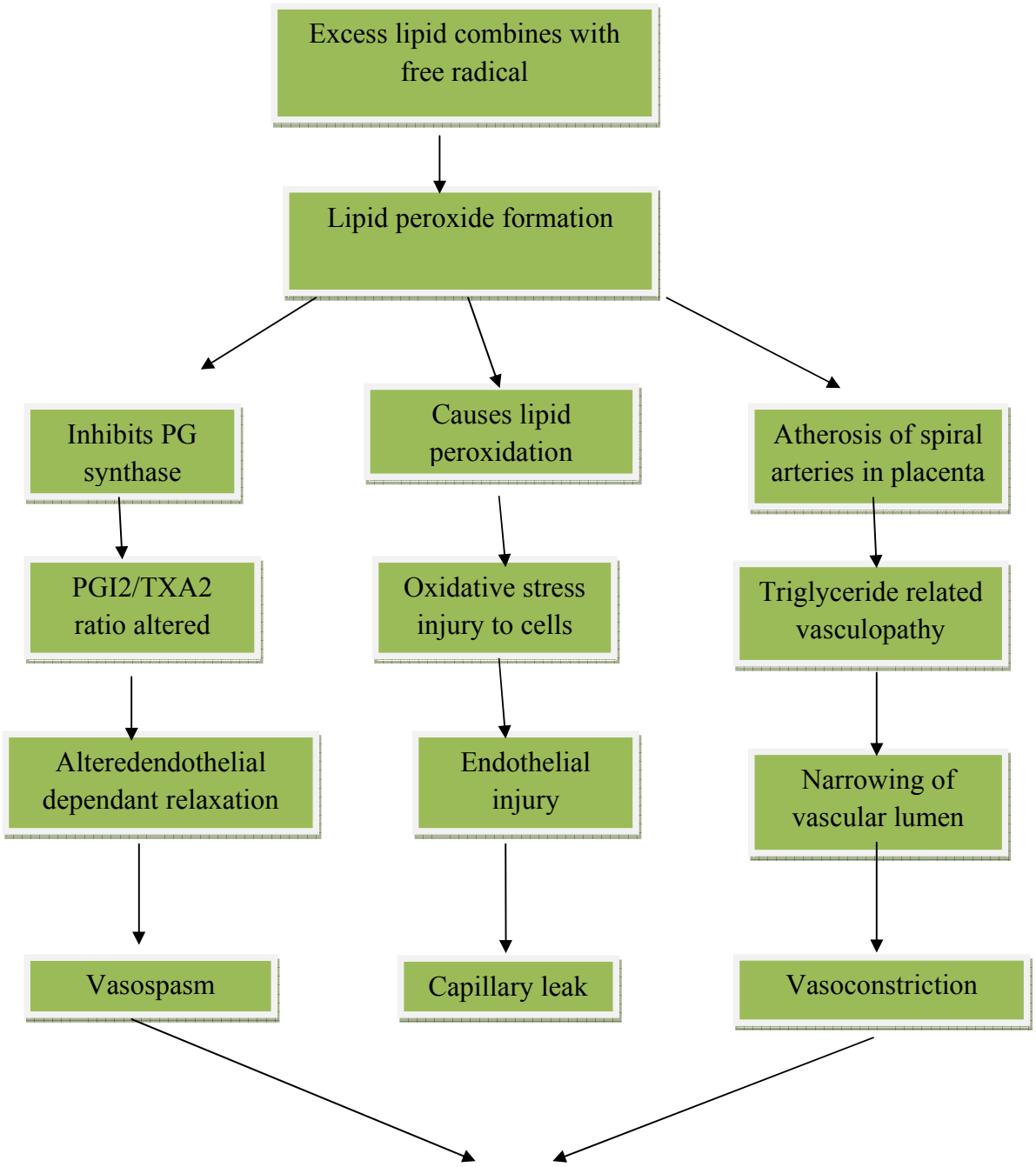
a) In chronic hypertension patient whenever there is sudden increase in blood pressure or, proteinuria, platelet count.

b) In chronic hypertension patient whenever there new onset of proteinuria of more than 300mg/24 hours.

5. CHRONIC HYPERTENSION

Systolic BP of greater than or equal to 140mmHg or Diastolic BP of greater than or equal to 90mmHg before 20 weeks not including gestational trophoblastic disease, twin . Hypertension diagnosed after 20 weeks of gestation and persisting after 12 weeks post partum.

ASSOCIATION OF DYSLIPIDEMIA AND PREECLAMPSIA



DEVELOPMENT OF PREECLAMPSIA

Figure-1.Role of altered lipid profile in the pathogenesis of preeclampsia

The changes in lipid profile are due to changes in hepatic and adipose tissue metabolism that alter circulating concentrations of TG,fatty acids, cholesterol and phospholipids and it is attributed to higher concentration of estrogen and state of relative insulin resistance[19], and also characterised by increased hepatic lipase activity and decreased lipoprotein lipase activity, leading to increase in circulating triglycerides[20]. Because of reduction in adipose tissue lipoprotein lipase activity, there is reduction in clearance of triglyceride rich lipoproteins[21].

NORMAL PREGNANCY ASSOCIATED WITH HYPERTRIGLYCERIDEMIA

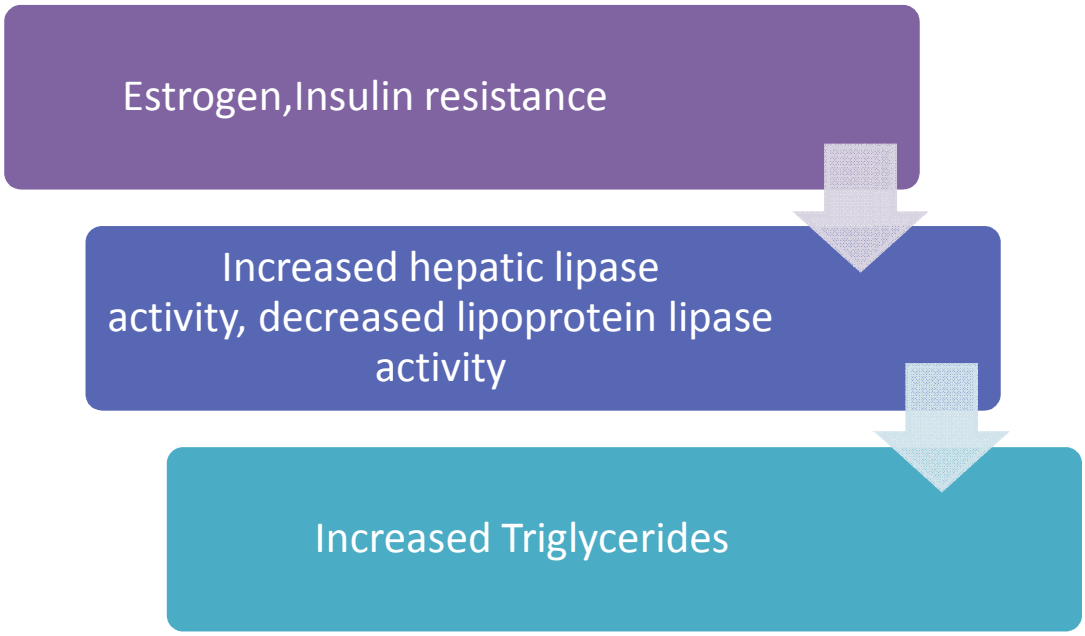


Figure-2:Cause of altered lipid profile in normal pregnancy

There was increasing evidence that in pathophysiologic mechanism of preeclampsia, lipid metabolism and circulating lipids play a major role[22], because lipid peroxides and oxidative imbalance act as cytotoxic and lead to endothelial injury. Compared to normal pregnant women ,women with preeclampsia have elevated lipid peroxides, and also severity of preeclampsia have a correlation with lipid peroxide levels[22].In particular levels of antioxidant in plasma and antioxidant activity are low in preeclamptic women. Normally lipid peroxidation was under control by variety of antioxidant mechanisms. But in women with preeclampsia, the balance of oxidant-antioxidant system was impaired. In women with preeclampsia, lipid peroxide production by placental tissue also elevated that lead to elevated concentration of lipid peroxides. Lipids interacts with oxygen free radical and forms lipid peroxide, which are unstable,highly reactive and damaging compounds[23]. They are toxic to the cells, enzymes by stimulating peroxidation reactions. In preeclampsia, the causal factor implicated is uncontrolled lipid peroxidation[24,25].

Elevated lipid peroxides act by modulating prostocyclin synthesis, alter important biochemical reactions in the cell and lead to endothelial cell dysfunction. Lipid peroxides alter the ratio between prostacyclin and thromboxane A_2 by inhibiting prostacyclin synthase[25]. In preeclampsia ,major clinical symptoms are due to this imbalance between prostacyclin

and thromboxane[23]. Lipid peroxides lead to impaired endothelial dependent relaxation by altering prostacyclin mechanism[25].In preeclampsia , proteinuria is explained by endothelial cells damage by lipid peroxides in kidney. Oxidative stress causes endothelial dysfunction.In cell membrane unsaturated lipids and thiol containing proteins are susceptible to free radical attack[24].There is lot of evidence supports that in preeclampsia , there is increased free radical activity and free radicals will cause lipid peroxidaion. Severity of preeclampsia have positive correlation with high levels of oxidation products. During pregnancy, the increase in lipid peroxides and increase in preeclampsia were confined to lipoprotein bound factors.Free&LDL bound lipid peroxides exhibit cytotoxicity on endothelial cells[24]. In preeclamptic women , atherogenic lipid profile is seen,which is characterised by increase in triglycerides and small dense LDL. Increase in triglycerides predispose to preeclampsia **by placental vasculopathy[27]**.

According to study conducted by Anne Catherine, he observed that higher concentration of phospholipid , lipid peroxides and TC in placental deciduas basalis tissue derived from women with Preeclampsia[27]. Atherosis of spiral arteries in placental layers heighten the risk of placental disease. As Preeclampsia is multicausal disease,one of the

plausible etiological factor **is 'TRIGLYCERIDE RELATED VASCULOPATHY"**[27].

In women with PIH, vascular changes in the placental bed is described as "acute atherosis" due to lipid laden macrophages (foam cells) in atherosclerotic plaque[14,17].

ACUTE ATHEROSIS:

In preeclampsia distinct pathological lesion of decidual arterioles are termed as acute atherosis. The arteriopathy involves the spiral and myometrial arteries region,where physiologic transformation changes were absent. Acute atherosis resembles atherosclerotic lesions of coronary arteries by showing endothelial disruption,platelet aggregation and accumulation of foam cells(lipid laden macrophages)[4,17]. In preeclampsia,acute atherosis of spiral areries have two outstanding features. They are vessel wall necrosis and fatty change in intimal cells,which are analogous in systemic arterial disease.

It is essential to explain why some women in pregnancy develop preeclampsia, while others not , that is because of the existence maternal predisposing factors and abnormal lipid metabolism could be one of the factor.

Alteration in lipid promote oxidative stress in preeclampsia.In pathogenesis of preeclampsia,insulin resistance syndrome, (syndrome X-includes dyslipidemia, resistance to insulin mediated glucose uptake, obesity) have an important role[4].

Multiple factors converge at particular point of oxidative stress and result in endothelial dysfunction,clinical features of preeclampsia.Primary or secondary maternal dyslipidemia lead to decrease of antioxidants results in preeclampsia[4].

Women with preeclampsia also predisposed to develop cardiovascular manifestation and coronary heart disease in later life[5].In subsequent pregnancies also, They are prone to develop metabolic and hypertensive complications[17]. In particular, if preeclampsia diagnosed early in index pregnancy,the risk of recurrence is high.This was supported by Sibai and colleagues that nulliparous women diagnosed preeclampsia before 30 weeks have 40% recurrence risk in subsequent pregnancy[16]. Compared to recurrence in nulliparous women developing preeclampsia, the recurrence risk is high in multiparous women developing preeclampsia[17]. So, to prevent maternal and fetal morbidity and mortality, preeclampsia to be predicted as early as possible.

Saleh R et al noted inflammatory and atherosclerotic lesions in the placenta of preeclamptic women[28] Presence of dyslipidemia in gestational hypertension and preeclampsia can aggravate the atherosclerotic plaque formation in uterine spiral arteries leading to narrowing of their lumen. This leads to significant reduction in the blood flow and placental ischemia thus setting up a vicious cycle of placental ischemia _ inflammation _ insulin resistance _ dyslipidemia _ atherosclerosis _ placental ischemia.

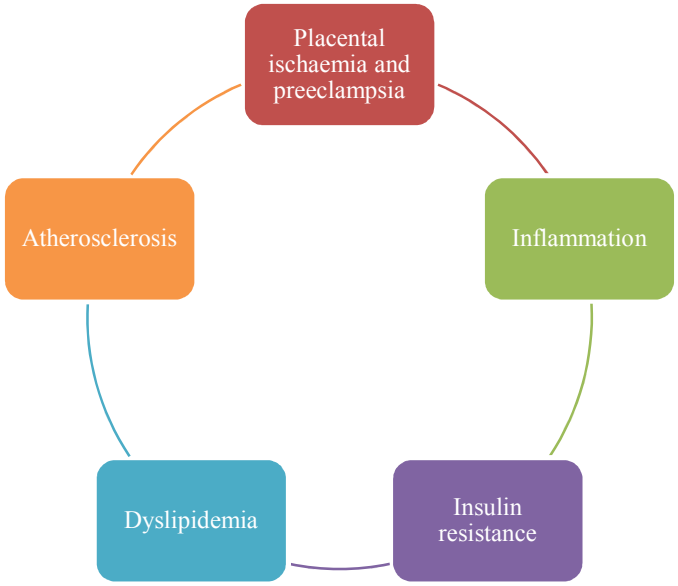


Figure-3:Dyslipidemia and preeclampsia

STUDIES RELATED TO LIPID PROFILE &PREECLAMPSIA

A study conducted in primigravida about lipoprotein subfractions by **Sattar N et al** also concluded that high triglyceride concentration in preeclampsia is a main contributor to endothelial dysfunction.

A study conducted by **Akhavan Setareh et al** and **Van den Elzen HJ et al** concluded that dyslipidemia in early pregnancy associated with preeclampsia development.**Van den Elzen HJ et al** , in his study demonstrated a significant association of diastolic BP with serum total cholesterol in first trimester and from first to late second trimester the change in systolic and diastolic BP showed linear relationship with serum total cholesterol and HDL-C[17].

According **to Akhavan Setareh et al** study,in women with serum triglyceride concentration >175mg/dl the risk of preeclampsia was13 fold more than women with triglyceride concentration<100mg/dl[13]. **Wakatsuki** concluded in his study that in preeclampsia women the plasma level of triglyceride and LDL were significantly higher than normals.According to JC Ray study,the risk of preeclampsia increase with increase in triglyceride concentration[51].According to **Cong KJ et al** study ,compared to non pregnant women the increase in lipid level didnot occur in mid trimester of pregnancy,significant increase occur in late trimester.In his study,in normal late pregnancy and mild , moderate degree of preeclampsia on significant difference in lipid levels, but in severe preeclampsia serum triglycerides was significantly higher.Type IV hyperlipidemia was seen in severe preeclampsia, because increase in serum triglyceride may result in lipid peroxide level elevation[17].

Farah Khaliq et al concluded in his study that the levels of serum VLDL-C,triglyceride were significantly increased with parity.In his study,according to parity subjects were grouped into primigravida and multiparous.In subgroups of multiparous women lipid levels were compared, there was a significant increase in VLDL-C and serum triglyceride in preeclampsia women having third or more pregnancy compared to second pregnancy. No other lipids showed significant change[2].

Risto Kaaja et al concluded in his study that in preeclampsia metabolic characteristics resemble the features of "insulin resistance syndrome" (hypertriglyceridemia, hyperuricemia, low HDL_2, hyperinsulininemia), which may result in endothelial dysfunction. In normal pregnancy, lipid profile changes are physiological because of hormonal variation[5]. According to Chiang AN et al study the levels of serum LDL-C, HDL-C, serum triglyceride, serum TC, which is physiological hyperlipidemia[18.]

According to **Belo L et al** study, there is rise in triglyceride and decrease in the size of LDL with proportional increase of small dense LDL which is atherogenic. But other studies concluded that physiological hyperlipidemia seen in normal pregnancy characterised by increase in

cholesterol, triglyceride. The alteration in levels of phospholipids, fatty acids,triglyceride,cholesterol are because of changes in adipose tissue and hepatic metabolism and they are attributed to relative insulin resistance and high concentration of estrogen[19].The rise in circulating triglyceride also explained by characteristic rise in the activity of hepatic lipase and reduced lipoprotein lipase activity[20].There is decrease in clearance of triglyceride rich lipoproteins from circulation, due to decrease in the activity oflipoprotein lipase in adipose tissue[21].

RISK FACTORS[3,11,17,18]

1. It is common in extremes of age (less than 18 years and more than 35 years.)
2. It is 2 fold more in black women compared to white.
3. Obesity
4. Inadequate diet like deficiency of Zinc, calcium, vitamins C&E and n-3 essential fatty acids.
5. Primigravida
6. In multigravida with previous history of PIH the risk increases by 40-50%.

7. Pre -existing medical disorders causing increased risk are,
   a) Chronic hypertension
   b) Hypercoagulable states like Anti-Phospholipid syndrome, Factor 5 Leiden mutation
   c) Diabetes mellitus
8. Genetic susceptibility-chromosomes 1,3,9,18 are being implicated.
9. Increased gene polymorphism in angiotensin T235 allele gene, rennin gene, IGF-2, gene involved in lipid metabolism
10. Genotype of fetus - paternally and maternally transmitted
11. Environmental factors
12. Conditions associated with large placenta like multiple pregnancy and molar pregnancy

CLINICAL FEATURES OF PREECLAMPSIA[17]

1.Hypertension:

Rise of BP greater than or equal to 140/90 mmHg,or increase in systolic BP of 30 mmHg,increase in diastolic BP of 15 mmHg.

The rise in BP is due to excess pressor substances in circulation and vascular system showing increased sensitivity to them.

2.Proteinuria:

In the 24 hours urine sample presence of protein more than 0.3 gm,or in random urine specimen more than 1+(>30mg/dl)

Glomerular afferent arterioles undergoes vasospasm lead to anoxic change and altered capillary permeability.That lead to protein leak in urine.

3.Oedema&excess weight gain:

In a week weight gain more than 1 Ib and in a month more than 5Ib in last trimester,after 12 hours of bed rest pitting edema over ankle may be earliest evidence of preeclampsia.

Decrease in osmotic pressure because of proteinuria and capillary permeability increase lead to development of oedema.

4.Epigastric pain:

In preeclampsia, there is hepatocellular necrosis that is the cause for epigastric pain. Stretching of glissons capsule and ischaemia aggravates pain.

5.Thrombocytopenia:

Due to severe vasospasm there is activation of platelet leading to platelet aggregation and microangiopathic hemolysis causes thrombocytopenia.

6.Other symptoms:

Due to cerebral hyperperfusion headache and visual disturbance(blurring of vision) develops. Because of decreased renal blood flow and GFR reduced urine output develops.

Abnormality	Mild	Severe
Diastolic BP	<100 mmHg	>110mmHg
Proteinuria	Trace to 1+	2+ or more
Headache Visual disturbance Epigastric pain Oliguria	Absent Absent Absent Absent	Present Present Present Present
Serum creatinine	Normal	Elevated
Thrombocytopenia	Absent	Present
Liver enzyme elevation	Minimal	Marked
Fetal growth restriction	Absent	Present

Table-1:Indicators of severity of preeclampsia

Preeclampsia is known as“ Disease of theories”[3]. It is associated with multiple organ involvement, multifactorial etiology, so various theories were proposed in understanding of its pathogenesis[13]. Even though exact etiology remain obsure, some most accepted hypotheses are abnormal trophoblast invasion of uterine vessels, increased vasopressor response ,vasospasm, immunological intolerance to fetus and genetic abnormalities[3].

The most common basic abnormalities consistently seen are

a) Incomplete invasion of cytotrophoblast in to spiral arteries,

b) Inflammation

c) Immunological intolerance

d) Endothelial dysfunction

A. **ABNORMAL PLACENTATION**

Placenta plays a major role in the pathogenesis of preeclampsia , as it is proved by delivery of placenta resolves this condition. Severe preeclampsia is associated with pathological evidence of placental ischaemia and hypoperfusion. This states to “Two stage theory”. That theory explains preeclampsia as a systemic disorder with

characteristic origin in the placenta and associated with maternal widespread endothelial dysfunction & vasospasm and arterial constriction lead to reduced intravascular volume compared to normal pregnancy[3].

Abnormal placentation as a cause of placental ishcaemia and hypoxia

Normally during placental development maternal spiral arteries are invaded by invasive cytotrophoblast of the fetal origin that leads to transformation of small calibre resistance vessels to high calibre capacitance vessels capable of maintaining adequate placental perfusion to growing fetus. During vascular invasion a specific process named as"**Pseudovasculogenesis or Vascular mimicry**" occurs[3,4,12] . That means differentiation of cytotrophoblast from epithelial phenotype to endothelial phenotype[3].

In Preeclampsia this event fails to occur ,so cytotrophoblast are not converted to endothelial type. At the same time invasion also shallow, so spiral arteries remain as small calibre resistance vessels. Switching cell surface molecules over the surface of cytotrophoblast fails to occur, because of that they are not able to invade the spiral arteries that lead to placental ischaemia and hypoxia[10].

This vascular remodelling process starts around 10-12 weeks of gestation and is completed by 18-20 weeks of pregnancy.This invasion extends from decidua to inner third of myometrium. But in Preeclampsia only decidual vessels are lined by endovascular trophoblasts[17] .Vessels of myometrium are not invaded, so deep myometrial vessels do not lose their endothelial lining and musculoelastic tissue, because of that vessels mean external diameter is reduced half than normal placental vessels.This lead to reduced uteroplacental blood flow and because of diminished perfusion hypoxia. Hypoxia leads to release of placental debris that creates systemic inflammatory response.

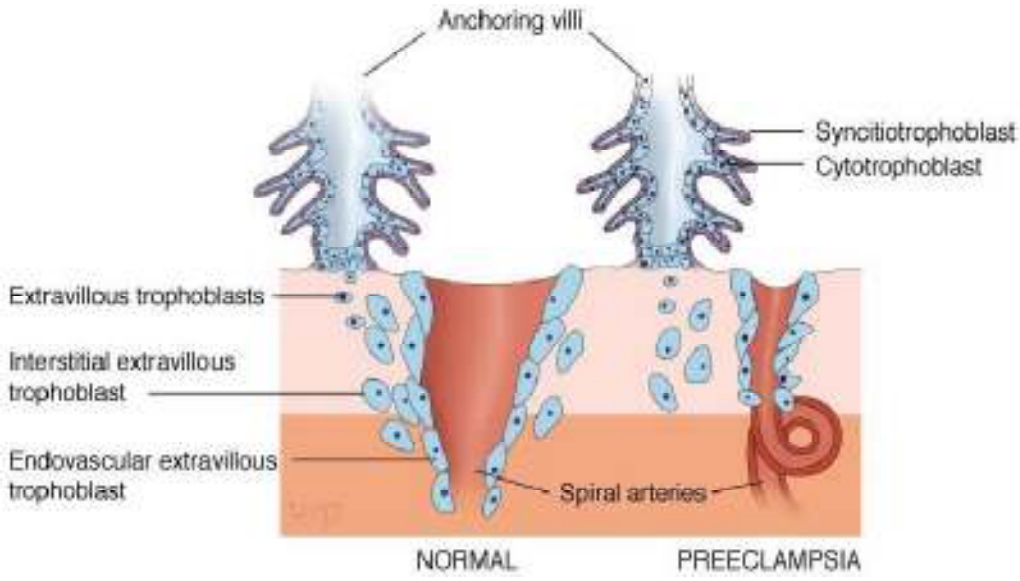


Figure-4:Difference in invasion of trophoblast among normal pregnancy&preeclampsia[17].

On examination under electron microscope fibrinoid material occludes the arteries at the implantation site and there was medial necrosis. First in the myointimal cells lipid accumulation occurs then in the macrophages. This is termed as atherosis[25].In placental stem vessels there is atheromatous changes and degeneration of endothelium,all this leads to progressive fibrosis and lumen obliteration. Placental perfusion is diminished because of all this changes and lead to preeclampsia syndrome[25]. Acute atherosis and thrombosis leads to placental infarct ,which are common in preeclampsia.

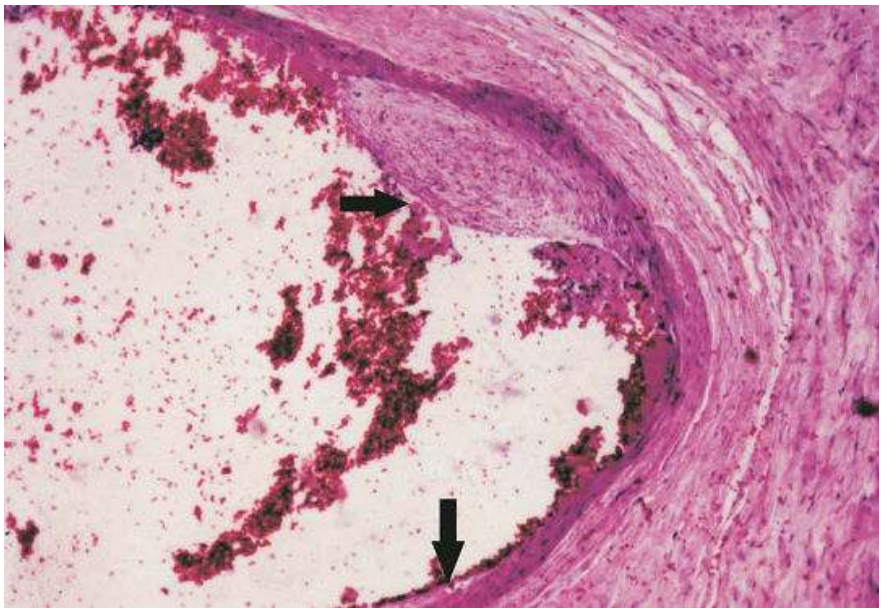


Figure-5: Endothelial degeneration and atheromatous plaque formation in umbilical vessels –Villi of preeclamptic placenta(H&EX100)[35]

Eventhough the pathology of Preeclampsia starts at placenta the ultimate target is maternal endothelium. Placental ischaemia leads to release of factors or substances into the systemic circulation that causes endothelial injury. So, in Preeclampsia many serum markers of endothelial activation and dysfunction like platelet derived growth factor(PDGF), endothelin, soluble tissue factor, soluble E-selectin, cellular fibronectin, von willebrand factor are deranged[17].

2.**Inflammatory changes of normal pregnancy**[17]

In normal pregnancy:

a) There is reduction in the synthesis and secretion of inflammatory cytokines.

b) Placenta secretes angiotensinase enzyme that destroys Angiotensin-2 .

c) There is increased vascular synthesis of VEGF, (PGI_2) Prostacyclin & nitric oxide (NO), the potent vasodilators and inhibitors of platelet aggregation. Because of this changes vascular system shows decreased response to pressor agent.

In Hypertensive disorders of pregnancy:

a) Because of decrease in activity of Angiotensinase enzyme, there is increase in half life of Angiotensin-2 occurs. The sensitivity to Angiotensin-2 also increases.

b) Activated leucocytes release inflammatory mediators like TNF-a&IL-6 that substances act directly and also indirectly by inducing oxidative stress cause endothelial injury.

c) Human endothelium produces potent vasoconstrictors like endothelin. Even though in normal pregnancy itself their levels are elevated, in Preeclampsia levels are very much higher than normal pregnancy.

d) In Vascular syncytiotrophoblast and endothelial cells L-Arginine synthesizes nitric oxide. Nitric oxide is a potent vascular smooth muscle relaxant ,inhibitor of platelet aggregation. It also prevents thrombosis in intervillous space.

e) In platelet, there is increased synthesis of vasoconstrictors like thromboxane A_2 , but reduced synthesis of vasodilators like prostocyclin.

The sum of over all changes is increase in vasoconstrictors & decreased vasodilators and elevated response to pressors. All this leads to platelet aggregation and endothelial dysfunction.

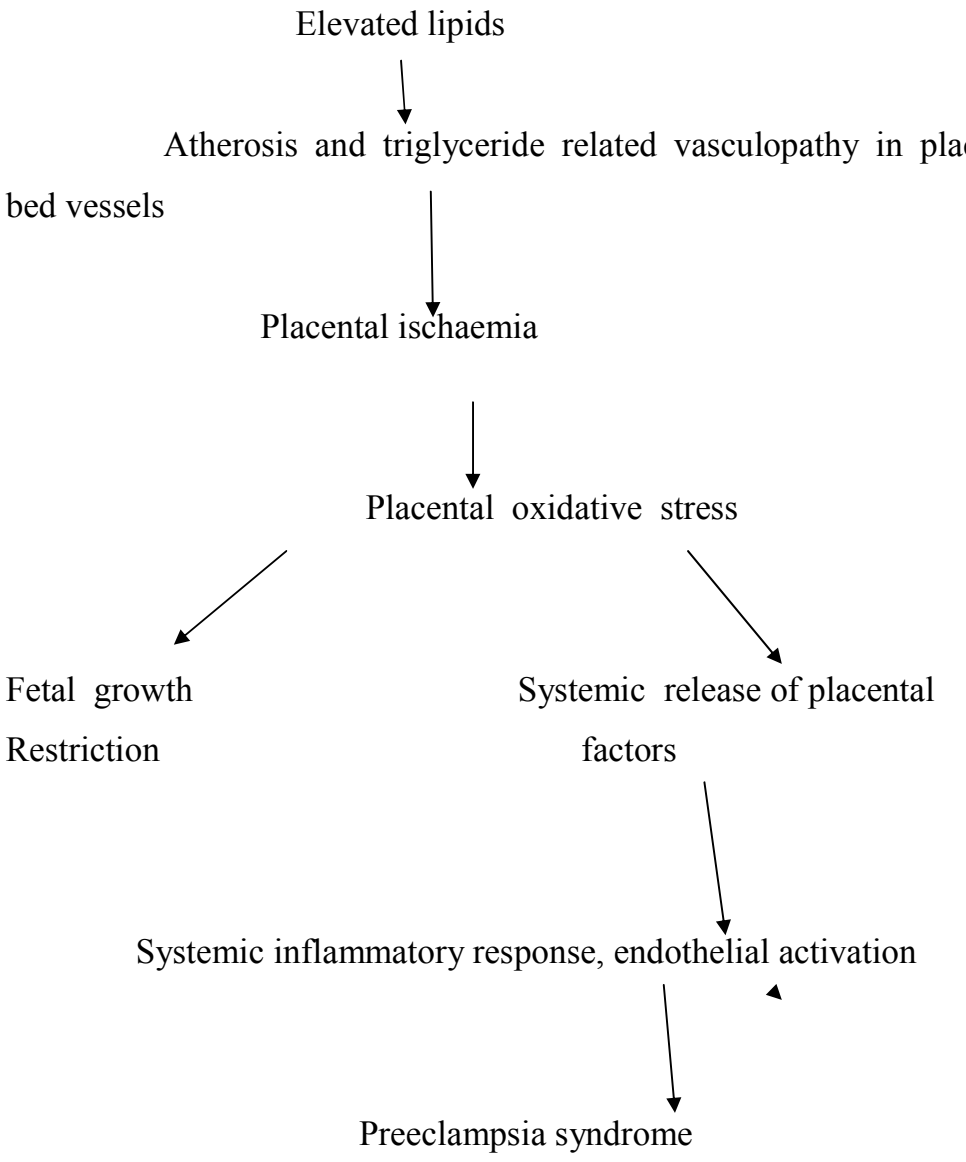


Figure-6:Role of dyslipidemia in development ofpreeclampsia

3.**Immunological intolerance**[17]:

Compared to normotensives women destined to develop preeclampsia have lower proportion T-Helper cells in eary second trimester itself. There is imbalance in Th1/Th2 ratio . There is predominance of Th1 cells, that leads to secretion of cytokines which causes inflammation.

The maternal immune tolerance to paternally derived placental or fetal tissues are dysregulated and lost, that lead to changes at placental surfaces which is suggestive of acute graft rejection. The ratio of maternal blocking antibodies to placental antigenic sites and fetal antigenic sites are not in balance in preeclampsia. In support of this, the incidence of preeclampsia is more in multiple pregnancy, molar pregnancy (excess of fetal antigenic load) and nulliparity (absence of blocking antibodies).So in immune suppressed states and in consanguineous marriages the incidence is decreased.

4.Endothelial dysfunction:

In several tissues including kidney and placenta to maintain endothelial health VEGF and TGF-b1 are needed. The regulators of vascular hemostasis in normal pregnancy are VEGF ,TGFb1. Levels of VEGF ,TGE-b1 are decreased in preeclampsia because of excess

secretion of S-flt and S-eng. Production of nitric oxide and prostacyclin also reduced. All this changes lead to endothelial dysfunction.

At the site of endothelial injury,

1. Increased membrane permeability
2. Increased procoagulants synthesis, decreased anticoagulants synthesis
3. Promotion of platelet aggregation
4. Clot formation, vasospasm

This is mechanism operating in both preeclampsia and atherosclerosis.

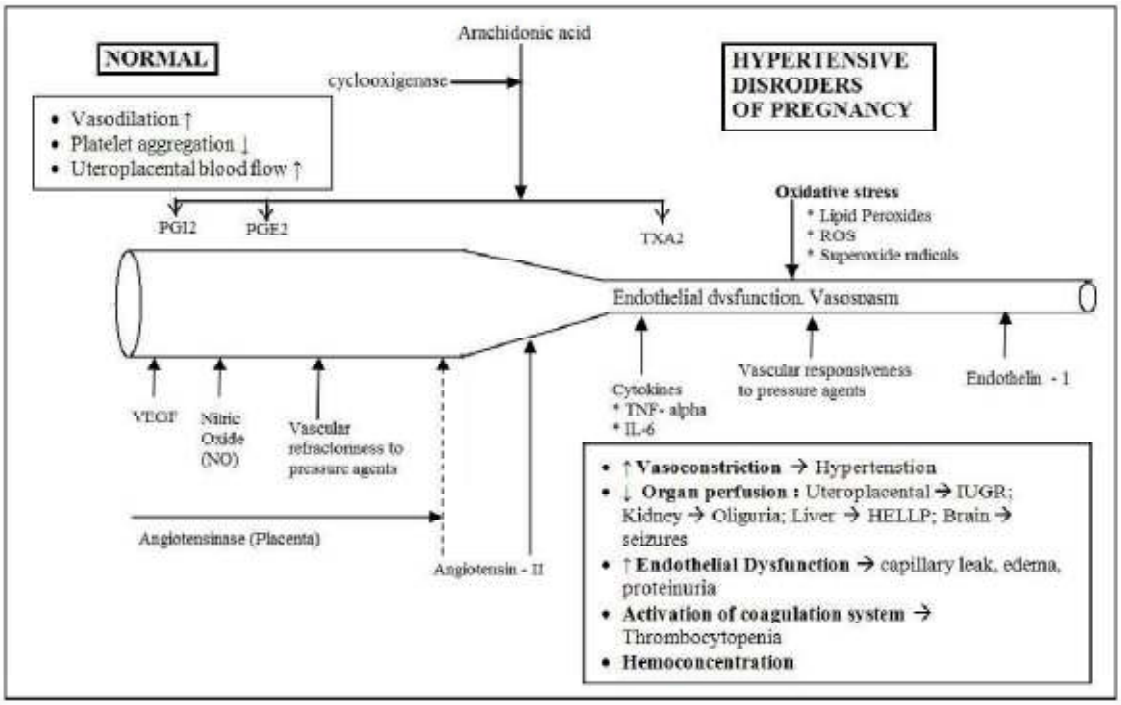


Figure7-: In Hypertensive disorders of pregnancy,pathophysiological role of endothelial dysfunction[32]

In pathogenesis of preeclampsia, role of lipids in endothelial dysfunction

One of the predisposing factor in mother that lead to development of preeclampsia is constitutional lipid abnormalities[14]. Lipid metabolism abnormality is not a mere manifestation,but various lines of evidence indicate that it is involved in pathogenesis of preeclampsia.Oxidative stress due to lipid causes hyperstimulation of endothelium which may lead to dysfunction and damage.

In most recent studies it was stated that women in first and second trimester there is elevation of triglycerides and free fattyacids.In vitro experiments reported in preeclampsia plasma the endometrial stimulatory activity depend on lipid fraction.Recent studies shown that there is predominance of atherogenic small dense low density lipoprotein(LDL) in preeclampsia women,which is characteristic of atherosclerosis[14]

The association between endothelial dysfunction and lipids in preeclampsia could be oxidative stress.By different enzymatic process freeradicals are generated.Free radicals are extremely reactive and they interact with polyunsaturated free fattyacids & produces lipid peroxide.

PATHOLOGICAL CHANGES IN DIFFERENT SYSTEMS[32]

Various significant changes in different organ systems in body takes place in gestational hypertension and preeclampsia.

1.BRAIN:

In hypertensive disorders of pregnancy brain damage is explained by two theories.

a) Because of extravasation of plasma through endothelial capillary leak during sudden increase in systolic BP

b) Vasospasm due to cerebral autoregulation during sudden rise in BP lead to cerebral ischaemia,ifarction,oedema.

This changes causes headache,blurring of vision, convulsion, confusion, coma.

2.CARDIO VASCULAR SYSTEM:

Because of vasoconstriction and hypertension causes increase in afterload and due to expansion of blood volume increase in preload occurs,all this changes predispose to increase in left ventricular mass.Conducting system may affected due to changes in the myocardium like necrosis at focal areas and hemorrhage that may lead to cardiac failure.

3.KIDNEY:

In kidney characteristic change known as "Glomerular endotheliosis" occurs.It consist of swelling of endothelium,cytoplasm hypertrophy and vacuolization.Due to this changesthere is reduction in renal blood flw,GFR,tubular absorption and secretion occurs.

4.LIVER:

From areas of infarct hepatic hemorrhage may extend and forms various degrees of ischaemic damage,periportal hemorrhage,thrombosis of portal vessels,subcapsular hematoma.Elevation of liver enzymes ocuur due to necrosis of parenchyma.

5.HELLP SYNDROME:

In severe preeclampsia HELLP syndrome occurs,due to hepatocellular necrosis.The components of HELLPsyndrome are hemolysis(intra vascular).rise in liver enzymes,thrombocytopenia.

6.BLOOD AND COAGULATION:

Various changes occuring in this system are there is increase in formation of intravascular thrombin and decrease in platelet count and its life span and rise in thromboxane A_2 due to excess degranulation. Endothelium releases PAI and fibronectin that lead to DIC.DIC is

characterised by thrombocytopenia due to platelet consumption and decrease in hemoglobin,schistocytes in peripheral smear due to microvascular hemolysis.

7.DYSLIPIDEMIA AND INSULIN RESISTANCE[34]:

There is decrease response to circulating insulin by liver,muscle,adipose tissue.Normal pregnancy is characterised by increase in insulin levels and peripheral resistance to insulin.Due to hormonal changes like rise in estradiol,progesterone,cortisol,human placental lactogen there is insulin resistance,which is maximum in third trimester.In preeclampsia,this changes are exaggregated as evidenced by various biomarkers like leptin,decreased sex hormone binding globulin,PAI-1. Changes in lipid profile occurs due to insulin resistance. That leads to atherogenic lipid profile which is characterised by rise in the total cholesterol,free fatty acids, triglycerides, small dense LDL and reduced HDL cholesterol. In the pathogenesis of preeclampsia atherogenic lipid profile plays a vital role.

8.ENDOCRINE SYSTEM[36]:

Because of enlargement of pituitary there is increase levels of growth hormone occurs. Placental growth hormone which is secreted by

syncytiotrophoblasts, the difference between the two is 13 amino acid residue. Insulin resistance is determined by placental growth hormone.

Due to glandular hyperplasia and vascularity increase there is enlargement of thyroid gland. In pregnancy HCG levels are also increased. Due to structural similarity between HCG and TSH there is increase in thyroid hormones(T_3,T_4) occurs that leads toinsulin resistance.

In Preeclampsia there is increase in levels of aldosterone,ANP and cortisol seen.Vascular system shows increased sensitivity to renin and angiotensinII.

PREDICTORS FOR PREECLAMPSIA[36,37]

There are various biochemical and clinical tests are proposed for prediction in early pregnancy. Even though various test are available, there is no simple, reliable and valid screening test.

Predictors are classified as:

a. Non - laboratory methods.

b. Laboratory methods.

a . Non laboratory methods:

1. History & Examination

- Nulliparity
- Past history or family history of hypertensive disorder

2. Blood pressure monitoring:

Mean arterial pressure in early pregnancy

3. Pressor Tests:

a) Roll over test:

After measuring BP in lateral position, Patient is asked to rolled over to supine position. The test is said to positive when there is rise of 20mmHg or more than normal. But it has poor sensitivity and specificity.

b) Isometric exercise (Hand grip) test:

In hand grip test the increase in systolic BP of 15mm Hg predicted the development of preeclampsia with high sensitivity(81.8%) and specificity (68.4%). But the test has poor reproducibility.

c) Angiotensin sensitivity test:

It is a screening test based on degree of sensitivity to angiotensin. The patient are destined to develop to preeclampsia may have abnormal vascular reactivity. That may be detected several weeks before manifestation of disease. In this test to raise the BP

to 20mmHg the dose of angiotensin-2 needed is calculated. This test also has low sensitivity and specificity.

3. Doppler velocimetry:

To evaluate diminished placental perfusion and uterine artery resistance Doppler examination of uterine and umbilical arteries are used.

b) Laboratory tests:

1. Micro albuminuria:

Urinary excretion of albumin more than 300 mg in 24 hours is labelled as micro albuminuria. Detection of microalbuminuria in second trimester is a good predictor.

2. Urinary calcium /creatinine ratio:

Preeclampsia is associated with hypocalciuria, due to increased tubular reabsorption and decreased renal filteration. So, decreased calcium/creatinine ratio is seen in preeclampsia. The sensitivity of this is 70% and specificity is 95%.

3.Serum uric acid :

Preeclampsia is associated with reduced glomerular filteration, increased tubular reabsorption, decreased tubular secretion. So serum

uric acid level are elevated in preeclampsia. But it is not sensitive and specific.

4.Serum Fibronectin:

Following endothelial injury, endothelial cells release fibronectin which is a glycoprotein and constituent of connective tissue& basement membrane involved in cellular adhesions. In normal pregnancy during third trimester 20% rise in serum level occurs. But in preeclampsia the rise is more.

5. Serum Antithrombin:

Even though the levels of Antithrombin are reduced in preeclampsia, there is overlap in levels in between hypertensive and normotensive.

6.Free fetal DNA:

The main component involved in pathogenesis of preeclampsia are endothelial activation, placental ischaemia and inflammation all lead to apoptosis. Because of accelerated apoptosis free DNA are released in circulation.

7. Oxidative stress:

As preeclampsia is associated with vasospasm, there is oxidative stress that leads to increased lipid peroxides.

8. Homocysteine:

Preeclampsia is associated with hyperhomocystinemia that causes endothelial damage & oxidative stress.

9. Cytokines:

Preeclampsia is associated with elevation of cytokines which are released by vascular endothelium and macrophages , leucocytes. But they are non specific because they are also elevated in inflammatory diseases and infections.

10. Coagulation activation:

Because of endothelial injury,vasospasm and platelet aggregation preeclampsia is associated with platelet dysfunction and thrombocytopenia.

COMPLICATIONS OF PREECLAMPSIA[17]

a. Accidental Hemorrhage

b. Acute renal failure

c. Cerebro vascular accid

d. HELLP syndrome

e. Microangiopathic hemolytic anaemia

f. Acute lef tventricular failure with pulmonary edema

g. Eclampsia

h. Aspiration pneumonia

i. Preterm labour

j. Sepsis &Shock

k. Recurrence of Preeclampsia in next pregnancy

l. Metabolic syndrome at later life-They are prone for diabetes, Hypertension at later life

FETAL COMPLICATIONS

a. Intra uterine death

b. Prematurity

c. Intra uterine growth restriction-due to chronic placental insuffiency. The duration of hypertension is more important than the level of blood pressure.

d. Neonatal encephalopathy-The link between preeclampsia and neonatal encephalopathy is a systemic inflammatory response secondary to oxidative stress.

e. Antepartum and intrapartum asphyxia due to impaired placental flow lead to anoxia

PREVENTION OF PREECLAMPSIA

METHODS PROPOSED TO PREVENT PREECLAMPSIA

1. Salt restriction
2. Antioxidants
3. Fish oil supplementation
4. Calcium supplementation
5. Low dose aspirin
6. Heparin

1.SALT RESTRICTED DIET

Though the earliest research efforts proposed that restriction of salt prevent the development of preeclampsia,but recent studies proved that it is ineffective in preventing the development of preeclampsia[45]

ANTIOXIDANTS

Preeclampsia is associated with increased oxygen free radical and decreased antioxidants. The level of oxygen free radical are decreased byantioxidant vitamins like vitamin-C, vitamin-E. But the levels of this vitamins are decreased in women at risk for developing preeclampsia. So,to increase the oxidative capacity vitamin-C, vitamin-E are provided.

Recent trials proved that antioxidant supplementation in antenatal women does not decrease the incidence of preeclampsia compared to placebos.

However two recent studies **(Poston et al and Rumbold et al 2006**) on role of Vit C(1000 mg)and Vit E 400 IU per day have shown little benefit and potential for harm[53,54].

3. FISH OIL SUPPLEMENTATION

It is the common dietary source of alpha-linoleic acid (ALA), eicosapentaenoic acid (EPA). It was supplemented with the

proclamation that , these fatty acids would prevent atherogenesis due to inflammation. But recent studies showed that no beneficial effect on supplementation.

Makrides et al (2001) have clearly shown insufficient evidence it for prevention of preeclampsia[46].

4.CALCIUM SUPPLEMENTATION

Women who consume low calcium diet are at risk of developing preeclampsia, was postulated by studies performed outside united state at1980's. Number of trials regarding calcium supplementation proved that supplementation has no salutary effects unless women is calcium deficient.

Some studies have shown decreased incidence of preeclampsia with calcium supplementation of 1.5-2 gms/day. Historically also a relationship between calcium deficiency and preeclampsia was suggested**. (Villar et al 2006)[51]**

Recently Cochrane systematic review noted protective effects of calcium supplementation only in women with low calcium intake **(Hofmeyr 2000[52]).WHO(2006**) published results of a large multicentric randomized place to controlled trial of calcium supplementation in pregnant subjects with lowcalcium intake(<600 mg/day).

Supplementation with1.5 gm of calcium/day did not result in statistically significant decrease in overall incidence of preeclampsia.

5.LOW DOSE ASPIRIN

There is inhibition of synthesis of thromboxane (TXA_2)in platelet by low dose aspirin, but action on PGI_2 is minimal. Dose is 50 to 150 mg daily.In meta analysis of 31 randomised trials the women consumed aniplatelet agents the relative risk of preeclampsia reduced significantly by 10%. Paris Collaborative Group trial - (**CLASP, 1994; COMMARASAMY A 2003 ; CARBILLON 2005)** showed that the use of aspirin decrease the relative risk of PIH by 10 percent[48,49,50].

6.HEPARIN

Because of high prevalence of placental thrombotic lesions found withsevere preeclampsia, there have been several trials to evaluate heparin treatment for affected women. Prophylaxis with loe molecular weight heparin plus low dose aspirin on pregnancy outcomes in women with a history of severe early onset preeclampsia and low birth weight infants. There were better pregnancy outcomes in women given low dose aspirin plus low molecular weight heparin compared with those given low dose aspirin alone[47].

SERUM LIPID PROFILE

LIPOPROTEINS:

Lipoproteins are spherical particles with free or non-esterified cholesterol and triglycerides on their surface as amphipathic coat and core contains triglycerides and cholesterol esters which are hydrophobic lipids.

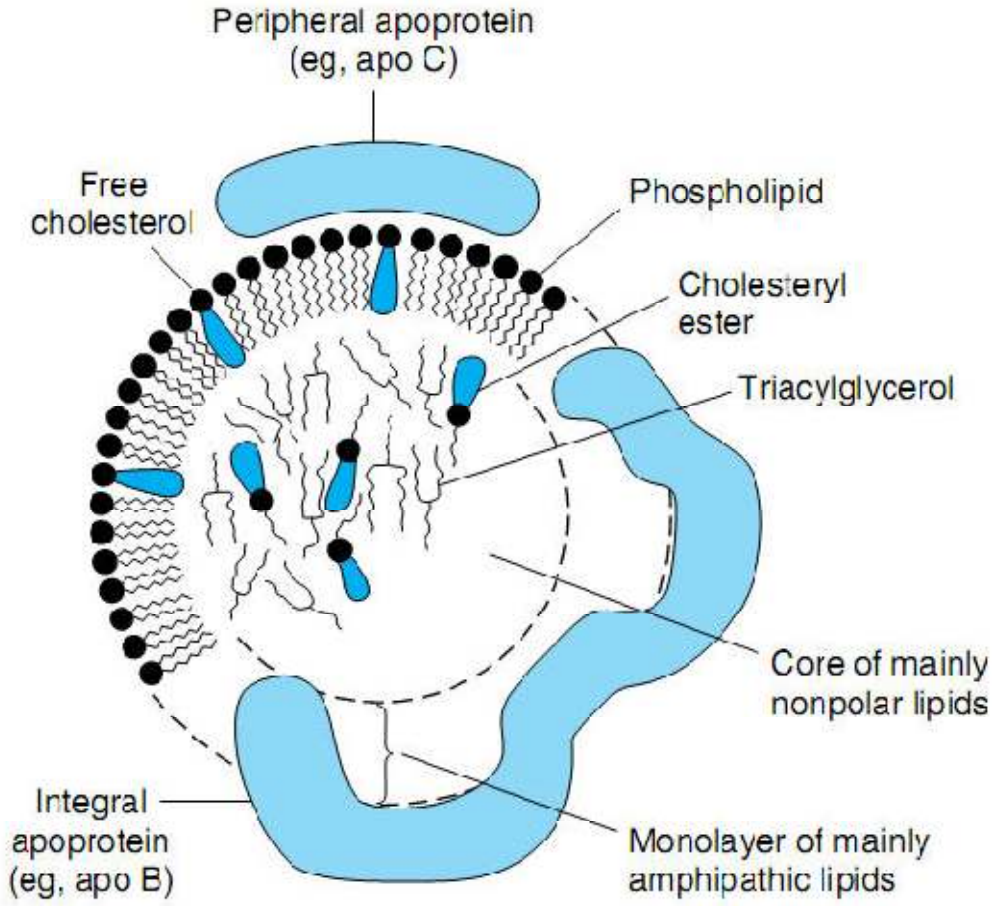


Figure-8 Structure of lipoprotein[55]

Classification of lipoproteins:[57]

Lipoproteins are mainly classified into five groups according to their density on ultracentrifugation and their mobility on electrophoresis.

- Chylomicrons
- Very low density lipoproteins (VLDL)
- Intermediate density lipoproteins (IDL)
- Low density lipoproteins (LDL)
- High density lipoproteins (HDL)

1.CHYLOMICRONS:

Chylomicrons are made of mainly triglycerides with cholesterol and specific apolipoproteins ApoB-48,ApoA-1,A-2,C-1,C-2,C-3.

Metabolism:

In intestine synthesis of chylomicrons takes place. By chyomicrons exogenous/dietary triglycerides are transported to skeletal muscles and adipose tissue and dietary cholesterol are transported to liver.

In intestine fat in diet are converted to monoglycerides and free fatty acids and absorped in to villi. In villi they are converted to triglycerides. In golgi apparatus and smooth endoplasmic reticulum triglycerides combined with cholesterol esters.In rough endoplasmic reticulum ApoA-I ApoA-II and ApoB-48 which are combined with lipids and form chylomicrons in intestinal cell. This chylomicrons are absorped in to lymphatics and thoracic duct then to systemic circulation. While in circulation chylomicrons combined with ApoE and Apo C and form mature chylomicrons.

Through systemic circulation they enter peripheral tissues. ApoC-II activates lipoprotein lipase present in capillary endothelial cells which causes hydrolysis of triglyceride core of chylomicrons leaving chylomicron remnants. During hydrolysis phospholipids ,cholesterol and ApoC from the surface are transported to HDL particle.

Cholesterol ester, ApoB-48 and ApoE are present in chylomicron remnant. ApoE is responsible for chylomicron remnant uptake by high affinity hepatic receptors. Hepatic lysosomes Cholesterol ester, Apo B-48 and ApoE are present in chylomicron remnant. ApoE is responsible for chylomicron remnant uptake by high affinity hepatic receptors. Hepatic lysosomes degrades it. Chylomicron remnant are having atherogenic potential.

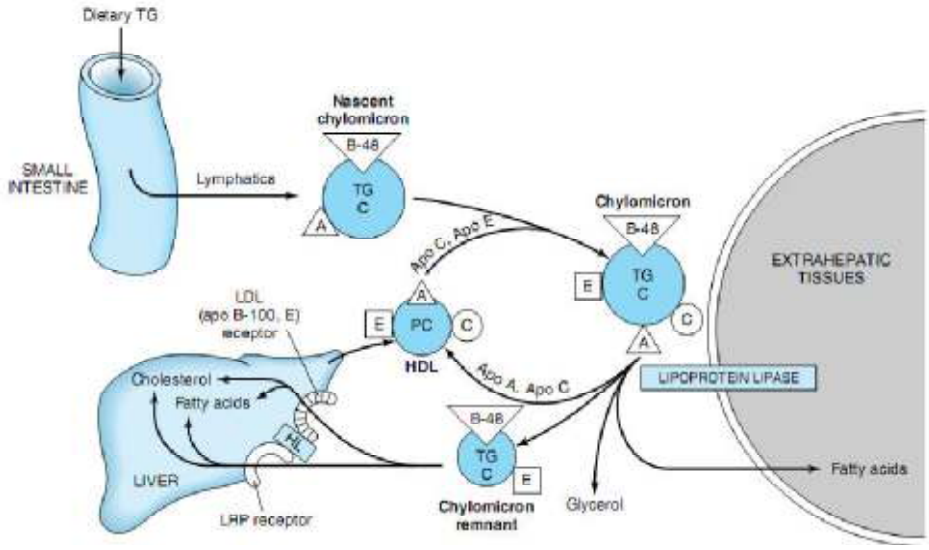


Figure-9 Chylomicron metabolism[58]

2.VERY LOW DENSITY LIPOPROTEINS[56,59]:

Triglycerides, cholesterol, phospholipids and proteins are present in VLDL. Apo B-100,C-I,C-II,C-III,Apo-E -II,E-III and E-IV are apoproteins present in VLDL[59].

Metabolism:

In peripheral tissues glucose and chylomicron remnant-TG are not hydrolysed, which are utilised for hepatic VLDL-TG synthesis. This is evidenced by post prandial rise in chylomicron-TG and a secondary rise in triglyceride concentration 4-6 hours after meal[59].

TG, cholesterol, Apo B-100, Apo E and Apo C are present in nascent VLDL . Apo C-II on VLDL's surface activates lipoprotein lipase present on endothelial cells, which causes hydrolysis of VLDL-TG and releases free fatty acids.

VLDL particles are converted to VLDL remnants because of transfer of Apo C to HDL during hydrolysis. Thus formed VLDL remnant are known as intermediate density lipoproteins.

3. INTERMEDIATE DENSITY LIPOPROTEIN(IDL)[59]:

During VLDL catabolism IDL are derived. Through Apo-E mediated process IDL are taken by liver. Lecithin cholesterol acyl transferase(LCAT) in plasma catalyses esterification of free cholesterol of HDL with fatty acids derived from lecithin which is major phospholipid in plasma membrane. Through the action of plasma cholesterol exchange protein this newly synthesized cholesterol is transferred to IDL .Most of original TG core of VLDL are replaced with cholesterol ester.

IDL particle from capillary wall are released in to circulation after hydrolysis. Then because of further conversion remaining TG's and apolipoproteins except Apo B are lost lead to production

of LDL which contains pure cholesterol ester in the core and Apo B at the surface.

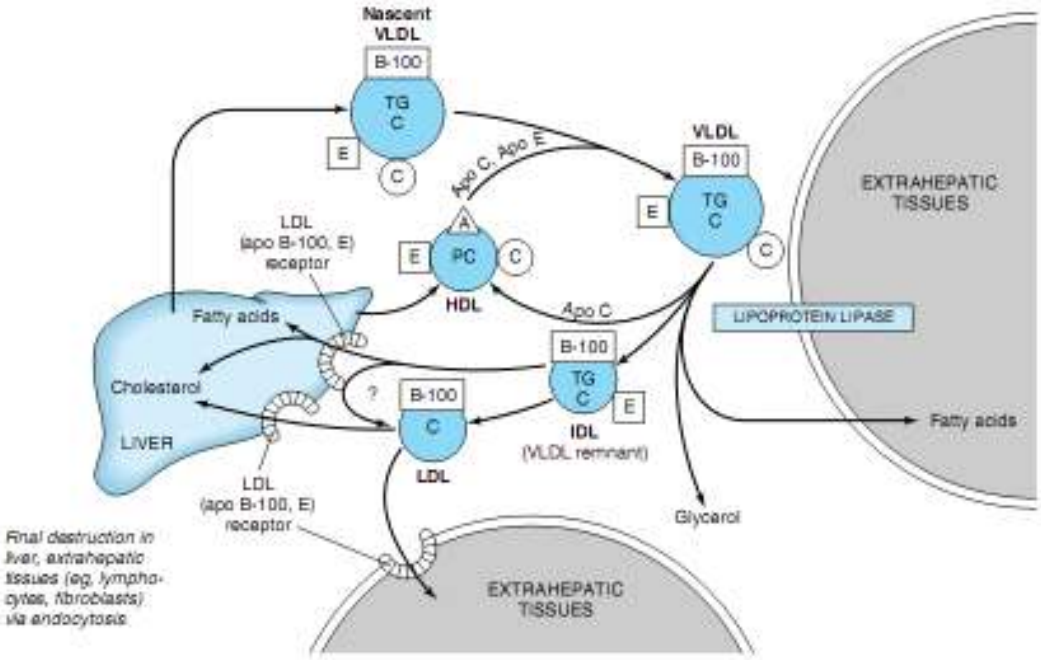


Figure-10 Metabolic fate of VLDL and LDLproduction[55]

4.LOW DENSITY LIPOPROTEIN(LDL)[59]:

Cholesterol, phospholipids and triglycerides are component of LDL. LDL is major carrier of cholesterol which formed from breakdown of VLDL. LDL is the atherogenic lipoprotein. LDL-B (small dense particles) and LDL-A(large buoyant particles) are the two sub fractions of LDL.

Compared to LDL-B which are formed from LDL-A ,LDL-A contain more cholesterol ester .Higher small dense LDL particles in plasma makes the patient more prone for preeclampsia[60] .

Metabolism:

Delivery of cholesterol to extra hepatic tissue and liver is by LDL.

LDL binds to clathrin coated pits which are high affinity receptors present at extra hepatic tissues. After binding endocytic vesicle are formed by invagination of pits into the cell. Endocytic vesicle fuse with lysosome and LDL released from receptor because of acidic pH. In lysosomes degradation of Apo B to small peptides and aminoacids and degradation of cholesterol takes place. For the synthesis of cell membrane and steroid hormones the cholesterol liberated are used.

The cholesterol supplied is regulated at cellular level. Increased level of cholesterol lead to:

a) Activation of enzyme acyl cholesterol acyl transferase (ACAT) and increased formation cholesterol ester occurs.

b) Inhibition of HMG CoA reductase and decreased rate of endogenous cholesterol synthesis.

c) Suppression of gene transcription causes inhibition of synthesis of new LDL receptors[56].

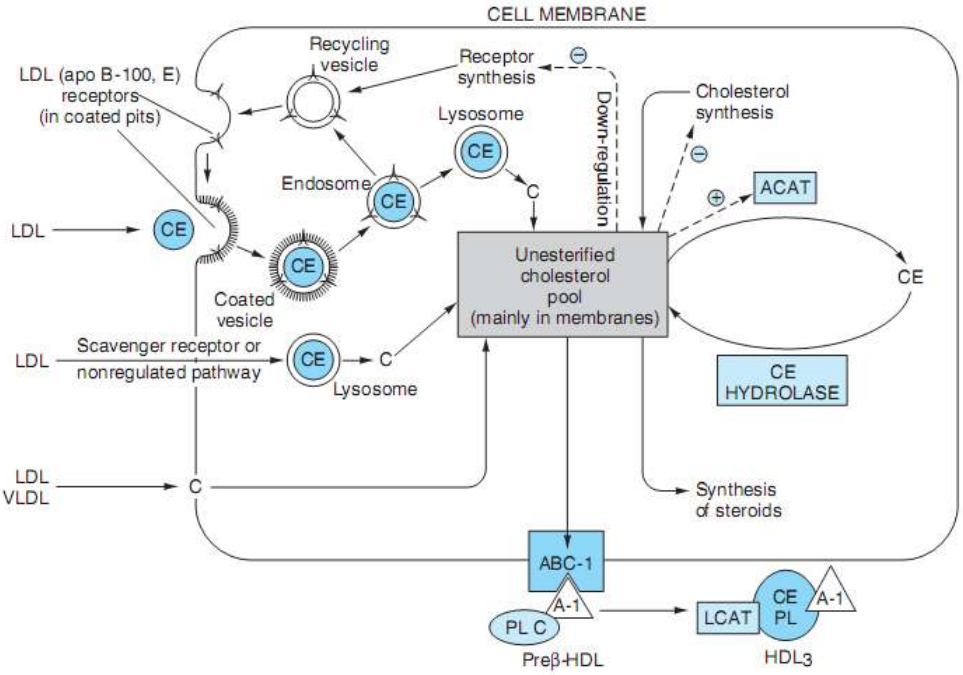


Figure-11: Factors affecting cholesterol balance at the cellular level[61]

5. HIGH DENSITY LIPOPROTEINS:

Smallest and densest of the lipoproteins is HDL because of it's high protein content which forms 50% of it's mass. Among the total protein content 70% formed by Apo A-I which plays a major role in esterification of cholesterol catalysed by Lecithin cholesterol acyl transferase[59].

In liver and intestine synthesis of HDL takes place. In liver synthesis of Apo C and Apo E takes place, which are required for chylomicron and VLDL mechanism, HDL acts as a repository for them.

The component of nascent HDL is discoid phospholipid bilayer which consist of Apo-A and free cholesterol. Apo-A I activates LCAT, which converts surface phospholipids and free cholesterol in to cholesterol ester and lysolecithin. Cholesterol ester which are nonpolar goes into hydrophobic interior of bilayer and lysolecithin is transferred to plasma albumin. Spherical pseudomicellar HDL-3 is formed by non polar core covered by a surface film of polar lipids and apolipoproteins. From peripheral tissues via scavenger receptor(SRB-1) and ATP binding cassette receptor G-1(ABCG-1) cholesterol transferred to HDL-3 ,then LCAT esterifies the cholesterol and increases it's size and forms less dense HDL-2. By SRB-1 from HDL-2 cholesterol ester are delivered to liver which is called as "reverse cholesterol transport". Hepatic lipase hydrolyses the phospholipids and triglycerides and forms HDL-3, this HDL-2 and HDL-3 interchange is called as HDL cycle[56,59].

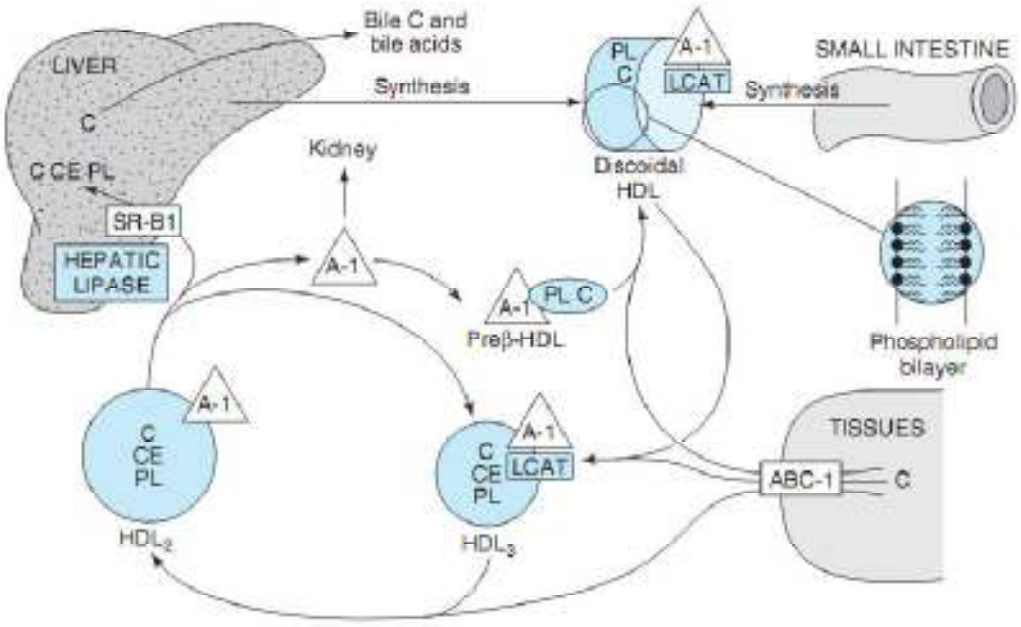


Figure-12: Metabolism of HDL and reverse cholesterol transport[55]

METHODOLOGY

A cross sectional study of lipid profile was conducted taking women with gestational hypertension and preeclampsia as cases and healthy pregnant women as controls from November 2012 to October 2013. The study was conducted in Department of obstetrics at Coimbatore medical college. It was approved by Ethical and Research Committee of Coimbatore Medical College. Informed consent was taken from each participant.

1. Selection of study subjects:

A total number of 90 subjects were selected on the basis of inclusion and exclusion criteria. Patient's data and relevant information were recorded in a proforma.

Cases:

60 women with Hypertensive disorders of pregnancy were selected on the basis of definitions given by National High blood pressure education programme (NHBPEP 2000) Case subjects were divided into two groups.

Group I-30 diagnosed cases of Gestational hypertension in age group of 20-30years.

Inclusion criteria: Pregnant female of 28-40 weeks of gestation with blood pressure _140/90 mm of Hg noted first time during pregnancy on _2 occasions at least 6 hours apart without proteinuria was considered as having gestational hypertension.

Group II- It included 30 diagnosed cases of preeclampsia in age group of 20-30 years.

Inclusion criteria:

Pregnant female of 28-40 weeks of gestation with blood pressure _140/90 mm of Hg noted first time during pregnancy on _2 occasions atleast 6 hours apart with proteinuria of _1+ (_30mg/dl) by dipstick method in arandom urine sample was considered as having preeclampsia.

Control group- It included 30 pregnant women.

Inclusion criteria:

Age matched healthy pregnant women of 28-40 weeks of gestation without any major illness and who are not on any medication were included.

Exclusion Criteria:

The pregnant women with following history were excluded from the study:

- History of chronic hypertension that was present before pregnancy.
- History of diabetes mellitus and/or who are on insulin therapy or hypoglycaemic drugs.
- Obese women with pre pregnancy BMI > 25
- Those who are taking antihypertensive or hypolipidemic drugs.
- Those with diagnosed liver, cardiac or renal diseases or any other major illness.

Sample collection is a invasive procedure performed in the study. The need for overnight fasting was explained to the controls and subjects. Informed consent was taken. While conducting the test subjects and controls were treated with due respect.

Detailed history about present pregnancy and previous pregnancy incase of multi and past history and family history of diabetes, hypertension, renal disease, thyroid disorder and any chronic drug intake was obtained. Height and weight during first trimester noted from antenatal card, weight gain also made from antenatal records.

BMI was calculated as per formula:

Weight(Kg)/Height in meter^2

Blood pressure was measured by palpatory method and auscultatory method in supine and sitting position.Systolic BP was taken by Korotkoff sound(phase I) and diastolic BP was taken by Korotkoff sound (phase V)[17].

Diagnosis of hypertension was made when systolic BP greater than 140 mmHg and Diastolic BP greater than 90 mmHgafter 20 weeks of gestation first time during pregnancy,after taking one more reading six hours later.

Then relevant investigations like blood urea,creatinine,blood sugar,serum uric acid, liver function test, complete hemogram, urine albumin were done.

Estimation of urine albumin by Dipstick method

Bottle with a tightly fitting cap contains reagent urine strips.It has several separate reagent areas affixed on plastic strip. Within 1 to 2 minutes it produces colour change of standardized range, when analytes reacts with specific reagent area on the test strip.

Testing method:

Under aseptic precautions freshly voided urine 2 ml is collected in a bulb. If patient is on urinary catheter, from indwelling catheter urine sample is obtained . From the air tight sealed containers dipsticks are removed, without touching the reagent areas of thestrip, to avoid alteration in test results.

After dipping the reagent area in urine, excess urine to be removed by tilting the strip and to allow the urine to run off the edges. It prevents the mixing of reagents and their dilution.

Principle of urine albumin test:

It is based on “protein error of pH dye indicator”, principle using bromphenol blue. Whenever protein (albumin) present in urine, because of its negative charge there is increase in pH and positive result occurs

Positive reaction is interpreted by development of range of colour from yellow to green then to blue. Yellow is interpreted as negative. colour change through yellow green and then green to green blue for positive reaction.

Test area	Results	Negative	Traces	Positive			
Protein	Conc(mg/dl)	0	10	30	100	300	1000
				1+	2+	3+	4+

Table-2: Sensitivity/limit of detection of Dipstick test

METHOD OF COLLECTION OF DATA:

Blood samples are taken from antecubital vein after overnight fasting and collected in red capped vacutainer tube which contains clot activator. The tube was kept at room temperature for half an hour for clotting and then centrifuged at 1200rpm to separate the serum which was analysed using Siemens dimension RxLMaX.

Following parameters were analysed:

ESTIMATION OF TOTAL CHOLESTEROL[58,59]:

Method: Enzymatic cholesterol oxidase – Phenol aminoantipyrine method[59].

PRINCIPLE:

The total cholesterol concentration is directly proportional to N,N diethyl aniline-Hcl/4-aminoantipyrine(DEA-HCL/AAP), formed at the end of reaction.

Cholesterol esters+ $H_2O \xrightarrow{\text{Cholesterol esterase}}$ cholesterol + fatty acids

Cholesterol +$O_2 \xrightarrow{\text{Cholesterol oxidase}}$ cholest-4-ene 3-one + H_2O_2

2 H_2O_2 + 4-Aminoantipyrine + Phenol $\xrightarrow{\text{Peroxidase}}$ Quinoneimine+ $4H_2O$

ESTIMATION OF HDL CHOLESTEROL:

Method:

Phosphotungstic acid and enzymatic cholesterol oxidase-phenol aminoantipyrine (CHOD-PAP)[58]

Principle:

On mixing the sample with phosphotungstic acid and magnesium,chylomicrons,VLDL and LDL are precipitated. On centrifugation ,HDL lies in supernatant portion which is measured by CHOD-PAP method.

Serum $\xrightarrow{\text{phosphotungstic acid}}$ $HDL_{(supernatant)}$ +LDL, VLDL, chylomicrons $_{(precipitate\ down)}$

ESTIMATION OF SERUM TRIGLYCERIDES:

Method:

Enzymatic glycerol phosphate oxidase – Phenol aminoantipyrine method[58].

Principle:

The red coloured quinoneimine was measured at 505 nm,the intensity of which is directly proportional to triglyceride concentration.

$$\text{Triglycerides} + H2O \xrightarrow{\textbf{Lipoprotein lipase}} \text{Glycerol} + \text{Free fatty acid}$$

$$\text{Glycerol} + \text{ATP} \xrightarrow{\text{Glycerol kinase}} \text{Glycerol-3-phosphate} + \text{ADP}$$

$$\text{Glycerol-3-phosphate} \xrightarrow{\text{Glycerol}-3-\text{phosphate oxidase}} H_2O_2 + \text{Dihydroxy acetone phosphate}$$

$$2\ H_2O_2 + \text{4-Aminoantipyrine} + \text{Phenol} \xrightarrow{\text{Peroxidase}} \text{Quinoneimine} + 4\ H_2O$$

ESTIMATION OF LDL CHOLESTEROL[58]:

Friedwald's formula

LDL(mg/dl)=totalcholesterol(mg/dl)-HDL(mg/dl)-triglycerides(mg/dl)/5

RESULTS

STATISTICAL ANALYSIS:

The collected data was analysed with SPSS 16.0 version. To describe about the data descriptive statistics frequency analysis, percentage analysis, mean, S.D were used. To find the significance difference between the multiple comparison one way ANOVA with Tukey's Post Hoc test was used and to assess the relationship between the variables Pearson's Correlation was used.In both the above statistical tools the probability value P=.05 is considered as significant level.

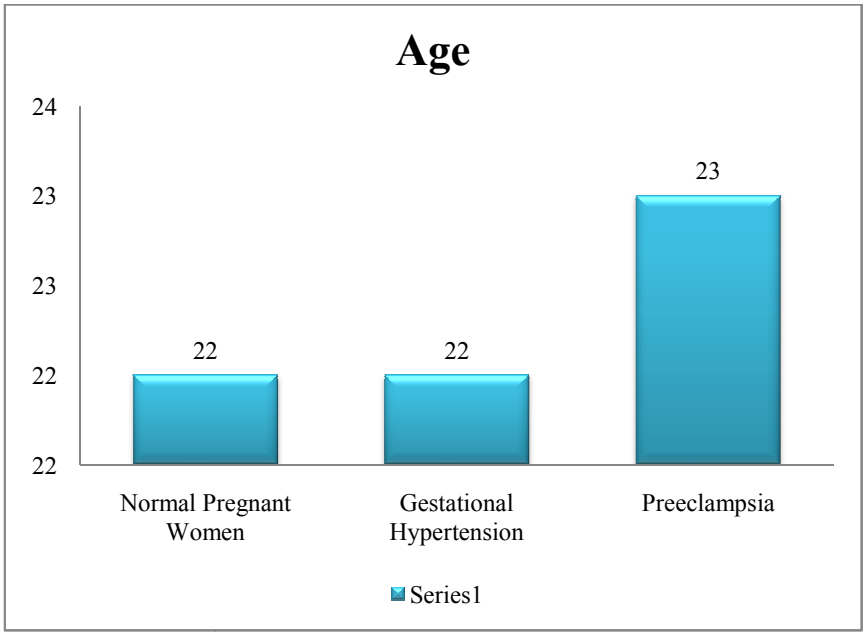
Table-3: Comparison of age among study subjects

Group	Variable	Age of mother
Control	Mean ± SD	24.98
	Range	20-29
Gestational hypertension (GroupI)	Mean ± SD	24.68
	Range	20-29
Preeclampsia Group II)	Mean ± SD	25.09
	Range	20-28
't' test between Group I & Group II	t value	0.890
	p value	0.377
't' test between Group I & controls	t value	0.245
	p value	0.807
't'test between Group II & controls	t value	1.054
	p value	0.296
One way ANOVA	F value	0.637
	p value	0.531

Unpaired student's t test:$p>0.05$: Non-significant;

$P<0.01$&$p<0.05$:significant ; $p<0.001$: Highly significant

Graph-1: Comparison of age among study subjects



The mean age in controls was 22.13±2.84 years, in Group I it was 22.30±2.38 years and in Group II it was 22.83±2.26 years. There was **no significant difference in age among study groups.(p-0.531).**

GESTATIONAL AGE

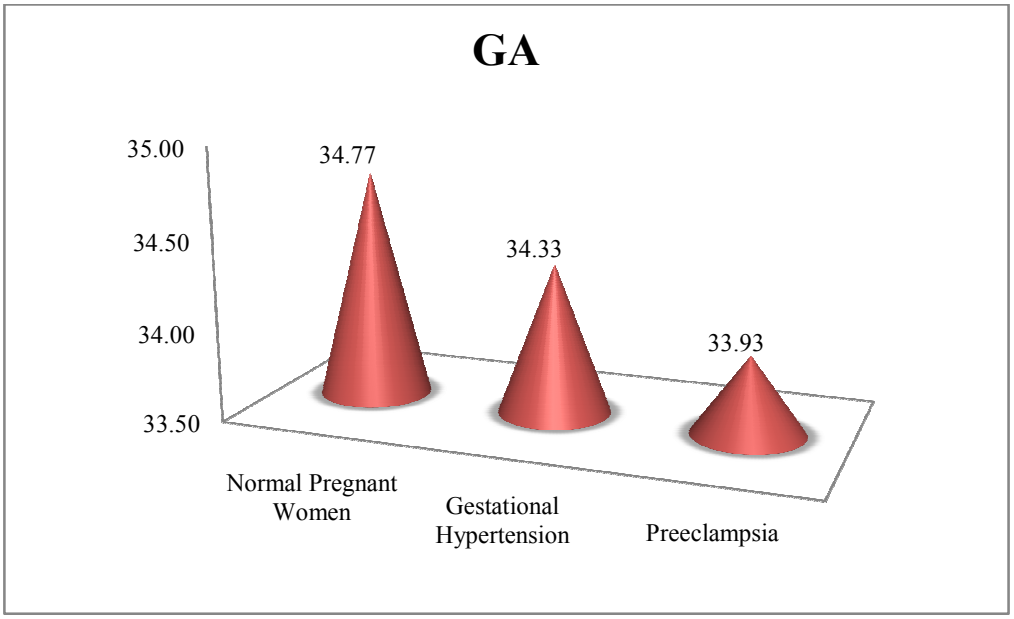
Table-4:Comparison of period gestation among study subjects

Group	Variable	Period of Gestation
Control	Mean ± SD	37.13
	Range	30-39
Gestational hypertension (GroupI)	Mean ± SD	37.25
	Range	30-40
Preeclampsia Group II)	Mean ± SD	36.25
	Range	30-39
't' test between Group I & Group II	t value	0.588
	p value	0.559
't' test between Group I & controls	t value	0.633
	p value	0.529
't'test between Group II & controls	t value	1.380
	p value	0.173
One way ANOVA	F value	0.804
	p value	0.451

Unpaired student's t test:p>0.05:Non-significant;

P<0.01&p<0.05:significant;p<0.001:Highly significant

Graph-2: Comparison of period of gestation among study subjects

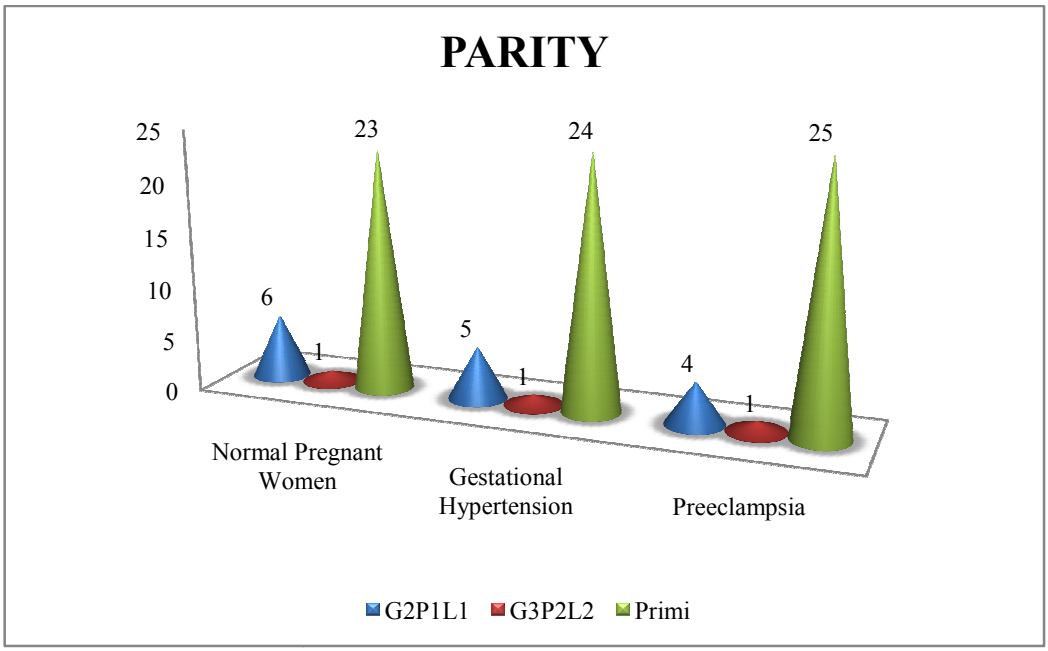


The mean period of gestation in controls was 34.77±2.36 weeks, in Group I it was 34.33±2.91 weeks and in GroupII it was 33.93±2.32 weeks. There was **no significant difference among study groups (p-0.451)**

PARITY

Table-5:Comparison of parity among study subjects

	Primi		G2P1L1		G3P2L2	
	No	**%**	**No**	**%**	**No**	**%**
Control	23	76.7	6	20	1	3.3
GHT	24	80	5	16.7	1	3.3
Preeclampsia	25	83.3	4	13.3	1	3.3



Graph-3 : Comparison of parity among study subjects

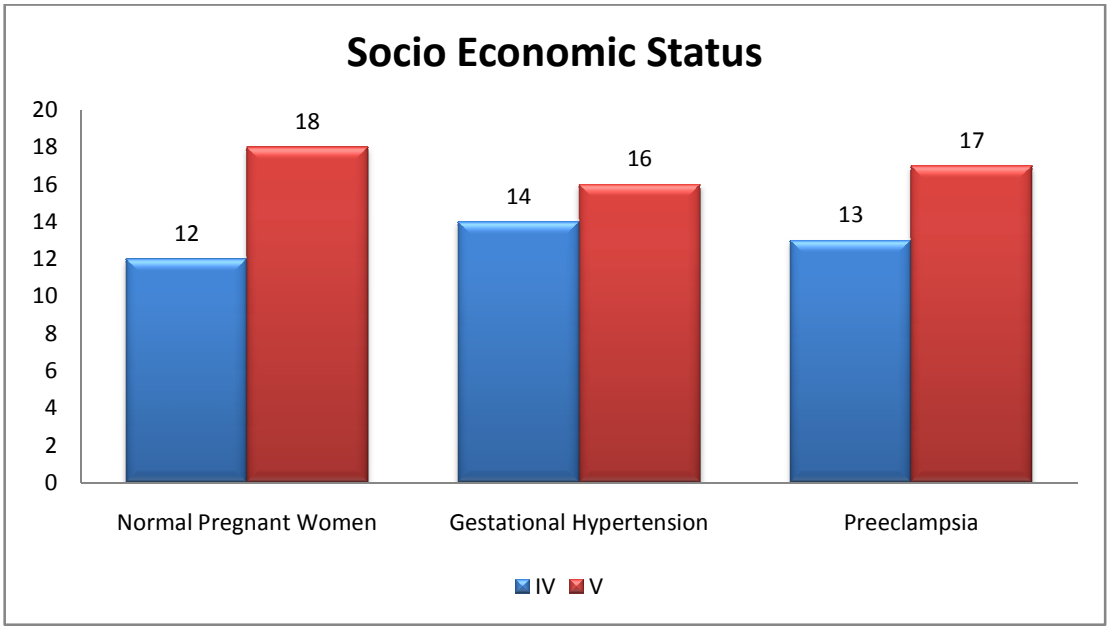
In all the groups, majority were nulliparous. But proportion nulliparous was little higher in cases compared to controls.

SOCIO-ECONOMIC STATUS

Table-6:Comparison of socio-economic status among study subjects

	Class - IV		Class - V	
	No	**%**	**No**	**%**
Control	12	40	18	60
GHT	14	46.7	16	53.3
Preeclampsia	13	43.3	17	56.7

Graph-4:Comparison of socio-economic status among study subjects



There was **no significant difference in socio-economic status** among study subjects.**(p>0.05)**

BMI

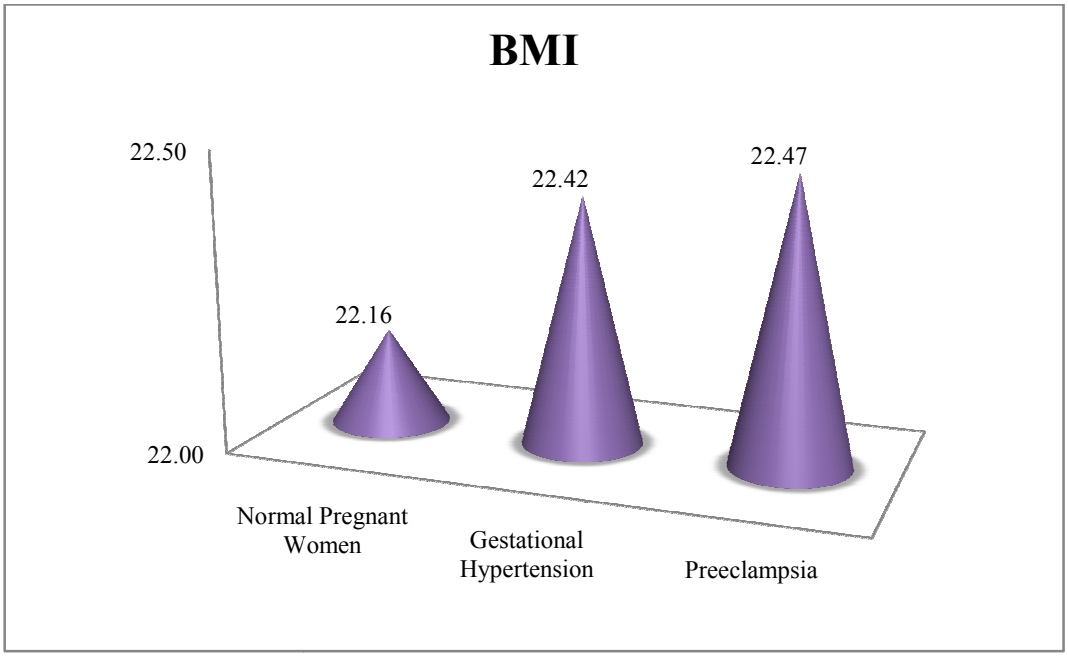
Table-7 : Comparison of BMI among study subjects

Group	Variable	BMI
Control	Mean ± SD	23.05
	Range	21.09-23.80
Gestational hypertension (GroupI)	Mean ± SD	23.72
	Range	21.09-25.00
Preeclampsia Group II)	Mean ± SD	22.83
	Range	20.70-24.00
't' test between Group I & Group II	t value	1.210
	p value	0.233
't' test between Group I & controls	t value	0.228
	p value	0.821
't'test between Group II & controls	t value	1.521
	p value	0.134
One way ANOVA	F value	1.037
	p value	0.359

Unpaired student's t test:$p>0.05$:Non-significant;

$P<0.01$&$p<0.05$:significant;$p<0.001$:Highly significant

Graph-5:Comparison of BMI among study subjects



The mean BMI of controls was 22.42±0.63, In Group I it was 22.47±1.25 and in Group II it was 22.16±0.67. There was **no significant difference in BMI** among study subjects**. (p0.359)**

SYSTOLIC BLOOD PRESSURE

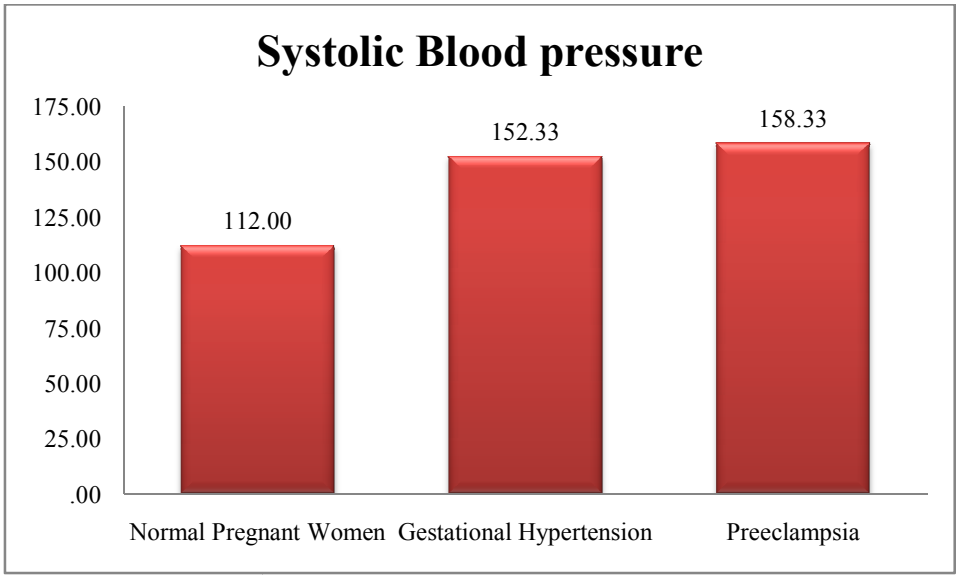
Table-8: Comparison of Systolic blood pressure among study subjects

Group	Variable	SBP
Control	Mean ± SD	117.010
	Range	100-120
Gestational hypertension (GroupI)	Mean ± SD	161.007
	Range	140-168
Preeclampsia Group II)	Mean ± SD	167.174
	Range	140-170
't' test between Group I & Group II	t value	2.556
	p value	0.013
't' test between Group I & controls	t value	21.434
	p value	0.001
't'test between Group II & controls	t value	24.278
	p value	0.001
One way ANOVA	F value	300.137
	p value	0.001

Unpaired student's t test:$p>0.05$:Non-significant;

$P<0.01$&$p<0.05$:significant;$p<0.001$:Highly significant

Graph-6: Comparison of systolic blood pressure among study subjects



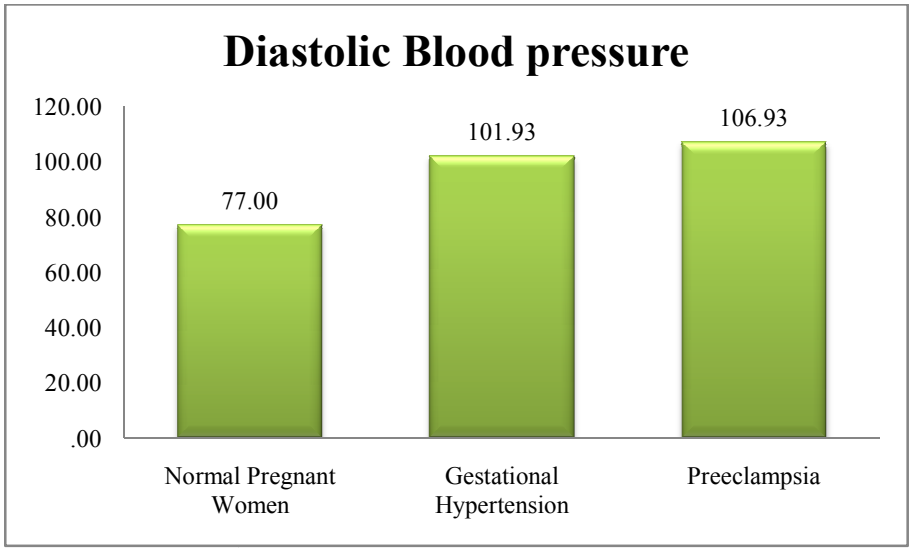
The mean systolic BP of controls was 112±5.010, In Group I it was 152±9.007 and in Group II it was 158.33±9.174. There was **significant difference in systolic BP** among study subjects**.(p-0.001)**

DIASTOLIC BLOOD PRESSURE

Table-9: Comparison of Diastolic blood pressure among study subjects

Group	Variable	DBP
Control	Mean ± SD	102.936
	Range	70-88
Gestational hypertension (GroupI)	Mean ± SD	109.509
	Range	90-114
Preeclampsia Group II)	Mean ± SD	115.604
	Range	90-120
't' test between Group I & Group II	t value	2.254
	p value	0.028
't' test between Group I & controls	t value	13.162
	p value	0.001
't'test between Group II & controls	t value	15.598
	p value	0.001
One way ANOVA	F value	126.527
	p value	0.001

Graph-7: Comparison of Diastolic blood pressure among study subjects



The mean Diastolic BP of controls was 97±5.936, In Group I it was 101±8.509 and in Group II it was 106.93±8.674. There was significant difference in **diastolic BP** among study subjects**(.p-0.001)**

TRIGLYCERIDES

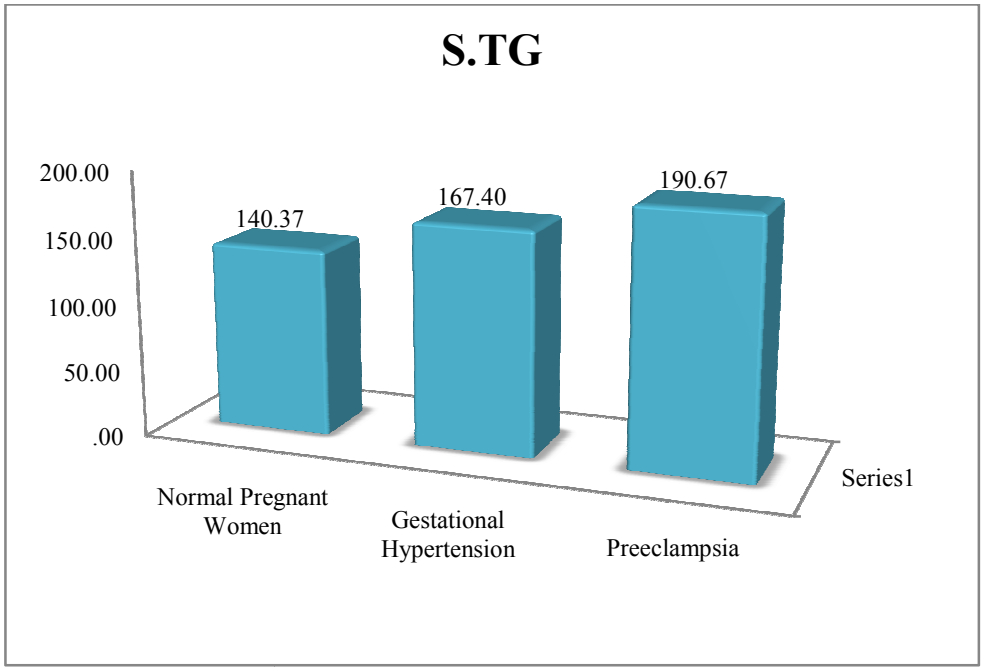
Table-10:Comparison of triglycerides among study subjects

Group	Variable	Triglycerides
Control	Mean ± SD	170.03
	Range	91-230
Gestational hypertension (GroupI)	Mean ± SD	199.55
	Range	101-233
Preeclampsia Group II)	Mean ± SD	223.23
	Range	133-259
't' test between Group I & Group II	t value	2.785
	p value	0.007
't' test between Group I & controls	t value	3.385
	p value	0.001
't'test between Group II & controls	t value	6.255
	p value	0.001
One way ANOVA	F value	19.17
	p value	0.001

Unpaired student's t test:p>0.05:Non-significant;

P<0.01&p<0.05:significant;p<0.001:Highly significant

Graph-8:Comparison of triglycerides among study subjects



The mean serum concentrations of triglycerides in controls is 140.37±29.65mg/dl, Group I it is 167.40±32.15 mg/dl and in Group III it is 190.67±32.56 mg/dl.

TOTAL CHOLESTEROL

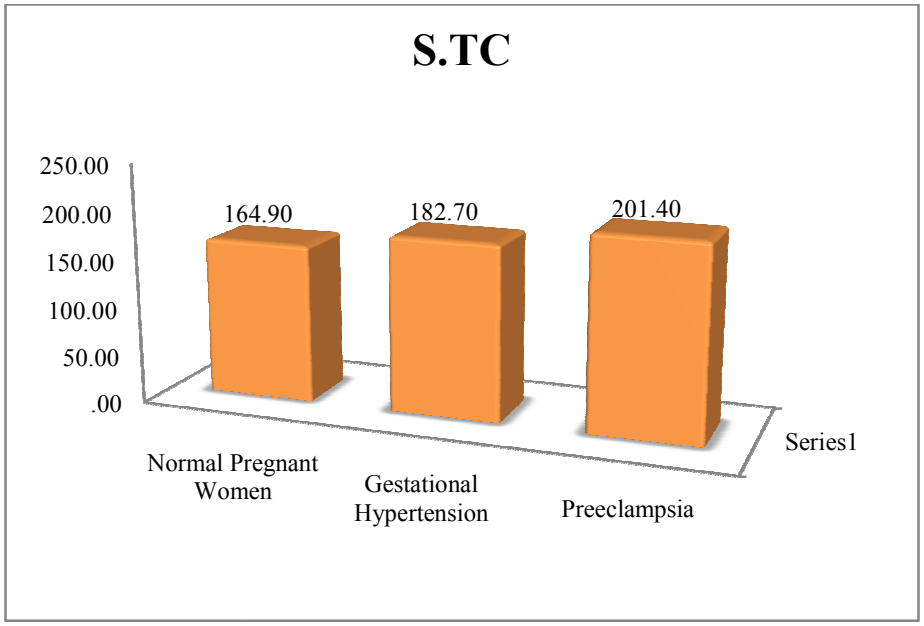
Table-11:Comparison of total cholesterol among study subjects

Group	Variable	Total Cholesterol
Control	Mean ± SD	188.61
	Range	121-218
Gestational hypertension (GroupI)	Mean ± SD	211.15
	Range	125-259
Preeclampsia Group II)	Mean ± SD	225.30
	Range	166-266
't' test between Group I & Group II	t value	2.756
	p value	0.008
't' test between Group I & controls	t value	2.632
	p value	0.011
't'test between Group II & controls	t value	5.937
	p value	0.001
One way ANOVA	F value	15.43
	p value	0.001

Unpaired student's t test:p>0.05:Non-significant;

P<0.01&p<0.05:significant;p<0.001:Highly significant

Graph-9:Comparison of total cholesterol among study subjects



The mean serum concentrations of total cholesterol in controls is 164.90±23.71mg/dl, Group I it was 182.70±28.45 mg/dl and in Group III it was 201.40±23.90 mg/dl.

LDL

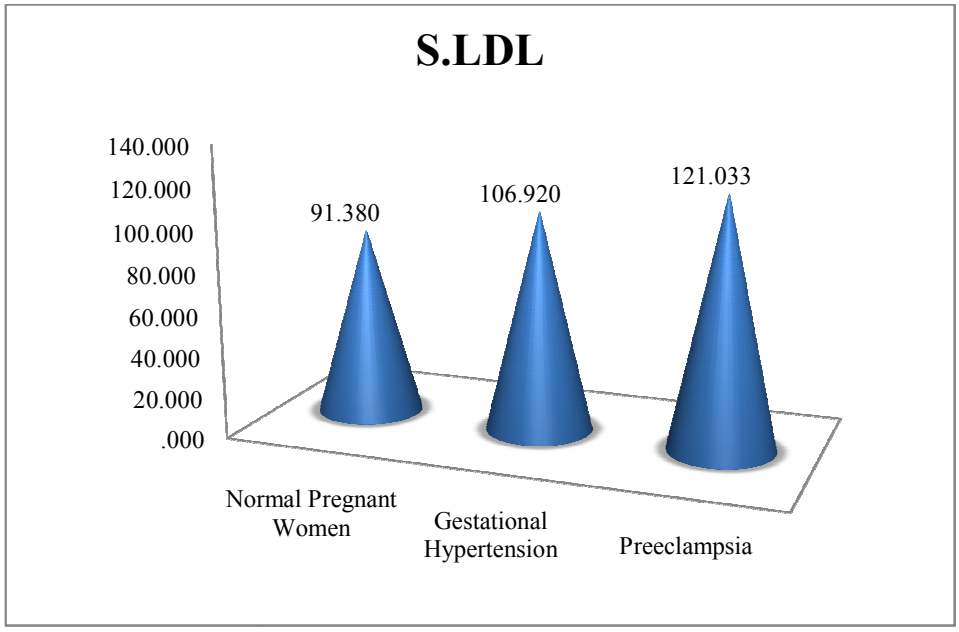
Table-12:Comparison of LDL among study subjects

Group	Variable	LDL
Control	Mean ± SD	112.43
	Range	48.4-136.4
Gestational hypertension (GroupI)	Mean ± SD	133.36
	Range	56.2-168.8
Preeclampsia Group II)	Mean ± SD	145.09
	Range	83.4-181.8
't' test between Group I & Group II	t value	2.162
	p value	0.035
't' test between Group I & controls	t value	2.518
	p value	0.015
't'test between Group II & controls	t value	5.080
	p value	0.001
One way ANOVA	F value	11.50
	p value	0.001

Unpaired student's t test:p>0.05:Non-significant;

P<0.01&p<0.05:significant;p<0.001:Highly significant

Graph-10:Comparison of LDL among study subjects



The mean serum concentrations of LDL cholesterol in controls is 91.38±21.05mg/dl, Group I it was 106.92±26.44 mg/dl and in Group III it was 121.03±24.06 mg/dl.

HDL

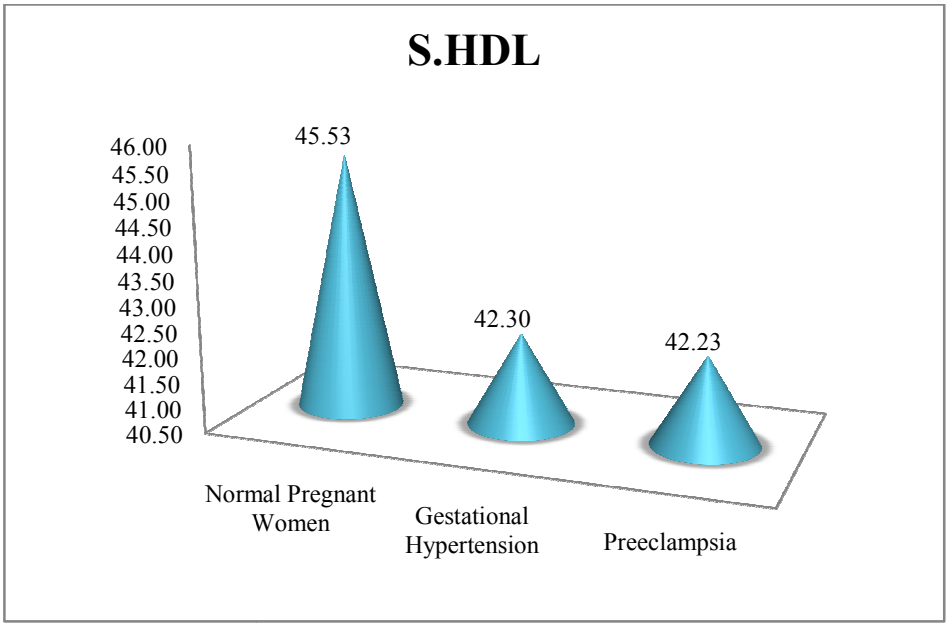
Table-13:Comparison of HDL among study subjects

Group	Variable	HDL
Control	Mean ± SD	50.94
	Range	35-58
Gestational hypertension (GroupI)	Mean ± SD	47.41
	Range	30-51
Preeclampsia Group II)	Mean ± SD	46.40
	Range	32-49
't' test between Group I & Group II	t value	0.055
	p value	0.956
't' test between Group I & controls	t value	2.378
	p value	0.021
't'test between Group II & controls	t value	2.644
	p value	0.011
One way ANOVA	F value	4.395
	p value	0.015

Unpaired student's t test:$p>0.05$:Non-significant;

$P<0.01$&$p<0.05$:significant;$p<0.001$:Highly significant

Graph-11:Comparison of HDL among study subjects



The mean serum concentrations of HDL cholesterol in controls is 45.53±5.41mg/dl, Group I it was 42.30±5.11 mg/dl and in Group III it was 42.23±4.17 mg/dl.

The statistical analysis by student's t-test shows that the mean serum levels of triglycerides, total cholesterol and LDL cholesterol are significantly increased in subjects with preeclampsia when compared to healthy controls ($p<0.001$) except the mean serum HDL cholesterol level which is significantly decreased ($p<0.01$).

The mean serum levels of triglycerides, total cholesterol and LDL cholesterol are significantly increased in subjects with gestational hypertension when compared to healthy controls ($p<0.01$, $p<0.05$ &

p<0.05 respectively) except the mean serum HDL cholesterol level which is significantly decreased (p<0.05).

The mean serum levels of triglycerides, total cholesterol and LDL cholesterol are significantly increased in subjects with preeclampsia when compared with gestational hypertension subjects. (p-0.001, p-0.001, p-0.001 respectively). There was significant decrease in mean serum HDL cholesterol concentration among these subjects (p-0.015).

The statistical analysis by one way ANOVA shows that the mean serum levels of triglycerides, total cholesterol and LDL cholesterol are significantly increased in subjects with gestational hypertension and preeclampsia when compared to healthy controls (p<0.001) except the mean serum HDL cholesterol level which is significantly decreased (p<0.05).

CORRELATION OF SEVERITY

The correlation of serum triglyceride levels with systolic blood pressure, serum triglycerides with diastolic blood pressure and serum triglyceride with urine albumin is represented in table-14.

There is a highly stastical significant correlation between

a) Serum triglyceride and systolic blood pressure(r=0.905)

b) Serum triglyceride and diastolic blood pressure(r=0.969)

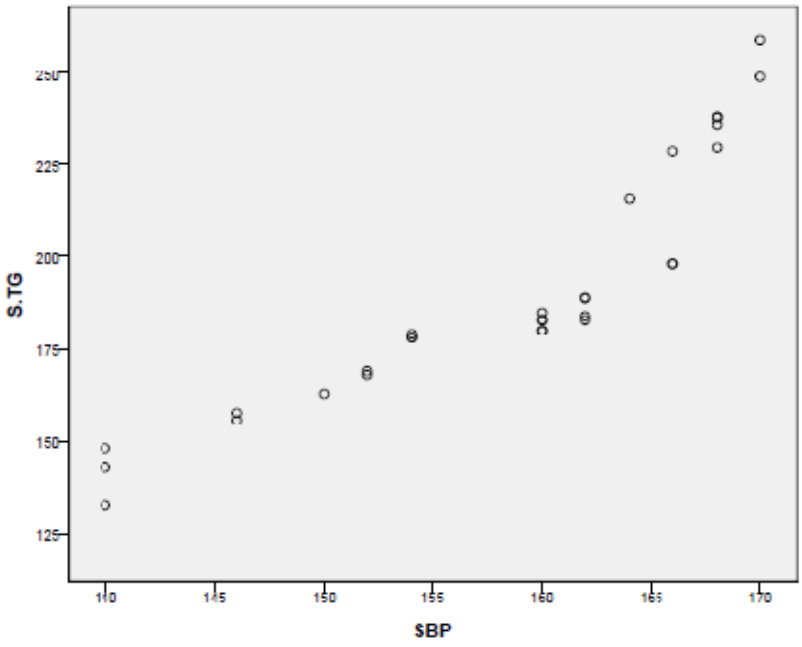
c) Serum triglyceride and urine albumin(r=0.936)

Table-14:Correlation of serum triglyceride with different parameters

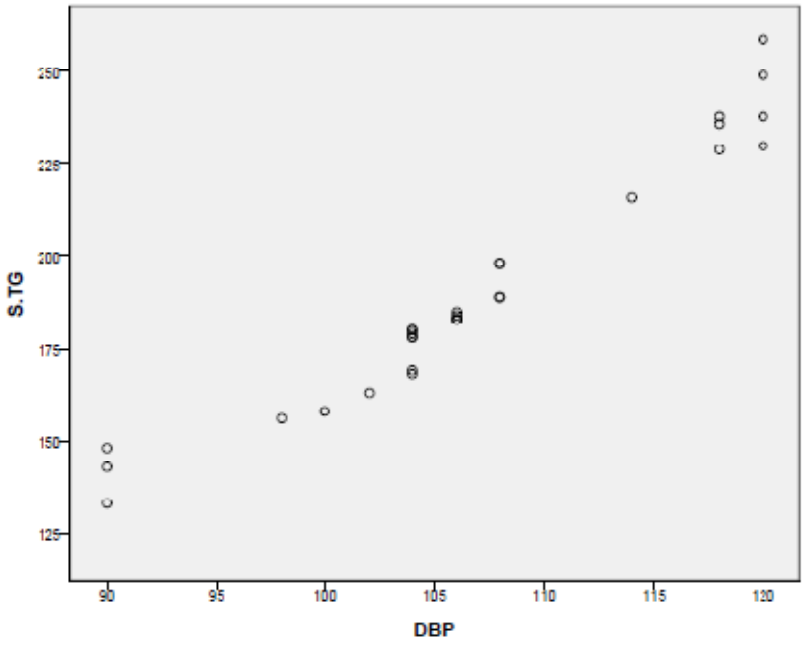
Parameter	'r' value	'p'value	Significance
Systolic BP	0.905	0.001	HS
Diastolic BP	0.969	0.001	HS
Urine albumin	0.936	0.001	HS

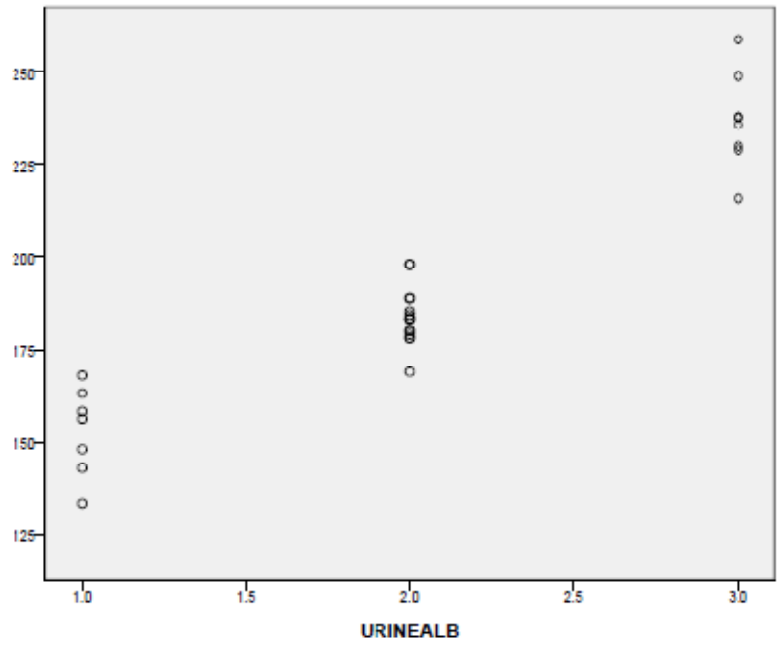
r-Karl Pearson correlation Co-efficient

HS-Highly significant



Graph-13:serum triglyceride with Diastolic blood pressure





Graph-14:serum triglyceride with urine albumin

DISCUSSION

SERUM LIPID PROFILE:

SERUM TRIGLYCERIDES:

The mean serum concentrations of triglycerides in controls is 140.37+29.65mg/dl,Group I it is 167.40+32.15 mg/dl and in Group III it is 190.67+32.56 mg/dl.

In my study mean **serum triglyceride are significantly elevated** in gestational hypertension and preeclampsia**.(p value-0.001)**

The finding of the studies done by Q Lei et al[49], Torun Clausen et al[62], S.WareJauregui et al[50], Shruthi Mohanty et al[53] and many other researchers coincides with these finding[62,64,65,66,67,68,69,70,71,72,74,75].

There is increase in hepatic lipase activity(by increasing the synthesis of TG in liver) and decrease in lipoprotein lipase activity(by decreased catabolism of TG at tissue level) are the cause for increased triglyceride concentration. There is delay in uptake of remnant by the liver leads to rise in TG concentration[64].

SERUM TOTAL CHOLESTEROL:

The mean serum concentration of total cholesterol in controls is 164.90+23.71 mg/dl; in group I, it is 182.70+28.45mg/dl, and in group II, it is201.40+23.90 mg/dl. In my study it was found that the mean serum

levels of **total cholesterol are significantly increased** in subjects with gestational hypertension and preeclampsia when compared to healthy controls **(p-0.001).**

The finding of the studies done by,Md.Zakir H et al[65] S.WareJauregui et al[50], Shruthi Mohanty et al[53] and many other researchers coincides with these finding[66,67,69,70,71,74].

The increase in cholesterol concentration is due to insulin resistance and reverse transport of cholesterol to liver because of reduced HDL level.

LDL CHOLESTEROL:

The mean serum concentration of LDL cholesterol in controls is 91.38+21.05 mg/dl; in group I, it is 106.92+26.44 mg/dl and in group II, it is 121.03+24.06 mg/dl. In present study it was found that the mean serum levels of **LDL cholesterol are significantly increased** in subjects with gestational hypertension and preeclampsia when compared to healthy controls **(p-0.001).**

The finding of studies done by Carlos A. Negrato et al, S.Ware-Jauregui et al[50], Q Lei et al49, S. Ware-Jauregui et al50, Torun Clausen et al51 and many other researchers.[64,65,66,67,69,70,71,73,74,75]

HDL CHOLESTEROL:

The mean serum concentration of HDL cholesterol in controls is 45.53+5.41 mg/dl; in group I, 4 mg/dl and 42.30+5.11 in group II, it is 42.23+4.17 mg/dl. In present study it was found that the mean serum levels of **HDL cholesterol are significantly decreased** in subjects with gestational hypertension and preeclampsia when compared to healthy controls **(p-0.015).**

The studies of **Carlos A. Negrato et al, S. Ware-Jauregui et al**, **Q Lei et al** and many other researchers are correlating.[64,65,66,67,68,69,71,73,74,75]

Reduction in HDL cholesterol is due to hypertriglyceridemia, which forms TG rich HDL particles through CETP mediated exchange with TG rich VLDL particles. Hepatic lipase rapidly catabolises TG rich HDL particles and decreasing it concentration.

A study conducted in primigravida about lipoprotein subfractions by 200 subjects divided into 4 groups. There were 50 normotensive nonpregnant normal women (group A), 50 normotensive pregnant normal women (group B), 50 pregnant women with preeclampsia (group C) and 50 pregnant women with eclampsia (groupD). Authors found that serum

triglyceride, serum VLDL levels were significantly high in preeclamptic women when compared with group A and B.

In the year 2010, **Uzma Iftikhar** and co-workers found significant increase in serum levels of total cholesterol, triglycerides, LDL and VLDL and significant decrease in serum levels of HDL in preeclamptic women when compared with controls[67].

In the same year**, Kashinakunti S.V.** and co-workers found significantly increased fasting serum levels of triglycerides in preeclamptic cases when compared with controls. They found positive correlation between serum triglycerides and systolic and diastolic blood pressure in cases[68].

In the same year, **Adiga Usha and a co-worker** found significantly increased serum levels of total cholesterol and total cholesterol:HDL ratio and significantly decreased serum levels of HDL in PIH cases when compared with controls. There was significant positive correlation between serum total cholesterol and Atherogenic index (AI) and significant negative correlation between serum HDL and AI. Total cholesterol levels were higher by 25% and HDL levels were lower by 36% in PIH cases when compared with controls[69].

In the same year, **Vidyabati RK** and co-workers found significantly increased serum levels of total cholesterol, triglycerides, LDL and VLDL in PIH cases when compared with controls. For 1 unit increase in Total Cholesterol, Triglycerides, VLDL and LDL, there were increased chance of developing PIH by 12.6%, 0.3%,12.4% and 7.1% respectively. With 1 unit increase in HDL, woman has 11.4% less chance of developing PIH[70].

In the year 2011, **Shalini Maksane** and co-workers found significantly increased serum levels of total cholesterol, triglycerides, LDL, VLDL and significantly decreased serum level of HDL in preeclamptic cases when compared with controls[71].

In the same year, **Valmir Jose de Lima and co-workers** conducted a case controlstudy with 42 preeclmaptic women as cases and 35 normal healthy pregnant women as controls at third trimester. Authors found significantly elevated serum levels of triglycerides and VLDL in cases when compared with controls. They found positive correlation between increased proteinuria and higher VLDL and triglyceride levels in patients with preeclampsia[72].

In the same year, **Zinat Begum and co-workers** conducted a case-control study with 75 preeclampsia cases and 75 normal healthy pregnant

women as controls.Authors found significantly reduced levels of serum HDL in cases when compared with controls.

In the same year, **Gohil JT and co-workers** conducted a study with 200 women divided into four groups. Group A- 50 nonpregnant normotensive women, Group B- 50 healthy pregnant normotensive at 32-36 weeks of gestation, Group C- 50 antenatal preeclamptic women at 32-36 weeks of gestation, Group D- 50 post partum preeclamptic women at _15 days after delivery. There was significant increase in serum levels of total cholesterol, triglycerides, LDL and VLDL and significant decrease in serum levels of HDL in group C when compared with group A, B and D[74].

SUMMARY

A total number of 90 subjects were included in this study of which 30 normal pregnant women were taken as Controls, 30 gestational hypertensive women were taken as Group I and 30 preeclamptic women were taken as Group II. All subjects were more than 28 weeks of gestation with no major illness.

In all the subjects, concentrations of, serum triglycerides, serum total cholesterol and serum HDL cholesterol were estimated.

The results showed that mean value of serum triglycerides, serum total cholesterol, serum LDL cholesterol concentration were significantly increased in women with gestational hypertension and preeclampsia when compared with healthy pregnant women. The mean serum HDL cholesterol concentration was significantly decreased in cases when compared with controls.

This study shows that there is presence of dyslipidemia in women with gestational hypertension and preeclampsia. Dyslipidemia might be involved in pathogenesis of these diseases.

The women who develop preeclampsia had disturbed lipid metabolism. Increased triglyceride levels and delayed triglycerides clearance and high blood pressure are reasons for the development of preeclampsia. This association may be significant in understanding the pathophysiological process of preeclampsia and may help in developing strategies for prevention and early diagnosis.

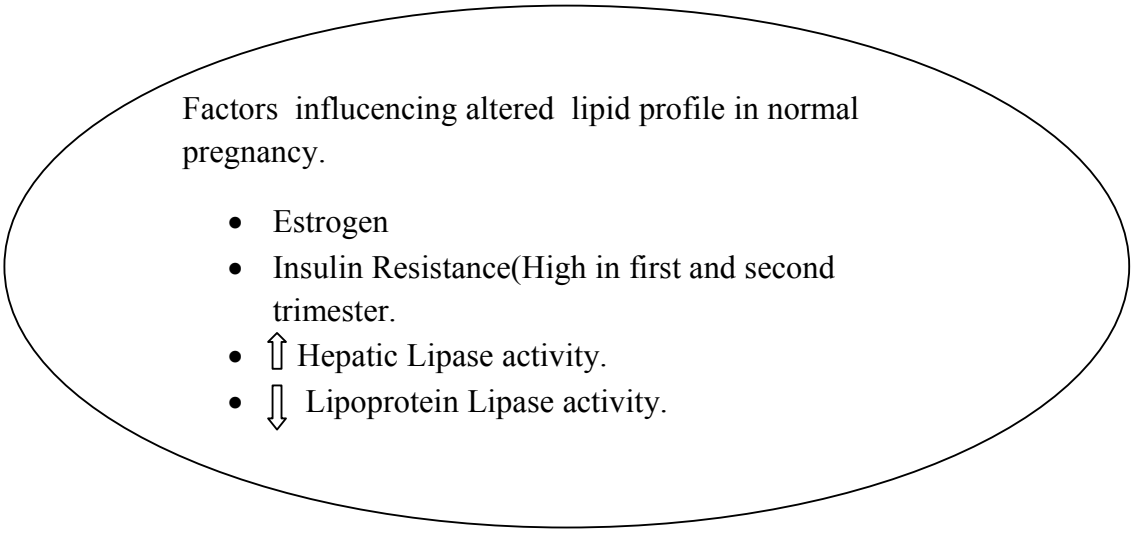
CONCLUSION

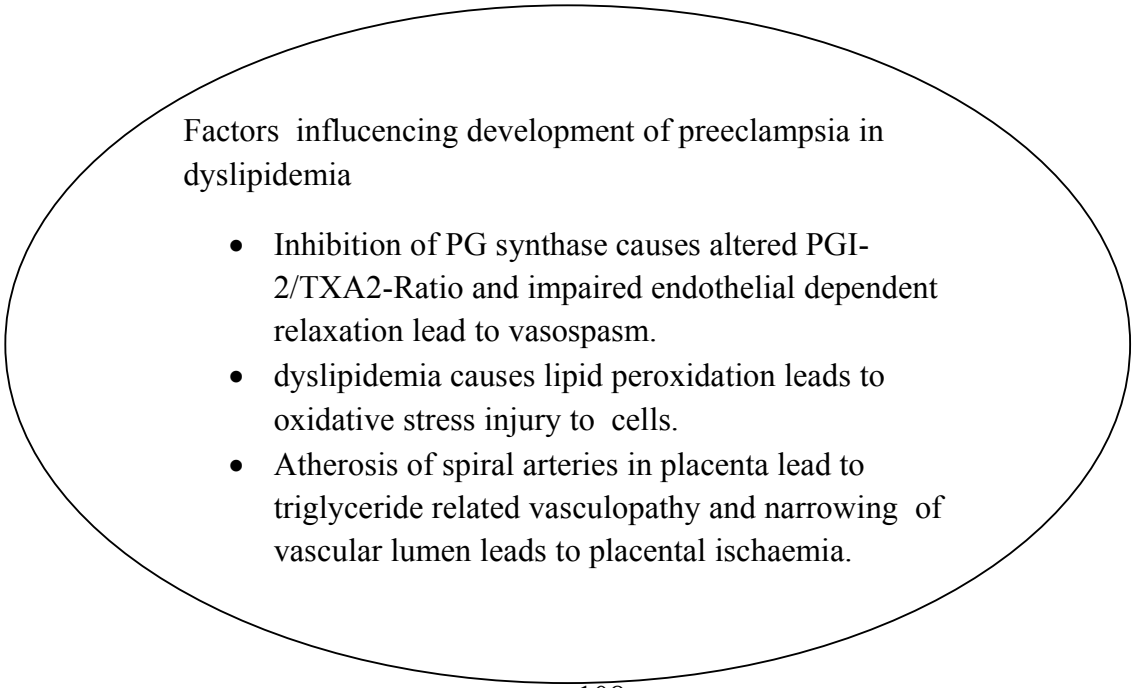
Due to hormonal changes there is physiological hyperlipidemia seen in normal pregnancy. In Preeclampsia triglycerides are elevated abnormally beyond the physiological rise of normal pregnancy,so it was implicated in pathophysiology of Preeclampsia. Atherogenic lipid profile that is raised triglycerides, LDL-C and decreased HDL-C lead to development of Preeclampsia by causing oxidative stress and endothelial dysfunction.

Systolic Blood Pressure, Diastolic Blood Pressure and proteinuria have positive correlation with triglyceride levels. So, the severity of Preeclampsia indicated by serum triglyceride concentration. If Preeclampsia diagnosed in present pregnancy the chance of recurrence in next pregnancy is high. So, by controlling the risk factors like obesity and altered lipid profile the chance of recurrence can be minimized.

This study helps in understanding the role of altered lipid profile in the pathophysiology of Preeclampsia. This may lead to development of preventive strategies and early diagnosis. By detecting this lipid profile changes in early pregnancy, it may be helpful to prevent and to slow

down the disease progression either by medication or life style modification.





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ANNEXURE-1

PROFORMA

I.Particulars of the Individual:

1.Name

2.Age

3.Sex

4.Religion

5.Occupation

6.Address

7.Educational status

8.Socio-economic status

9.Date of admission

10.In patient/Out patient number

11.Case-Booked/Unbooked

II.Present History:

1.H/O Amenorrhoea

2.H/O pedal edema

III.Obstetric History:

1.Parity index (G-P-L-A)

2.Married life

3.H/O present pregnancy-1st trimester

2nd trimester

3rd trimester

4.H/O previous pregnancy-DM, HT, Epilepsy

IV.Menstrual History:

Last menstrual period(LMP)

Expected date of delivery(EDD)

V.Past History:

1.H/O Hypertension

2.H/O Diabetes Mellitus

3.H/O Altered lipid profile

4.H/O Drug intake

5.H/O Obesity

VI.Family History:

1.H/o Diabetes mellitus

2.H/o Hypertension

3.H/o Preeclampsia in mother or sister

VII.Personal History:

1.Diet

2.Appetite

3.Sleep

4.Bowel and bladder habits

5.H/o smoking

VIII.General Physical Examination:

1.Height

2.Weight

3.Prepregnancy BMI from ante natal records

4.Temperature

5.Nutrition

6.Pallor,Icterus,Clubbing,Cyanosis,Lymphadenopathy,Pedal edema

7.Breast,Spine,Thyroid

IX.Vital Data:

1.Pulse rate

2.Blood pressure

3.Respiratory rate

X.Systemic Examination:

1. Respiratory system

2.CVS

3.CNS

4.Per Abdomen Examination

a)Abdominal wall edema

b)Uterine size(gestational age)/Fundal height

c)Position of Head

d)Fetal heart rate and fetal movements

XI.Investigations:

1.Hb%

2.Blood group

3.Blood sugar,urea,creatinine

4.Urine albumin

5.Liver function test

6.Serum uric acid

4.Serum lipid profile-Triglycerides,Total cholesterol,LDL,HDL

INFORMED CONSENT

I,..... the undersigned agree voluntarily to participate in the study , entitled **"Study of Serum Lipid Profile in Gestational Hypertension and Preeclampsia"** I understand that this is an invasive procedure wherein the blood investigations will be done.

The procedure of study have been explained to me in my own language.

Date:

Place :

Signature of the subject

Signature of investigator

MASTER CHART

Group – II Women with PREECLAMPSIA

S.NO	NAME	IP NO	AGE	PARITY	GA	SES	SBP	DBP	URINEALB	HEIGHT	WEIGHT	BMI	S.TG	S.TC	S.HDL	S.LDL
1	Ruby	31841	21	Primi	34	V	140	90	1+	152	50	21.64	133	178	41	110.4
2	Floramary	29978	21	Primi	36	IV	168	118	3+	156	52	21.36	236	196	49	99.8
3	Patteswari	28845	23	Primi	36	IV	162	106	2+	145	48	22.82	184	259	49	173.2
4	Jancyrani	26894	20	Primi	37	V	160	106	2+	153	51	21.78	183	189	45	107.4
5	Rifanabegam	27865	22	Primi	35	V	166	118	3+	161	54	20.83	229	219	41	132.2
6	Ruckmani	25674	24	Primi	34	V	160	106	2+	155	52	21.64	183	187	41	109.4
7	Sulthana begam	23345	23	Primi	35	V	164	114	3+	152	50	21.64	216	266	41	181.8
8	Rahamath nisha	26678	22	Primi	31	IV	168	118	3+	156	52	21.36	238	190	42	100.4
9	Bannari	27731	21	Primi	33	IV	162	108	2+	150	50	22.22	189	187	44	105.2
10	Umamaheswari	23331	21	Primi	34	IV	160	106	2+	163	55	20.7	185	221	43	141
11	hithaya fathima	31199	24	Primi	32	V	170	120	3+	155	52	21.64	249	192	44	98.2
12	Sangeetha	29990	25	G2P1L1	36	V	162	106	2+	155	53	22.06	183	215	44	134.4
13	Madha	25531	25	Primi	31	V	168	120	3+	157	51	20.69	230	215	44	125
14	Gayathri	28881	26	Primi	31	V	140	90	1+	150	50	22.22	143	220	43	148.4
15	Jasmin	24415	23	Primi	32	V	152	104	1+	155	52	21.64	168	166	49	83.4

S.NO	NAME	IP NO	AGE	PARITY	GA	SES	SBP	DBP	URINEALB	HEIGHT	WEIGHT	BMI	S.TG	S.TC	S.HDL	S.LDL
16	Thangamani	25891	22	Primi	35	IV	154	104	2+	153	52	22.21	179	174	38	100.2
17	Sameemma	30981	21	Primi	36	IV	170	120	3+	150	50	22.22	259	203	49	102.2
18	Priya	30897	26	G2P1L1	32	V	166	108	2+	155	52	21.64	198	192	47	105.4
19	Sreeja	31674	27	G2P1L1	32	IV	140	90	1+	153	52	22.21	148	187	40	117.4
20	Katheeza banu	32189	21	Primi	37	IV	152	104	2+	150	50	22.22	169	215	47	134.2
21	Nancy salomin	38765	28	G3P2L2	37	V	162	108	2+	160	54	21.09	189	207	38	131.2
22	Annalakshmi	27865	27	G2P1L1	37	V	150	102	1+	157	53	21.5	163	205	38	134.4
23	Jumaila	32214	21	Primi	34	IV	168	120	3+	152	51	22.07	238	184	42	94.4
24	Vasanthi	31114	20	Primi	32	IV	166	108	2+	150	51	22.66	198	228	39	149.4
25	Sakila banu	29810	21	Primi	30	V	160	104	2+	155	53	22.06	180	184	44	104
26	Naseema	30021	22	Primi	32	V	146	100	1+	155	52	21.64	158	178	32	114.4
27	Gandhimathi	27018	23	Primi	34	IV	154	104	2+	155	53	22.06	178	195	40	119.4
28	Mohanapriya	27099	22	Primi	32	V	146	98	1+	160	54	21.09	156	231	39	160.8
29	Samsath banu	29055	23	Primi	39	IV	154	104	2+	155	53	22.06	178	184	36	112.4
30	Mercy	31964	20	Primi	32	V	160	104	2+	152	50	21.64	180	175	38	101

Group – I Women with Gestational Hypertension

S.NO	NAME	IPNO	AGE	PARITY	GA	SES	SBP	DBP	URINEALB	HEIGHT	WEIGHT	BMI	S.TG	S.TC	S.HDL	S.LDL
1	Umarani	23453	20	Primi	30	V	140	90	NIL	152	57	24.67	138	172	40	104.4
2	Thilagavathy	25567	21	Primi	32	IV	154	106	NIL	156	60	24.69	178	172	44	92.4
3	Sujitha	27899	21	Primi	34	IV	148	98	NIL	145	52	24.76	149	151	47	74.2
4	Padmapriya	24456	22	Primi	36	V	152	104	NIL	153	57	24.35	167	195	43	118.6
5	Nithya	21134	20	Primi	34	V	162	112	NIL	161	65	25	192	228	31	158.6
6	Selvi	23378	25	G2P1L1	32	V	164	114	NIL	152	50	21.64	203	170	48	81.4
7	Loganayaki	29913	24	Primi	31	IV	162	106	NIL	160	54	21.09	185	188	44	107
8	Divya	32110	23	Primi	32	IV	140	90	NIL	150	50	22.22	101	153	38	94.8
9	Rathi	24675	22	Primi	30	IV	148	98	NIL	152	50	21.64	152	246	50	165.6
10	Rabithbaseera	28895	21	Primi	34	IV	140	90	NIL	160	54	21.09	119	125	45	56.2
11	Narmadha	23342	21	Primi	36	V	150	106	NIL	155	52	21.64	174	206	46	125.2
12	Malar	25591	20	Primi	37	IV	160	112	NIL	155	53	22.06	196	154	37	77.8
13	Kanniyammal	28294	23	Primi	39	V	160	110	NIL	155	53	22.06	193	179	41	99.4
14	Shakira	23399	24	G2P1L1	38	V	164	114	NIL	150	51	22.66	202	197	30	126.6
15	Malarvizhi	31312	23	Primi	38	V	162	110	NIL	155	53	22.06	195	176	41	96
16	vellammal	31112	21	Primi	37	IV	164	112	NIL	152	50	21.64	231	259	44	168.8
17	Victoria	31162	21	Primi	33	IV	168	114	NIL	150	52	23.11	233	181	40	94.4

S.NO	NAME	IPNO	AGE	PARITY	GA	SES	SBP	DBP	URINEALB	HEIGHT	WEIGHT	BMI	S.TG	S.TC	S.HDL	S.LDL
18	Bhuvanewari	31716	20	Primi	32	V	162	104	NIL	160	54	21.09	183	176	48	91.4
19	Radhikamani	31271	20	Primi	34	V	152	104	NIL	159	54	21.35	171	169	45	89.8
20	Geetharani	29467	21	Primi	33	IV	150	100	NIL	150	52	23.11	166	224	43	147.8
21	Logu	31322	20	Primi	32	IV	140	90	NIL	150	51	22.66	129	147	42	79.2
22	Ranjani	30736	23	Primi	31	V	144	94	NIL	155	53	22.06	138	158	42	88.4
23	Chinnammal	30377	22	Primi	30	V	142	92	NIL	155	53	22.06	134	189	47	115.2
24	Murugeswari	31064	21	Primi	39	V	150	104	NIL	150	52	23.11	171	185	51	99.8
25	Pradeepa	31143	27	G2P1L1	40	IV	142	90	NIL	152	50	21.64	133	184	44	113.4
26	Anusiya	31124	26	G2P1L1	38	IV	160	106	NIL	160	54	21.09	185	183	32	114
27	Mallika	31177	25	G2P1L1	34	V	146	94	NIL	133	43	24.3	137	172	38	106.6
28	Maryloosiya	31144	24	Primi	35	V	140	90	NIL	150	51	22.66	131	170	45	98.8
29	Radhamani	30848	21	Primi	35	V	150	98	NIL	152	50	21.64	158	187	42	113.4
30	Revathy	31897	29	G3P2L2	34	IV	154	106	NIL	160	54	21.09	178	185	41	108.4

Controls – Normal Pregnant Women

S.NO	NAME	OP NO	AGE	PARITY	GA	SES	SBP	DBP	URINE ALB	HEIGHT	WEIGHT	BMI	S.TG	S.TC	S.HDL	S.LDL
1	Chitra	2500213	24	Primi	32	V	110	70	NIL	152	50	21.64	127	187	46	116
2	Saharbanu	2411907	20	Primi	34	V	120	80	NIL	150	50	22.22	230	218	46	126
3	Manimegalai	2567900	25	G2P1L1	34	V	116	76	NIL	145	48	22.82	145	167	48	90
4	Ranjithadevi	2346567	28	G2P1L1	36	V	110	74	NIL	150	51	22.66	131	171	39	108
5	Indhu	2476747	21	Primi	39	IV	120	86	NIL	155	53	22.06	182	180	44	99.6
6	Sathya	2743786	27	G2P1L1	32	IV	116	84	NIL	145	48	22.82	167	163	49	80.6
7	Subbulakshmi	2577886	21	Primi	34	V	118	86	NIL	155	53	22.06	171	154	47	72.8
8	Kasthuri	2388787	20	Primi	30	IV	110	80	NIL	155	52	22.21	148	121	43	48.4
9	Jothi	2778678	22	Primi	36	V	120	88	NIL	153	52	22.21	180	213	47	130
10	Fathima	2177876	21	Primi	36	V	110	80	NIL	155	52	22.06	152	134	53	50.6
11	Kalpana	2278687	20	Primi	37	V	110	70	NIL	150	50	22.22	119	162	48	90.2
12	Ramya	2447689	20	Primi	36	IV	110	70	NIL	145	48	22.82	131	159	42	90.8
13	Jeya	2337896	20	Primi	38	V	120	86	NIL	150	51	22.66	170	178	52	92
14	Vidhya	2679854	20	Primi	38	V	110	70	NIL	150	51	22.66	91	124	40	65.8
15	Veni	2877986	21	Primi	32	V	110	78	NIL	145	48	22.82	135	184	47	110
16	Bharathi	2668945	20	Primi	33	IV	110	70	NIL	155	53	22.06	97	130	38	72.6

S.NO	NAME	OP NO	AGE	PARITY	GA	SES	SBP	DBP	URINE ALB	HEIGHT	WEIGHT	BMI	S.TG	S.TC	S.HDL	S.LDL
17	Tamilponni	2453189	20	Primi	37	V	110	78	NIL	150	52	23.11	138	178	47	103.4
18	Nagalakshmi	2998766	26	G2P1L1	37	V	110	80	NIL	150	51	22.66	141	171	37	105.8
19	Pavithra	2987654	23	Primi	39	IV	110	74	NIL	145	48	22.82	106	156	42	92.8
20	Sridevi	2778994	25	G2P1L1	35	IV	114	76	NIL	160	54	21.09	129	167	42	99.2
21	Shanthi	2113445	20	Primi	36	V	100	70	NIL	151	51	22.36	114	149	52	74.2
22	Angel	2889576	20	Primi	33	IV	114	70	NIL	150	52	23.11	116	159	35	100.8
23	Nirmala	2897564	23	Primi	34	V	110	74	NIL	155	53	22.06	124	145	42	78.2
24	Kavitha	2747868	24	Primi	35	V	110	76	NIL	145	50	23.8	129	158	49	83.2
25	Marumalar selvi	2786235	29	G3P2L2	34	V	114	80	NIL	150	53	23.5	140	163	39	96
26	Ambika	2995234	25	G2P1L1	33	IV	118	86	NIL	150	51	22.66	173	215	44	136.4
27	Beena	2333678	22	Primi	31	IV	110	80	NIL	159	54	21.35	160	169	54	83
28	Sudha	2666678	21	Primi	32	IV	110	70	NIL	155	53	22.06	124	154	58	71.2
29	Masilamani	2999967	20	Primi	34	IV	110	78	NIL	160	54	21.09	140	149	46	75
30	Shantha	3266456	20	Primi	36	V	100	70	NIL	145	48	22.82	101	169	50	98.8

ABSTRACT

Background:

Gestational hypertension and preeclampsia are classified as hypertensive disorders of pregnancy. They are one of the major causes for increased mortality and morbidity in mother and fetus. In these disorders, Placental ischemia and inflammation occur due to impaired trophoblastic invasion into uterine spiral artery. Inflammatory mediators released from ischemic placenta into the circulation lead to insulin resistance and dyslipidemia which further lead to endothelial dysfunction and hypertension.

Keywords: Dyslipidemia; gestational hypertension; preeclampsia.

AIMS

1.To compare the serum lipid parameters(triglycerides,total cholesterol,LDL,HDL) of normal pregnant women with gestational hypertension and preeclampsia.

OBJECTIVES

1. To measure serum lipid profile in gestational hypertension,preeclampsia and normal pregnant women.
2. To compare serum lipid profile levels in three groups.

3.To know the role of altered lipid profile in the pathophysiology of preeclampsia.

4.To establish the relationship between serum lipid profile and preeclampsia

5.To correlate the lipid profile levels with the severity of preeclampsia.

Methods:

Case control study was done taking 30 women with gestational hypertension as Group-I, 30 women with preeclampsia as Group-II and 30 age matched healthy pregnant women as controls.

In all the subjects, concentrations of serum triglycerides, total cholesterol and HDL were estimated using enzymatic methods in semiautoanalyser. LDL calculated by Friedwald's formula using triglyceride,total cholesterol,HDL values.

Results:

The mean concentrations of triglyceride,total cholesterol,LDL were significantly increased and HDL concentration significantly decreased in women with hypertensive disorders of pregnancy when compared with healthy pregnant women. Systolic blood pressure , diastolic blood pressure and urine albumin have positive correlation with triglyceride concentration.

Interpretation and conclusion:

This study suggests that dyslipidemia is present in women with gestational hypertension and preeclampsia. The serum lipid profile in these conditions may help to detect the disease progression.It leads to development

strategies to prevent recurrence in next pregnancy by life style modification and medication.As Systolic blood pressure,Diastolic blood pressure and urine albumin have positive correlation with triglyceride concentration it indicates the severity of disease.