

**LIPID METABOLISM STUDY IN WOMEN OF
PREGNANCY INDUCED HYPERTENSION CASES**



Ph.D THESIS

By

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PREGNANCY INDUCED HYPERTENSION CASES**

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TO

**MY SISTERS, WHO BECAME VICTIM OF THIS
DEADLY DISEASE IN
A VERY YOUNG AGE**

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Chapter - 1

INTRODUCTION

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MATERIAL AND METHODS

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DISCUSSION

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Rubina Nazli

ABSTRACT

This cross sectional study was conducted on the pregnant women attending the Gynecology and Obstetrics Department of tertiary care hospitals of Peshawar, North West Frontier Province (NWFP) Pakistan. A total of 402 pregnant women at gestational age of ≥ 20 weeks were registered in the study after taking their informed consent. The study subjects were divided into four groups of pregnant women; with three patient groups (A, B, C) of Pregnancy Induced Hypertension (PIH) and one control group (D).

History of each participant was recorded on a pre designed questionnaire. Height, weight and blood pressure was measured and 5 ml of venous blood was drawn from patients and control groups. Biochemical analysis of lipoprotein included Total Cholesterol (TC), High Density Lipoprotein Cholesterol (HDL-C), Low Density Lipoprotein Cholesterol (LDL-C), Very Low Density Lipoprotein Cholesterol (VLDL-C), Triglycerides (TG), Apolipoprotein-A1 (APO-A1), Apolipoprotein- B100 (100), Lipoprotein-a (LPA) and hematological parameters including Hemoglobin (Hb) and Platelet count. These investigations were performed in PMRC Research Centre, Khyber Medical College, Peshawar and in the Pathology labs of Post Graduate Medical Institute (PGMI) Lady Reading Hospital, Peshawar. The data was processed on computer software package SPSS version 10.

Statistically highly significant ($P < 0.001$) differences were noted in most of maternal serum lipids and lipoprotein concentrations in the three individual patient groups when compared with the control pregnant women, except changes in LDL-C ($P > 0.05$). Changes in the TC were non significant in group A and B, while difference in group C were significant ($P < 0.05$) when compared with the control group D. Similarly was non significant ($P > 0.05$), markedly significant ($P < 0.01$) and highly significant ($P < 0.001$) in group A, B & C respectively when compared with group D. Mean concentrations of 100 were non significant in group B, while it was significant ($P < 0.05$) in group A and C when compared with group D. Changes in the mean values of LPA were non significant in group A and B, while it was highly significant ($P < 0.001$) in group C as compared to

control group D. Amongst the different lipoprotein ratio TC: HDL-C, LDL-C: HDL-C, TG: HDL-C and HDL-C: VLDL-C ratio were found highly significant ($P < 0.001$) in patient groups of A, B and C, as compared with group D. Women who developed hypertension (group A+B+C) had 5.45%, 3.5%, 39%, 38.6% and 26.98% higher concentrations of TC, LDL-C, VLDL-C, TG and LPA levels respectively, than control subjects. A significant decrease of (16.76%) and (18.5%) was respectively noted in HDL-C and APO-A1 of patient group when compared with control pregnant women, while no significant change in 100 levels was seen among the groups. TC: HDL ratios, LDL-C: HDL-C ratio and TG: HDL-C ratios were higher (32.3%, 29.8% & 66.4% respectively) among women with PIH and were found highly significant ($P < 0.001$) as compared to normotensive women. In the PIH group LDL-C: 100 was raised to the marked significant level of $P < 0.01$, while the difference between the two groups of test and control was found non significant for LDL-C: 100 ratio ($P > 0.05$). HDL-C: VLDL-C ratio were decreased by 38.23% in the patients and were highly significant as compared with control subjects ($P < 0.001$).

A significant difference was found in maternal TG levels, VLDL-C, TC: HDL-C, TG: HDL-C and HDL-C: VLDL-C ratio, when the PIH group of patients with systolic blood pressure (SBP) $<$ and ≥ 150 mmHg were compared. Similarly PIH patients had significantly elevated serum HDL-C, VLDL-C, TG, TC: HDL-C, TG: HDL-C, HDL-C: VLDL-C and LDL-C: 100 ratio when patients with diastolic blood pressure (DBP) < 110 were compared with DBP ≥ 110 mmHg.

Undesirable TC > 240 mg/dl in 35.8% patients, undesirable HDL-C in 50% patients, high concentrations of TG (73.2%), borderline high concentration of LDL-C (23.6%), undesirable TC ratio > 5.2 in 52.3% and undesirable LDL-C ratio > 1.6 were noted all in the patients of eclampsia group 'C'.

A 1.5-fold increase in the risk of PIH among women with TC > 240 mg/dl was noted, as compared with women whose TC concentration was < 200 mg/dl (95% CI (0.80-2.75) χ^2 1.81, P 0.17). Women in the lowest group of HDL-C concentration, experienced an 8.6-fold increased risk of PIH as compared with women in the highest group (95% CI (3.28-22.71) χ^2 27.9, $P < 0.0001$) as referent. The women having LDL-C in the range of 130-159 mg/dl experienced a 1.5-fold

increased risk of PIH as compared with women in the lowest group (95% CI (0.67-3.40). Women in the TG concentrations (200-499 mg/dl) experienced a 3.5-fold increased risk of PIH as compared with those women in the lowest group as referent (95% CI (1.50 to 8.22) χ^2 10.82, $P < 0.001$). The risk of PIH increased 4.5 times for HDL-C ratio > 5.1 (95% CI (2.-8.87) χ^2 24.39, $P < 0.0001$). Women with the highest LDL-C: HDL-C ratio experienced an almost 2.4-fold increased risk of PIH (OR 2.43, 95% CI 1.18 to 4.98, χ^2 7.09, P 0.007) as compared with women whose ratio values were < 1.21 (lower group).

A significant change was seen in the concentration of HDL-C ($P < 0.01$), VLDL-C ($P < 0.05$), triglycerides ($P < 0.05$), 100 ($P < 0.05$) and LPA ($P < 0.05$), when PIH women in the second trimester were compared with those in their third trimester. Significant changes were observed in the systolic ($P < 0.05$) and DBP ($P < 0.01$) of PIH women, when 2nd trimester was compared with the 3rd trimester.

In the patient group 85.6% pregnant women were anemic as compared to 84.5% in the control group. Majority of women with severe anemia (Hb < 7.7 g %) were present in the three patient groups as compared to the normal pregnant women. Normal platelet count > 150 thousand/ μ L was recorded in 85 (95.5%) of control pregnant women against 70 (78.3%) in the group of PIH. The number of women with severe thrombocytopenia (platelet count < 100 thousand/ μ L) were more in group C of eclampsia (13.6%) versus 1.1% in the control women.

In conclusion, the results of our study propose that an abnormal lipid metabolism and predominantly low HDL-C and high TG concentrations, may add to the promotion of vascular dysfunction and oxidative stress seen in pregnancy induced hypertension. It is, therefore, essential that, blood lipid concentrations be estimated in pregnant women during antenatal care since it could be useful in the early revealing and prevention of obstetric complications such as pregnancy induced hypertension.

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LIST OF ABBREVIATIONS

Abbreviations	Full Name
PIH	Pregnancy Induced Hypertension
GH	Gestational Hypertension
PE	Pre-eclampsia
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
TC	Total Cholesterol
HDL-C	High Density Lipoprotein Cholesterol
LDL-C	Low Density Lipoprotein Cholesterol
VLDL-C	Very Low Density Lipoprotein Cholesterol
TG	Triglycerides
APO-A1	Apo-lipoprotein-A1
100	Apo-lipoprotein-B100
LPA	Lipoprotein (a)
Hb	Hemoglobin
PLT	Platelet Count
BMI	Body Mass Index
EDTA	Ethylene diamine tetra acetate
SD	Standard Deviation
SEM	Standard Error of Mean
OR	Odd ratio
CI	Confidence Interval
HELLP	Hemolysis Elevated Liver Enzymes Low Platelet syndrome
NCEP III	The National Cholesterol Education Program, Adult Treatment Panel III

INTRODUCTION

1.1 Hypertension

High blood pressure, also called hypertension, is high pressure of the blood in the arteries. National Institute for Health and Clinical Excellence (NICE)¹ define hypertension as persistent elevated blood pressure above 140/90 mmHg.

There are two causes for the development of high blood pressure: First is that the heart pumps blood forcefully and second is the constriction of arterioles because of which the flow of blood will exert more pressure. The body stands with hypertension for some time, but finally the heart size is enlarged and this condition is called hypertrophy of heart. Cardiac hypertrophy is the main cause of cardiac failure. This persistent rise in the blood pressure effects arteries and arterioles in various organs; such as brain, kidneys, heart and retina.

Two components which are used to classify blood pressure are systolic and diastolic pressure respectively. When we measure blood pressure the systolic is the first reading and the diastolic is the second reading. Both systolic and diastolic blood pressures have their own significance. Various age groups are affected by hypertension and their consequences depend on whether systolic or diastolic blood pressure or both are raised. Pulse pressure is the third measurement which is main predictor of severity of the disease. Blood pressure is recorded by sphygmomanometer and its units are millimeter of Mercury (mmHg). Adult guidelines for hypertension propose three types: These types are as normal, prehypertensive and hypertensive. In normal adult the blood pressure should be 120/80 mmHg or less than this reading. Hypertension is usually present when

blood pressure is 140/90 mmHg or more than it. In that the upper reading 140 mmHg is systolic and lower reading 90 mmHg is diastolic. In prehypertensive type the range is 120-139 mmHg/80-89 mmHg, showing a high tendency towards raised blood pressure.

Systolic Blood Pressure: The systolic pressure is the force that blood exerts on the artery walls as the heart contracts to pump out the blood. Raised reading of systolic pressure is responsible for complications in various organs, such as heart, blood vessels and kidneys. It is also common cause of death in adults with middle and old age.

Diastolic Blood Pressure: The diastolic pressure is the measurement of force as the heart relaxes to allow the blood to flow into the heart. Raised pressure of the blood in the diastole is an important indicator of cardiac failure and stroke in young adult people.

Pulse Pressure: Pulse pressure is the difference between the systolic and the diastolic blood pressure readings. It is measured by subtracting systolic blood pressure from diastolic blood pressure. It shows hardness and damage to the arteries. High values of pulse pressure show more damage and stiffness to the arteries. It is proved that high value of pulse pressure is indicator of cardiac diseases especially in old age. In people over 45 years of age every 10 mmHg raise in that pressure will relatively increase the risk of stroke by 11%, cardiovascular diseases by 10% and overall mortality by 16%. In adults of young age the danger is more higher².

1.1.1 Hypertension Categories

High blood pressure is classified in different ways. One of the classifications is of the following type:

1. Essential Hypertension. Approximately 90% hypertension cases are of essential hypertension. The cause of that is unknown. That is why it is also called idiopathic or primary hypertension. The cause may be due to complex processes in the main body systems and organs i.e. blood vessels, heart, kidneys, nerves and hormones.
2. Secondary Hypertension. It is responsible of 5% cases of hypertension. A cause is known in this type of hypertension. Factors responsible for the secondary hypertension are as under:
 - a) Renal hypertension
 - b) Pregnancy induced hypertension (PIH)
 - c) Cushing's syndrome
 - d) Malignant Hypertension
 - e) Adrenal hypertension
 - f) Drugs
 - g) Coarctation of the aorta

Table-1.1: Blood pressure categories and ranges in adults.

Ranges of Blood Pressure	
Categories	Ranges for Adults (systolic/diastolic)
Normal Blood Pressure	Systolic ≤ 120 mmHg Diastolic ≤ 80 mmHg
Pre-hypertension	Systolic 120 - 139 mmHg Diastolic 80 - 89 mmHg
Mild Hypertension (Stage 1)	Systolic 140 - 159 mmHg Diastolic 90 - 99 mmHg
Moderate-to-Severe Hypertension (Stage 2)	Systolic >160 mmHg or Diastolic > 100 mmHg

1.1.2 Epidemiology

In European society the prevalence of hypertension increases with increasing age.

In adults 15-20 percent of people have raised blood pressure. Most of them have blood pressure which is mildly elevated. As high blood pressure become more severe the chances of cardiovascular complications increase³.

The major cause of ischemic cardiac diseases and hemorrhagic stroke is raised blood pressure. In Pakistan a study conducted by The National Health Survey of Pakistan (1990-94), pointed out that Pakistanis have a massive burden of hypertension⁴. The incidence of high blood pressure in Pakistani people aged 15 years and above was 19.0% (95% CI; 18.9-19.1)⁵.

Hypertension is prevalent⁴ in twenty-two percent of the urban Pakistani population age >15 years, and 1/3rd of persons aged ≥ 45 years and above. The prevalence based on age varied markedly, from 17.3 - 25.3% in men and from 9.9 - 41.4% in women between various ethnic groups, being highest in Balochi women and lowest in Sindhi women⁶. Higher occurrence of hypertension in the urban population is owing to more obesity in this area⁴. A direct relationship has been noted in age and systolic blood pressure⁵. It is imperative to note that > 70% of individuals with hypertension were unaware of their disease status, and < 3% had successfully controlled their blood pressure.

1.1.3 Complications

Stroke is the important complication of hypertension. Stroke is caused by high pressures in systole and diastole, but systolic blood pressure is more responsible. Women have two times more risk. Left ventricular hypertrophy, ischemic heart disease, cardiac failure, progressive renal disease, retinal vascular disease and dissecting aneurysm are its other complications.

1.1.4 Prognosis

Factors which influence prognosis include:

1. The possibility of a cardiovascular incident for any given blood pressure increases with age; control of hypertension is mainly helpful in elderly patients.
2. Diabetes, abnormal lipid profile and smoking are also major factors to cause heart diseases. If two or more risk factors occur in hypertensive patients the consequent danger of heart diseases increases. The possibility of cardiovascular disorders is higher as compared to the sum of the individual risk causes.
3. Left ventricular hypertrophy on ECG carries a poorer prognosis.

1.1.5 Pregnancy Induced Hypertension

Pregnancy induced hypertension contribute to the ancient times. Thiagarajha⁷ and Chesley⁸ have given its description in their reviews. Eclampsia was identified by the pre-Hippocratic Kahun Papyrus from Egypt 3000 years back. PIH was recognized by ancient Greeks. They believed that in pregnant women the appearance of heaviness, drowsiness and headaches is not a good sign. They have the possibility to develop some kinds of seizures. There was no explanation of this disease in any authentic books of Hippocrates, but Galen's commentary on Hippocrates' aphorisms recommends that he was familiar with the aggressive features in pregnant women. Likewise there is no talk about of it in the books of Susruta, the famous Indian clinician in the 6th century BC. St. Gall a well-known practitioner in the tenth century AD had a trick played on him. He was about to

examine the Duke of Bavaria and, as a deception the valuable nobleman replaced for his urine that of a woman who was pregnant. The high cleric after making his examination made the gloomy statement that the Duke would give birth to a child. This event is possibly the first evidence of finding protein in urine of pregnant women, although to some extent. Technical description on PIH actually started indirectly in the 17th century. Blundell, Mauriceau and Barton and all documented the signs of PIH. Rayer detected protein in urine of three pregnant women with edema in 1840. Although in 1843, Simpson and Lever detected protein in urine of pregnant women separately of each other. Old time practitioners had recommended raised blood pressure in women with PIH by examining their stiff bounding pulse. In, 1884 Vinay used ancient sphygmomanometer. He evaluated a blood pressures 160-200 mmHg in pregnant women with protein in urine. Blood pressures taken by his device was considered to be normal up to 160 mmHg. In 1897 Vaques and Nobecourt discovered eclamptic hypertension, but they believed that they had proved Vinay's examination.

Approximately 2-3% of pregnancies are complicated by raised blood pressure which is a frequent health problem during pregnancy. Blood pressure more than 140/90 mmHg before pregnancy or before 20 weeks⁹ pregnancy is called chronic hypertension. Hypertension after 20 weeks pregnancy in a woman with edema and proteinuria without previous history of hypertension is called pregnancy induced hypertension. When associated with proteinuria, the disorder is termed pre-eclamptic-eclampsia/toxemia, and when present without protein in urine it is called transient hypertension or gestational hypertension⁹. PIH is present in about 5% of the entire pregnancies, in 10% of primiparous women and 20 to 25% of

women with previous history of chronic hypertension. Raised blood pressure in pregnancy is the major cause of feto-maternal morbidity and mortality¹⁰.

A Pre-eclampsia

When blood pressure rises in pregnancy with significant protein in urine is called pre-eclampsia. Pre-eclamptic toxemia is actually a syndrome of signs and symptoms. It is suggested that placenta releases some substances that cause damage to endothelium of mothers blood vessels. High blood pressure is the major sign and that contributes to widespread damage to mother kidneys, liver and especially endothelium¹¹.

Pre-eclamptic toxemia may occur from 20 weeks pregnancy; the course of disease is different in different patients. Majority of cases are diagnosed preterm. When it occurs before 32 weeks, it is supposed to be associated with high mortality. Delivery of placenta is ultimate treatment which can be either to induce the labor, abortion or C-section. It can also occur up to six weeks postpartum. Among the serious complications of pregnancy pre-eclampsia is the most common; it may affect both the mother and the fetal survival¹¹.

B Eclampsia

This word originates from the Greek and means to a flash, a word used by Hippocrates to name a fever of rapid onset¹².

Eclampsia is a dangerous complication of pregnancy with a sudden onset and has the features of developing tonic-clonic fits in a patient who have developed pre-eclampsia. Eclampsia without onset of prior pre-eclampsia is rare. Pre-eclampsia

and eclampsia are collectively called hypertensive disorders or toxemia of pregnancy. Women developing fits and coma with previous history of organic brain lesions are not eclamptic.

C Gestational Hypertension

It is defined as the start of raised blood pressure before 20 weeks of pregnancy without protein in the maternal urine.

1.1.5.1. Pathophysiology

There are various theories to clarify eclampsia and pre-eclampsia and it is suggested that it is present till the placenta is present; once it is removed the situation improved¹³. It is proposed that hypo perfusion of placenta is the main factor responsible for the disease process. Maternal blood vessels become more sensitive to pressure agents causing constriction of blood vessels and hypo perfusion in various organs. Furthermore the condition is aggravated by the activation of coagulation chain causing microthrombi formation. Oedema developed by release of plasma into extra vascular tissues that further worsen the condition. These changes cause signs and symptoms of eclampsia as well as hypertension, renal, hepatic, and pulmonary dysfunction specifically cerebral dysfunction¹³. Endothelial activation and altered platelet counts are the markers of the disease progression before the development of signs and symptoms¹³.

Abnormal modeling of feto-maternal boundary can be immunologically mediated and is related to decrease placental perfusion¹³. Trophoblast seems to be involved incompletely¹⁴. In pre-eclamptic toxemia and eclampsia adrenomedullin is a strong vasodilator released in low quantity by the placenta¹⁵. Thromboxane A₂,

prostacyclin, endothelins and nitric oxide are the vasoactive involved¹⁶. Different studies have proposed that this is actually the mother immune system which is compromised by the paternal antigens which are present in the developing fetus¹⁷.

Eclampsia is seen as type of a hypertensive encephalopathy in the setting of those pathological changes that lead to pre-eclampsia. It is suggested that cerebral vascular resistance is decreased, causing to increased blood flow to the brain. In addition to abnormal function of the endothelium, this leads to cerebral edema¹⁷. Generally an eclamptic convulsion will not lead to permanent brain damage; but still, intracranial hemorrhage can occur¹⁸.

1.1.5.2. Causes

The cause of PIH in most of the cases is suggested to be because of shallow implantation of placenta because of which it becomes hypoxic and causes immune reaction. It is characterized by release of inflammatory mediators from the placenta, that act on vascular endothelium. This incomplete invasion is supposed to start from the mother's immunological response to the placenta. From this theory it is evident that maternal immunological responses to paternal antigen which are present in fetus play a key role. In few cases of PIH it seems that maternal receptors are lacking for protein which placenta secrete to down regulate the immune system response to it¹⁹. This theory also matches the theory of miscarriages; in which maternal immune system destroy the developing fetus. The mother's response to placental implantation appears to be acceptable in many cases. In women with raised base line levels of inflammation resulting from pre existing diseases such as chronic hypertension, acute immune disorders have low acceptance for the inflammatory processes of the pregnancy. If pre-eclampsia is

not treated it will lead to fulminant pre-eclampsia with visual disturbances, headache and epigastric pain. Abruptio of Placental and HELLP syndrome (Hemolysis Elevated Liver Enzymes Low Platelet) are also linked to pregnancies with hypertension. These are dangerous conditions for both the developing fetus and the mother.

Many hypotheses are proposed to clarify why PIH starts, and have related the syndrome to the occurrence of the following factors²⁰:

- I. Endothelial cell injury
- II. Immune rejection of the placenta
- III. Altered vascular reactivity
- IV. Compromised placental perfusion
- V. Decreased glomerular filtration rate with retention of salt and water
- VI. Decreased intravascular volume
- VII. Imbalance between prostacyclin and thromboxane
- VIII. Increased central nervous system irritability
- IX. Uterine muscle stretch (ischemia)
- X. Disseminated intravascular coagulation
- XI. Genetic factors
- XII. Dietary factors, including vitamin deficiency

The present perception of the syndrome is as a two step procedure, with an extremely changeable first step which influences the placenta to hypoxia, tracked by the discharge of soluble factor which affect many of the other observed phenomena. A number of the past theories can be included under this umbrella, as the soluble factors have been shown to affect, for example altered vascular

reactivity, endothelial cell injury, decreased intravascular volume, inflammation, the classic lesion of glomerular endotheliosis etc. Basic maternal susceptibility to the damage is probable concerned as well.

1.1.5.3 Epidemiology

Prevalence of pregnancy induced hypertension in pregnancies is 10% mainly in last two trimesters and after 32 weeks of gestation. In rare cases it is present as early as 20 weeks. Primiparous are more affected²¹ with the progress of parity the chances decreases. In women who have no family history of hypertension, change of paternity is also considered to decrease the risk²² in the next pregnancy. Still studies give contradictory data on this point whether paternal change decreases the risk. The age of mother is also important with increasing age the risk of pregnancy induced hypertension increases²³.

Pregnancy induced hypertension is common in women who have past history of raised blood pressure, autoimmune diseases like diabetes, renal disease, lupus, various inherited thrombophilias like Factor V Leiden, or, in women with a family history of PIH, in women with a multiple pregnancies (twins, triplets, and more) and obese women. Previous history of PIH is important risk factor for the development of pregnancy induced hypertension. The PIH can also present it self in the post partum period (6-8 weeks), but more common in just immediate postpartum period. Postpartum PIH usually started in first 24-48 hours after delivery, in that period the patient must be kept under observation²⁴ because it is most dangerous time.

Regarding perinatal and maternal mortality eclampsia is the leading cause. The incidence of eclampsia is described to be 0.56 per 1,000 births (US data from 1979-86) versus 26 per 1,000 births for pre-eclampsia²⁵. Proper antenatal checkups and services can decrease the mortality. Maternal mortality in India²⁶ is 32% and perinatal mortality 39%. It is most common to see eclamptic seizures in last trimester, in labor and in immediate 48 hours of delivery.

Approximately 585,000 women die each year of pregnancy related causes, 98% of these deaths are in the developing countries²⁷⁻²⁸. Out of these maternal deaths, 13% are in the women with pregnancy induced hypertension and eclampsia, the most terrible form that accounts for major cause of death²⁷. Complications of eclampsia in the developed countries is about 1 in 2000 deliveries²⁹ as compared to developing countries³⁰⁻³² where it varies from 1 in 100 to 1 in 1700. Same type of study³³ was conducted in Sri Lanka, according to that 4.9% of the pregnant women delivering in a tertiary care hospital have pregnancy induced hypertensive disorders. The prevalence of eclampsia in various parts of Pakistan³⁴⁻³⁶ is stated to be ranging from 1.6% - 3.1%, which is significantly elevated in contrast to statistics from the developed countries like UK (0.072%)³⁷, USA (0.028%)^{13, 38} and Finland (0.024%)³⁹, but is relatively lower in contrast to a study from Bangladesh (9%)⁴⁰. The national incidence of PIH is 15.2%, in India, while it is four times higher in primipara women than in multipara^{41, 16}. In Pakistan, maternal death from eclampsia is reported as 9 to 16.9 %^{34-36, 42}. The high incidence observed is pointing towards poverty, lack of education and unawareness regarding health care in this part of the world.

1.1.5.4 Signs and Symptoms

As the disease progresses and other organs become involved its sign also starts developing. These are raised blood pressure, edema, headache, visual disturbance, epigastric pain, excessive weight gain, hyperreflexia, and proteinuria. With the progress of the pathophysiological process the signs and symptoms of other organs also developing, these are liver failure, epigastric pain, oliguria, pulmonary edema, and signs of the HELLP syndrome. Raised blood pressure causes intrauterine growth retardation in developing fetus and also causes fetal distress. Antipartum hemorrhage (abruption) can also occur.

1.1.5.5 Risk Factors

Pregnancy induced hypertension is more common in primiparous and women of younger age. Multiple pregnancies, hydatiform mole in which the placenta is large in size are also risk for eclampsia. Moreover, women with underlining vascular disorders e.g. diabetes, hypertension and nephropathy or thrombophilic diseases such as the antiphospholipid syndrome are at more risk to start pre-eclampsia and eclampsia. In addition, the genetic factor is also involved; patients who have a family history of pregnancy induced hypertension, especially in mother or sister are at higher risk⁴³.

1.1.5.6 Diagnosis

Pregnancy induced hypertension can be diagnosed when we take two separate blood pressure readings of pregnant women at 4 hours apart, and it shows 140 mmHg systolic and 90 mmHg of diastolic or more and proteinuria of ≥ 300 mgs in

24 hours urine sample. Swelling of the hands, face and feet also called edema is an important sign of developing pregnancy induced hypertension.

Signs and symptoms of PIH help in its diagnosis. Pre-eclampsia/eclampsia have symptoms which can be some times confused with other common problems of pregnancy, like pain in epigastrium can be confused with heart burn although it is important symptom showing involvement of liver and HELLP syndrome.

1.1.5.7 Differential Diagnosis

Differential Diagnosis of pregnancy induced hypertension are; chronic hypertension, chronic renal disease, thrombocytopenia, primary seizure disorders, immune purpura, pancreatic and gallbladder disease or antiphospholipid syndrome and hemolytic-uremic syndrome. After 20 weeks of pregnancy in all pregnant women possibility must be considered. When underlining disease is present then it is difficult to diagnose, such as hypertension⁴⁴. In pregnant women when high blood pressure is noted for the first time associated with protein in urine it may be eclampsia, or underlying medical problem which is previously undiagnosed such as phaeochromocytoma. In rare cases it may be a pregnancy specific condition such as hydatidiform mole presenting as pre-eclampsia. If convulsions are started in pregnancy chances are of eclampsia but the other disorders must be excluded. These are the brain tumor, aneurysm of the brain and side effects of certain drugs. Commonly when preexisting pre-eclampsia is present it helps in the diagnosis of eclampsia.

1.1.5.8 Complications

Complications of PIH are serious as eclampsia itself. The most dangerous complication is cerebral hemorrhage, which is a lesion and it can make pregnant women victims. Other complication is acute respiratory distress syndrome, but it is not determined whether it is due to eclampsia or modern respiratory support technique. Another common and dangerous condition is HELLP syndrome.

1.1.5.9 Treatment

There is no specific treatment, but early diagnosis and close monitoring is essential to rapidly recognize pregnancy induced hypertension and its life-threatening complications such as HELLP syndrome and eclampsia. Anti hypertensive drugs are used for raised blood pressure in pregnancy, there are many drugs but they have side effects on fetus. Commonly used drugs are labetalol and methyldopa. The only known cure for progressing pre-eclampsia or eclampsia is abortion or delivery, either by caesarean section or induction of labor. Postpartum PIH is also treated with anti hypertensive drugs.

1.1.5.10 Prevention of Convulsions

Pregnant women with eclampsia once start, fit quick management must be done to stop the fits and to deliver the fetus. Convulsions are controlled by using magnesium sulfate (4-6 g loading dose in 100 mL iv fluid given over 15-20 minutes, then 2g per hour as a continuous infusion)⁴⁵. International MAGPIE study⁴⁶ shows the evidence for use of magnesium sulfate.

Control of blood pressure in eclampsia is more effective with hydralazine and labetalol. Dose of hydralazine is 5-10 mg IV every 15-20 minutes until desired response is achieved or 20 mg bolus iv followed by 40 mg if necessary in 10 minutes; the 80 mg every 10 minutes up to maximum of 220 mg⁴⁵.

1.1.5.11 Recurrence Of PIH In Subsequent Pregnancies

It is not uncommon that pre-eclampsia or gestational hypertension reoccur or reappear in several pregnancies of the same woman. According to some studies⁴⁷⁻⁴⁹, in subsequent pregnancies the recurrence of pre-eclampsia or gestational hypertension has been reported as elevated as 50%. The danger of reappearance of pre-eclampsia, however may not give the right image as evaluated by some retrospective studies. They have not been capable to confirm the diagnosis by examining case notes since strict criteria may not have been applied to diagnose the same state in the past. The incidence of pre-eclampsia⁵⁰ is markedly lowered in women with previous history of normal delivery or even abortion. With a change of partner the protective effect of multiparity is lost however; the word primipaternity was used to explain this fact, proposing that pre-eclampsia might be a problem of primipaternity rather than primigravidity because the patterns of changing paternity were significantly correlated with pre-eclampsia in multipara⁵¹⁻⁵⁴.

1.1.5.12 Early Prevention

In developing countries eclampsia remains one of the major obstetrical problems. The reasons of this situation are still not identified; therefore useful primary prevention is not feasible at this stage. Research in the earlier decade has recognized some main risk factors for pregnancy induced hypertension, and

treatment of these factors might result in reducing its frequency. In secondary prevention of PIH aspirin was suggested to be the drug of choice in the early 1990s. The current facts show that women with a low dietary calcium intake are probable to take advantage from calcium supplementation. In tertiary prevention of pregnancy induced hypertension good antenatal care and timed delivery are of utmost significance. High blood pressure in pregnancy should be treated early with anti hypertensive drugs, such as methyldopa, lebetalol, hydralazine and calcium channel blockers⁵⁵.

1.1.5.13 Morbidity and Mortality Associated With Hypertensive Disorders of Pregnancy

Pregnancy induced hypertension is one of the two most frequent causes of maternal mortality in the developed countries⁵⁶. Even though in the developing world, where pre-eclampsia is the third commonest cause of maternal death following hemorrhage and infection⁵⁷, that is responsible for the great number of the estimated 50, 000 annual maternal deaths from hypertensive problems of pregnancy. Pre-eclampsia and eclampsia is predicted to account for 20-25% of maternal deaths⁵⁸ in Africa, Latin America, and the Caribbean. In Sri Lanka on the whole maternal mortality rate⁵⁹ in 1995 was 2.4 per 10,000 deliveries as compared with 15 per 10,000 deliveries in 1970. In 1997 hypertensive disorders of pregnancy⁶⁰ accounted for 10.3% of maternal deaths. However, this does not mean that severe maternal morbidity associated with hypertensive disorders of pregnancy is any less than has been reported in other parts of the world⁶¹. As the treatment of pre-eclampsia also include delivery there is also a considerably increased morbidity and mortality from iatrogenic prematurity. In a Sri Lankan study⁶² as many as 34% of infants born of pregnancies complicated by pre-

eclampsia required special care. In the West^{61, 63}, perinatal mortality rates (PNMR) in pregnancies complicated by pregnancy induced hypertension are low where it is reported to be less than 5%. In different studies conducted in Srilanka^{33, 62, 64} perinatal mortality rates of 14.8%, 23.2%, and 24.1% have been reported

1.1.5.14 Lipid Metabolism In PIH

Lipoproteins' levels increases during pregnancy, but in PIH they increases two times more⁶⁵⁻⁶⁷. Changes in lipoproteins' concentration in essential hypertension are documented⁶⁸. Abnormal lipoproteins' levels are responsible for damage to endothelium that leads to high blood pressure and proteinuria; these are important signs of pregnancy-induced hypertention⁶⁹.

Changes in lipoproteins cause atherosclerosis, damage to endothelium and other heart diseases. The major sign of PIH is hypertension, suggesting that it is due to vasospastic events in the placenta, kidney, uterus and brain⁷⁰.

Changes in lipoproteins' levels have a key role in the pathogenesis of pregnancy induced hypertension. In PIH injury to endothelium and resulting endothelium function are important factors to cause damage to multiple systems of the body⁷⁰.

Abnormal lipid metabolism has a basic role in the pathogenesis of this disease⁷¹.

Relation of abnormal lipoproteins' levels in pregnancy with hypertension and protein in urine is highly suggestive to show some new diagnostic tools. Hormones are also involved in the pathogenesis of pregnancy related hypertensive disorders, their abnormal levels can be reflected by lipoproteins estimation, and one can avoid the expensive hormonal levels detection assay.

Pregnancy induced hypertension is the most important cause of maternal and neonatal mortality⁷². Vascular sensitivity to pressors⁷³ increases pregnancy induced hypertension. The coagulation and fibrinolytic cascades are highly activated⁷⁴. Endothelium dysfunction can explain protein in the urine⁷⁵. Serums from women with pre-eclampsia have some unknown substances that alter the metabolic and functional properties of cultured endothelial cells⁷⁶. Abnormal lipid metabolism is responsible for endothelial dysfunction⁷⁷ and it was proposed that small, dense low-density lipoprotein may add to endothelial dysfunction in pre-eclampsia⁷⁸⁻⁷⁹. Triglyceride-rich lipoproteins particularly may also activate endothelial dysfunction⁸⁰ and atherothrombosis⁸¹. In toxemia of pregnancy⁷⁸⁻⁷⁹ serum triglyceride concentration increases much more notably. The essential modulator of this hypertriglyceridemia is oestrogen as pregnancy is related with hyperoestrogenaemia. In pregnancy the level of oestrogen increases that causes increased hepatic biosynthesis of endogenous triglycerides, which is carried by very low-density lipoprotein⁷⁵. This process probably is modulated by hyperinsulinism that starts in pregnancy⁷⁶. All these mentioned interactions along with increased endothelial triglyceride accumulation may result in endothelial cell damage in pregnancy⁷⁹. In pregnancy-induced hypertension the level of TG increases, and it is likely to be deposited in predisposed vessels, such as the uterine spiral arteries and contributes to the endothelial damage, both directly and indirectly through generation of small, dense LDL⁸⁰. Moreover this hypertriglyceridemia can be related with hypercoagulability⁸¹. If women who have a history of PIH then according to current epidemiologic studies will have more risk of cardiovascular disease. According to a review of 7,543 hospital records from Iceland, it was found⁸² that a greater rate of death from ischemic heart

disease in women with a history of PIH was present compared with the general population (relative risk = 1.47; 95% confidence interval [CI] 1.05–2.02). According to a Scottish retrospective cohort study women with a history of pregnancy induced hypertension, an average of 19 years before, had a 2-time high risk of being admitted to the hospital for ischemic heart disease or dying from that disease.⁸³ Irgens et al⁸⁴, in a population-based retrospective cohort study from Norway, observed that women with a history of PIH had an increased mortality rate (OR = 1.65; 95% CI 1.01–2.70) from cardiovascular causes as compare to women without PIH, 13 years after the index pregnancy. These retrospective studies recommended a relation between PIH and long-term risk of cardiovascular disease, but they were inadequate in their ability to regulate for confounders and they could not propose the mechanisms underlying the relation.

Women in whom PIH ultimately develops are more likely to enter pregnancy overweight and to demonstrate, during pregnancy, some of the risk factors characterizing atherosclerosis, such as dyslipidemia (hypertriglyceridemia, low levels of high-density lipoprotein [HDL] cholesterol and high levels of small dense low-density lipoprotein [LDL] cholesterol)^{78,85}, insulin resistance^{86, 87}, and endothelial dysfunction⁸⁸. Certainly these metabolic changes (increased adiposity, hyperlipidemia, elevated blood pressure and hyperglycemia,) are indicative of the metabolic syndrome. This syndrome is proposed as an independent risk factor for cardiovascular disease^{89, 90}, and organizations such as The National Cholesterol Education Program, Adult Treatment Panel III (NCEP III)⁹¹, and the World Health Organization (WHO)⁹² have proposed criteria to better define people at risk for the metabolic syndrome. Obesity, hypertension, blood lipid profile, fasting blood

glucose concentration, and, for the WHO criteria, evaluation of insulin resistance are the main criteria.

A study from China⁹³ shows that serum levels of triglycerides (TG), apolipoprotein C-II (apo C-II) and apo C III were highly increased in normotensive pregnant women by 3.5, 2.4 and 2.8 times respectively, when compared with those in non-pregnant ones ($P < 0.001$); serum total cholesterol (TC), high density lipoprotein-cholesterol (HDL-C) and apolipoprotein AI (apo A1), B100 and E were also increased in normotensive pregnant women by 21%, 33%, 55%, 79% and 77% respectively, when compared with those in non-pregnant ones ($P < 0.001$). TG: HDL-C in normotensive pregnant women was also considerably higher than that in non-pregnant ones ($P < 0.01$). Serum HDL-C levels remained unchanged in both groups. Serum TG, apoC II and apoC III were highly increased in PIH patients by 2.3, 4.0 and 2.8 times respectively, when compared with those in non-pregnant ones ($P < 0.001$); serum TC, HDL-C and apoAI, B100 and E were also increased in PIH patients by 27%, 26%, 52%, 90% and 67% respectively, when compared with those to non-pregnant ones ($P < 0.001$) TG: HDL-C in PIH patients was also considerably higher than that in non-pregnant ones ($P < 0.01$). Serum HDL-C levels were increased in PIH patients by 29%, when compared with non-pregnant women. Only serum HDL-C level in PIH patients was higher than that in normotensive pregnant women. No significant differences were seen in other lipid and apolipoprotein levels between PIH patients and normotensive pregnant ones. There was no significant difference in the levels of serum lipid and apolipoprotein between the subgroups of PIH patients according to the severity of the disease.

Serum levels of MDA, total cholesterol, triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), Lp (a), and placental MDA were significantly elevated, and high-density lipoprotein cholesterol (HDL-C) and Apo A-I levels were significantly lower, in severely pre-eclamptic and mildly pre-eclamptic women than in the normal pregnant women, but no difference was seen in Apo B among groups. Serum level of Lp (a) was positively associated with body mass index in severely pre-eclamptic women ($r=0.489$, $p=0.008$). A significant positive association was also found between serum level of MDA and systolic blood pressure in women with severe pre-eclampsia ($r=0.375$, $p=0.049$)⁹⁴.

1.1.6.0 Lipoproteins

Lipoprotein contains both lipids and proteins. The proteins are bounded to the lipids or their derivatives covalently or non-covalently. Structural proteins transporters, several enzymes, antigens, toxins and adhesions are lipoproteins. Examples comprise of the high density and low density lipoproteins which facilitate fats to be carried in the blood stream, the transmembrane proteins of the mitochondrion and the chloroplast and bacterial lipoproteins⁹⁵.

Function

The transport of lipids and cholesterol around the body in the aqueous blood is the function of lipoprotein particles, in which they would not normally dissolve. All cells utilize and depend on fat; cholesterol is a building block of body cells, to create the multiple membranes which cells use to both control internal water content, internal water soluble elements and to systematize their protein enzymatic systems and internal structure.

The structure of lipoprotein particles have hydrophilic groups of cholesterol, phospholipids, and apoproteins directed outward; which helps them to become soluble in the salt-water based blood pool. Triglyceride-fats and cholesterol esters are transported internally, shielded from the water by the phospholipids monolayer and the apoproteins. The interaction of the proteins forming the surface of the particles with (a) enzymes in the blood, (b) with each other and (c) with specific proteins on the surfaces of cells, determine whether triglycerides and cholesterol will be added to or removed from the lipoprotein transport particles. Concerning atheroma development and progression vs. regression, the key issue has always been cholesterol transport patterns, not cholesterol concentration itself.

Classification of lipoprotein

Lipoproteins are classified on the basis of their functions and densities. Various types of lipoprotein are given below.

- a. Chylomicrons-carry triacylglycerol from the liver, skeletal muscles, and to adipose tissue.
- b. Very low-density lipoproteins (VLDL) - they carry endogenous triacylglycerol from the liver to adipose tissue.
- c. Intermediate density lipoproteins (IDL) - they are intermediate between VLDL and LDL. They are not usually detectable in the blood.
- d. Low-density lipoproteins (LDL) – they carry cholesterol from the liver to cells of the body. Sometimes referred as the ‘bad cholesterol’ lipoprotein.
- e. High-density lipoproteins (HDL) – they collect cholesterol from the body’s tissues, and bring it back to the liver, sometimes referred to as the “good cholesterol” lipoprotein.

Table-1.2: Classification of lipoproteins on the basis of densities.

Density (g/mL)	Class	Diameter (nm)	Protein %	TC %	Phospho lipid %	Triacyl glycerol %
>1.063	HDL-C	5-15	33	30	29	8
1.019-1.063	LDL-C	18-28	25	50	21	4
1.006-1.019	IDL-C	25-50	18	29	22	31
0.95-1.006	VLDL-C	30-80	10	22	18	50
<0.95	Chylo microns	100-1000	< 2	8	7	84

1.1.6.1 Total cholesterol

Total Cholesterol (TC) is a waxy, lipimic alcohol present in the cell membranes and transported in the blood plasma. It is an essential component of mammalian cell membranes where it is important to set up proper membrane permeability and fluidity. Cholesterol is classified as a sterol which is a contraction of steroid and alcohol. Even though cholesterol is crucial for life, elevated levels in circulation are linked with atherosclerosis. Cholesterol is ingested in the diet, recycled within the body through reabsorption of bile in the digestive tract. Cholesterol facilitates the body to make cells and produce hormones. Excessive cholesterol in the blood can assemble up in the surrounding of the arterial walls, forming plaques. Bulk amounts of plaque add to probability of having a heart attack or stroke.

1.1.6.2 High Density Lipoprotein Cholesterol

High-density lipoproteins-cholesterol (HDL-C) is one of the 5 major groups of lipoproteins (chylomicrons, VLDL-C, IDL-C, LDL-C, and HDL-C) which facilitate lipids like cholesterol and triglyceride to be transported within the water based blood stream. Approximately 30% of blood cholesterol is carried by HDL in healthy persons.

It is hypothesized that HDL can take away cholesterol from atheroma within arteries and carry it back to the liver for re-utilization and excretion, the main reason why HDL-bound cholesterol is often called “good cholesterol”. Low HDL-C levels (less than 40 mg/dL) raise the risk for heart disease, while a high level of HDL-C assists to defend against cardiovascular diseases. When determining cholesterol any contained in HDL-C particles is proposed to provide safety to the body’s cardiovascular health, in contrast to “bad” LDL cholesterol.

HDL-C carries several lipids and protein groups, a lot of which have very low concentrations but are biologically very active. For example, HDL-C and their protein and lipid components help to activation of the endothelium, inflammation, platelet aggregation or coagulation and decrease oxidation. All these properties may add to the ability of HDL-C to protect from atherosclerosis⁹⁶.

1.1.6.3 Low Density Lipoprotein Cholesterol

Low-density lipoprotein cholesterol (LDL-C) is a type of lipoprotein that transfers triglycerides and cholesterol from the liver to peripheral tissues. Similar to all lipoproteins, LDL-C make easier fats and cholesterol to move within the water based solution of the blood stream. LDL-C also controls cholesterol production at these spots. It frequently come out in the medical setting as part of a blood

cholesterol test and since elevated levels of LDL cholesterol can be a warning sign of medical disorders like cardiovascular disease. It is sometimes called bad cholesterol, as opposite to HDL-C, which is often referred to as good cholesterol. Every original LDL-C particle has a single apolipoprotein B-100 molecule, which circulates the fatty acids, keeping them soluble in the aqueous solution. Also, LDL-C has a highly-hydrophobic core consisting of polyunsaturated fatty acid known as linoleate and about 1500 esterified cholesterol molecules. This core is encircled by a shield of phospholipids and unesterified cholesterol, as well as a single copy of B-100 large protein. LDL-C particles are about 22 nm in diameter and have a mass of about 3 million Daltons, but since LDL-C particles have a changeable number of fatty acids, they in reality have a mass and size distribution⁹⁷.

1.1.6.4 Very Low Density Lipoprotein Cholesterol

Very low-density lipoprotein cholesterol (VLDL-C) is a kind of lipoprotein prepared by the liver. VLDL-C help cholesterol and fats to move inside the water based solution of the blood stream. VLDL-C collects in the liver from cholesterol and apolipoproteins. VLDL-C is altered in the bloodstream to low-density lipoprotein. VLDL-C particles have a diameter of 30-80 nm. Chylomicrons transport exogenous (dietary) products, whereas endogenous compounds are transported by VLDL-cholesterol.

VLDL-C transports endogenous phospholipids, cholesterol, triglycerides and cholesteryl esters. Its role is the body's internal transports mechanism for lipids. VLDL-C levels have been related with increased rates of atherosclerosis and are higher in metabolic states and in a number of diseases.

1.1.6.5 Triglyceride

Triglycerides, as main part of very low density lipoprotein cholesterol and chylomicrons, have a vital role in metabolism as energy sources and transporters of dietary fat. They provide additional energy (9 kcal/g) as compared to proteins and carbohydrates. In the intestine, triglycerides are split into fatty acids and glycerol which are then moved into the cells lining the intestine. The triglycerides are rebuilt in the enterocytes from their fragments and packaged together with proteins and cholesterol to form chylomicrons. These are excreted from the cells and collected by the lymph system and transported to the large vessels near the heart prior to being mixed into the blood. Different tissues can detain the chylomicrons, releasing the triglycerides to be used as a source of energy. Liver cells and fat can produce and store triglycerides. When the body needs fatty acids as an energy source, the hormone glucagons causes the breakdown of the triglycerides by hormone-sensitive lipase to liberate free fatty acids. As the brain can not make use of fatty acids as an energy source except when it is changed to a ketone, the glycerol part of triglycerides can be changed into glucose, via gluconeogenesis, for brain fuel when it is broken down.

Triglycerides cannot pass through cell membranes freely. Particular enzymes on the walls of blood vessels called lipoprotein lipases should break down triglycerides into glycerol and fatty acids. By the use of the fatty acid transporter (FAT) fatty acids can then be taken up by cells. High levels of triglycerides in the bloodstream have been associated to atherosclerosis in the human body, which increase the risk of stroke and heart disease. However, the relative negative impact of increased concentration of triglycerides compare to that of LDL: HDL ration is

so far unidentified. The danger can be partially accounted by a strong opposite association between triglyceride level and HDL- C level.

1.1.6.6 Apolipoprotein

Apolipoproteins are a kind of protein that binds to fats (lipids). They form lipoproteins, which take up dietary fats through the bloodstream. Dietary fats are digested in the intestine and transported to the liver. Liver also synthesizes fats by itself. Fats are stored in fat cells called adipocytes. Fats are metabolized because they are essential for energy in the heart, skeletal muscle, and other organs. They are secreted as milk from the breast.

The fatty, oily part of lipoproteins is not soluble in water. But because of their detergent-like (amphipathic) action, apolipoproteins help them to dissolve.

Apolipoproteins also serve as enzyme co-factors, receptor ligands and lipid transport carriers that control the metabolism of lipoproteins and their absorption in tissues. There are six main classes of apolipoproteins and several sub-classes which are as following:

1. A (apo A-I, apo A-II, apo A-IV, and apo A-V)
2. B (apo B48 and apo B100)
3. C (apo C-I, apo C-II, apo C-III, and apo C-IV)
4. D
5. E
6. H

Hundreds of genetic polymorphisms of the apolipoproteins have been evaluated, and several of them change their function and structure. Apolipoprotein production is controlled primarily by the fat part of the diet in the intestine.

Apolipoprotein synthesis in the liver is organized by multiple factors, including hormones (estrogens, glucagon, insulin, androgens, thyroxin), alcohol intake, dietary composition and various drugs (statins, niacin, and fibric acids).

1.1.6.7 Lipoprotein (a)

Lipoprotein (a) is a subclass of lipoprotein. Studies have recognized Lp(a) as a significant danger for atherosclerotic disorders such as stroke and coronary heart disease.

Lipoprotein (a) composed of an LDL-C like particle and the specific apolipoprotein (a), which is covalently bound to the apoB of the LDL-C like particle. Lp(a) plasma levels are highly hereditary and is frequently controlled by the apolipoprotein(a) gene. High Lp(a) levels in blood is a threat for cerebrovascular disease (CVD), coronary heart disease (CHD), thrombosis, atherosclerosis and stroke. Lp(a) levels may be affected by disease states, but are only slightly affected by exercise, diet and other environmental factors. High Lp(a) predicts risk of early atherosclerosis like to high LDL-C, but in advanced atherosclerosis, Lp(a) is a risk factor not dependent on LDL-C. Lp(a) show a coagulant threat of plaque thrombosis.

1.1.6.8 Test Overview

Cholesterol and triglyceride tests are blood tests that measure the total amount of fatty substances in the blood. Lipoprotein analysis (lipoprotein profile or lipid profile) assess blood levels of total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides⁹⁸⁻¹⁰⁰. The normal range and the range representing the borderline and high levels of lipoproteins are given in the following table.

Table-1.3: Levels of cholesterol and triglycerides in the blood.

Total cholesterol	Desirable:	1 Less than 200 mg/dL 2 Less than 5.2 mmol/L
	Borderline high:	3 200–239 mg/dL 4 5.2–6.2 mmol/L
HDL cholesterol	High:	5 240 mg/dL or higher 6 6.2 mmol/L or higher
	High (desirable):	7 More than 60 mg/dL 8 More than 1.6 mmol/L
	Acceptable:	9 40–60 mg/dL 10 1.0–1.6 mmol/L
	Low (undesirable):	11 Less than 40 mg/dL 12 Less than 1.0 mmol/L
Total cholesterol-to-HDL ratio	Desirable:	13 5:1 or less
	Undesirable:	14 More than 5:1
LDL cholesterol	Optimal:	15 Less than 100 mg/dL 16 Less than 2.6 mmol/L
	Near optimal:	17 100–129 mg/dL 18 2.6–3.4 mmol/L
	Borderline high:	19 130–159 mg/dL 20 3.4–4.1 mmol/L
	High:	21 160–189 mg/dL 22 4.1–4.9 mmol/L or higher
	Very high:	23 190 mg/dL or higher 24 4.9 mmol/L or higher
VLDL cholesterol	Optimal:	25 Less than 130 mg/dL 26 Less than 3.4 mmol/L
	Borderline high:	27 140–159 mg/dL 28 3.4–4.1 mmol/L
	High:	29 160 mg/dL or higher 30 4.1 mmol/L or higher
Triglycerides	Normal:	31 Less than 150 mg/dL 32 Less than 1.7 mmol/L
	Borderline high:	33 150–199 mg/dL 34 1.7–2.3 mmol/L
	High:	35 200–499 mg/dL 36 2.3–5.6 mmol/L
	Very high:	37 500 mg/dL or higher 38 5.6 mmol/L or higher

HDL: LDL ratio according to the severity of disease is given in the following table.

Table-1.4: Distribution of HDL: LDL levels according its severity.

Risk level	Men	Women
Very Low Risk	3.4	3.3
Low Risk	4.0	3.8
Average Risk	5.0	4.5
Moderate Risk	9.5	7.0
High Risk	>23	>11

According to the National Heart, Lung, and Blood Institute optimal, borderline and high levels for each component of lipoprotein are given the following table.

Table-1.5: Optimal, Borderline, and High Levels for Each Component.

Lipoprotein	Optimal	Borderline	High risk
LDL Cholesterol (mg/dL)	<100	130–159	160+
HDL Cholesterol (mg/dL)	>60	35–45	<35
Triglycerides (mg/dL)	<150	150–199	>200
Total Cholesterol (mg/dL)	<200	200–239	>240
Cholesterol to HDL Ratio	<4	5	>6

1.1.7.0 Hematological Changes in PIH

Many hemostatic abnormalities have been reported in relation with hypertensive disorders of pregnancy. Thrombocytopenia is the most common of these, existing in 11% to 29% of patients who have pregnancy induced hypertension¹⁰¹⁻¹⁰³. These pregnancies also are linked with qualitative alterations signifying increased platelet turnover. There are an increased number of megakaryocytes in the bone marrow, shortened platelet life span and an increased number of immature platelets seen in the peripheral blood smear¹⁰⁴⁻¹⁰⁵. Many investigators consider that the increased platelet utilization is due to disseminated intravascular coagulation while others propose an immune mechanism¹⁰⁴.

In pregnancy induced hypertension, the most frequent hematological abnormality found¹⁰⁶ is thrombocytopenia. The degree of thrombocytopenia increases with severity of disease and the occurrence of thrombocytopenia depend on the severity of the disease progression¹⁰⁶. Lower is the number of platelet; the greater is the maternal and fetal morbidity and mortality¹⁰⁷. Overt thrombocytopenia defined by platelet count $<1 \text{ lac/mm}^3$ point toward severity of disease process where in most cases delivery is indicated because platelet number continues to decrease after that¹⁰⁷. In HELLP syndrome having platelet count $<1 \text{ lacs/mm}^3$ demonstrate poor fetal outcome¹⁰⁸. It takes place in 2–12% women with severe pre-eclampsia or eclampsia¹⁰⁶. Early estimation of severity of PIH is essential to stop complications like HELLP syndrome and increased maternal and fetal morbidity and mortality. Whatever work has been done so far to study the severity of PIH, like platelet count by automated cell counter, in-direct and direct method, test for prothrombin time, partial thromboplastin time (PTT), decrease in α_2 antitrypsin, increase

fibronectin level/decrease antithrombin III level, increase in SF1f-1 (soluble Fms-like tyrosine kinase-1) concentration, decrease in circulating free placental growth factor (PGF) and vascular endothelial growth factor (VEGF) are though more receptive but expensive, time consuming and require well equipped hospitals^{107,109-110}. On the other hand platelet estimation method is rapid, reliable, easier, and cheaper and does not need any expensive materials; therefore prognosis of diseases could be supervised by simple estimation of platelet count.

1.1.8.0 Importance of Work

Pregnancy induced hypertensive disorders are frequent complications of pregnancy and are associated with increased maternal and fetal morbidity. Disorders of the lipoprotein metabolism are main cause of endothelial dysfunction that may result in proteinuria and hypertension, clinical hallmark of pregnancy induced hypertension. The PIH syndrome deserves a lot of awareness and attention from obstetrician and full compliance from the patient. It is a preventable disease. A good, thorough and regular antenatal care can easily identify the patients at risk and they can be managed on standard lines.

Simple measurement of serum lipid concentration may be of good predictive value in toxemia of pregnancy, avoiding the costly endocrinal investigations. Research work on the topic and particularly its related complications is lacking in our region where, because of illiteracy, lack of health awareness, education, poverty, and superstitious beliefs prevent women from seeking medical advice/antenatal care during pregnancy. The present work will provide a benchmark for evaluating blood pressure and serum lipid levels in pregnant

women and its correlation with different degrees of PIH complications. Further, the work will initiate a general public awareness and their concern over physical and antenatal checkups during pregnancy hence, improving their overall quality of living, and generating a healthier society.

1.1.9.0 Aims and Objectives

1. To determine and compare the serum lipids among pregnancy induced hypertensive women and women having normal pregnancy without hypertension.
2. To establish relationship/association between different fractions of serum lipids and sub types of PIH.
3. To associate PIH with the age, body mass index and parity of the women in different groups.

MATERIAL AND METHODS

The proposed, cross sectional/analytical study was conducted in the tertiary referral health care facilities of Peshawar, viz. Khyber Teaching Hospital, Post Graduate Medical Institute Lady Reading Hospital and PGMI Hayatabad Medical Complex Peshawar, North West Frontier Province (NWFP) Pakistan. The analytical work was done in PMRC Research Centre, Khyber Medical College, Peshawar and Pathology labs of Post Graduate Medical Institute, Lady Reading Hospital, Peshawar.

2.1.0 Study Population

Study population was women with pregnancy induced hypertension (PIH) and normotensive pregnant women at gestational age of ≥ 20 weeks. Pregnancy induced hypertension was defined as the occurrence of hypertension after 20 weeks of conception with or without proteinuria and edema with systolic blood pressure ≥ 140 mmHg and diastolic blood pressure ≥ 90 mmHg on repeated readings¹.

2.2.0 Categories of PIH

Pregnancy Induced Hypertension was sub divided into three groups as under:

- 1 Pre-eclampsia (PE) was defined by persistent hypertension and proteinuria of 2+ or greater on dipstick testing according to the International Society for the Study of Hypertension in Pregnancy.

- 2 Eclampsia was defined by women presenting with convulsions/coma during or soon after pregnancy, described by pathological edema, hypertension, and proteinuria.
- 3 When PIH was occurring without proteinuria it was expressed gestational hypertension (GH) or transient hypertension.

2.3.0 Study Groups

The study subjects were divided into four groups of pregnant women, with three patient and one control group as under:

- Group A:** Women with gestational hypertension (GH)
- Group B:** Women with pre-eclamptic toxemia (PE)
- Group C:** Toxemic women with eclampsia.
- Group D:** Women having normal uncomplicated pregnancy without Hypertension

2.4.0 Sample size calculation

Statistical formula used for sample size calculation was

$$n_0 = 4PQ/25$$

For gestational hypertension estimated prevalence (P) =20%

$$Q = (100-20) = 80$$

$$4*20*80/25=254$$

$$n_0 = 254$$

$$\text{As } n = n_0 / (1 + n_0/N)$$

Where N=15700 (total number of admitted obstetrics patients per year in tertiary care hospitals of Peshawar)

Sample size (n) will be = 249 +25% non response=312

2.5.0 Study Setting

The study was undertaken on 402 pregnant women. 312 pregnant women with PIH, admitted in the Gynea and Obstrectics units or undergoing prenatal care at tertiary referral health care facilities were randomly selected and screened for PIH at their outpatient prenatal visits and on labor and delivery. From the same health facilities 90 healthy pregnant women without a history of hypertension, diabetes mellitus, renal/cardiovascular diseases were randomly selected as an age/weight/body mass index, gestational period and socio-economic matched control group for comparison. After explaining aims and objectives, informed consent was taken from each subject for participation in this study.

Ethical approval for the study was obtained from the Institutional Ethical Research Board (IERD) at Post Graduate Medical Institute, Hayatabad Medical complex, Peshawar.

2.6.0 Variables

History of patients was recorded on a well designed questionnaire, which included information regarding sociodemographic characters, maternal age, age at marriage, gestation age at screening, para, gravida, nulliparous women, obesity, number of prenatal visits, history of diabetes/hypertension/kidney diseases, expecting twins or triplets, previous history of low birth weight, still birth babies, previous history of PIH, and family history of PIH/hypertension in the first degree relatives. Sign and symptoms of PIH like swelling in the hands, face and feet, severe headaches, abdominal pain, reduced output of urine or no urine, blood in the urine, a change in reflexes, convulsion/seizures, coma, dizziness, excessive

vomiting, nausea and rapid gain in weight were recorded. Any complications of eclampsia like cerebro vascular, cardio vascular, visual, pulmonary, renal, hepatic, haemostatic and obstetrical were also recorded (Annexure-1).

2.7.0 Specimen Collection & Processing

Venous blood samples were obtained from both cases and controls. 5 mL of blood was obtained through routine method applying aseptic technique and tourniquet for as short a time as needed. 1 mL of blood was transferred to an EDTA vacutainer. This sample was used to measure hemoglobin, absolute values and platelet count. 4.0 mL of blood was transferred to a vacutainer tube without a coagulant. All specimens were transferred over ice cubes to PMRC labs, Khyber Medical College. After coagulation of the blood, each blood sample was centrifuged for 10 minutes at 3000 rpm to get a clear and cell free serum. The samples were isolated with proper labeling.

Biochemical analysis of lipoprotein included Total Cholesterol (TC), High Density Lipoprotein Cholesterol (HDL-C), Low Density Lipoprotein Cholesterol (LDL-C), Very Low Density Lipoprotein Cholesterol (VLDL-C), Triglycerides (TG), apolipoprotein A1 (APO-A1), apolipoprotein B100 (APO-B100), Lipoprotein-a (LPA) and hematological parameters included Hemoglobin (Hb), platelet count and absolute values. Serum lipids were analyzed enzymatically by using Semi Auto Chemistry Analyzer Microlab 200 (Merck). Full blood count and absolute values were measured by using Hematology Auto Analyzer Humacount Plus, by Human (France). These investigations were performed in PMRC Research Centre, Khyber Medical College, Peshawar on daily basis. Rest of the serum from each subject was stored frozen at -20°C in capped epindorph plastic tube. Serum

APO-A1, APO-B100 and LPA were measured in the Pathology labs of Post Graduate Lady Reading Hospital, Peshawar by using kits of Roche Diagnostics, on Chemistry Auto analyzer, Modular P-800 by Roche, Cobas (Japan).

Serum triglycerides and total cholesterol were measured by using enzymatic method of Elitech Diagnostic kits of France. Serum HDL-C was measured by using kits of Merck Diagnostics. Serum LDL-C was calculated by Frederickson-Friedwald's formula according to which $LDL-C = TC - HDL \text{ cholesterol} - VLDL \text{ cholesterol}$. VLDL cholesterol was calculated as 1/5 of triglycerides.

2.8.0 Measurements

2.8.1 Methods and Test Procedures

2.8.1.1 Height

Heights of subjects were determined by the use of a vertical calibrated scale, in the standing position. Subjects removed their shoes prior to height measurement. Heel to head-crown length was measured in centimeters.

2.8.1.2 Weight

Weight of subjects was measured by means of an accurate physical balance, in the standing position, and with minimum clothing. The balance was pre tested with known standard weights.

2.8.1.3 Body Mass Index (BMI)

This was calculated from the measurement of weights and heights by using the following formula:

$$BMI = \text{Weight in Kg} / \text{Heights in (meter)}^2$$

2.8.1.4 Blood Pressure Recording

Both systolic and diastolic blood pressure was measured with a standard mercury sphygmomanometer and standard arm cuff at the right arm. Subjects were either in sitting or reclining positions and the recordings were taken after a period of 5 minutes rest in the position of recording. The recordings were taken at interval of 5 minutes each, and their mean values taken. The degree of hypertension was directly determined from the blood pressure measured. Women once found hypertensive, were screened for presence of protein in urine by using dipstick method.

2.9.0 Different Cut Offs

Cut off values for different variables were defined as under:

2.9.1 Hypertension¹¹²

Normal Blood Pressure (BP)	Systolic < 120 mmHg Diastolic < 80 mmHg
Prehypertension	Systolic 120-139 mmHg
Normal to High-Normal BP	Diastolic 80-89 mmHg
Mild Hypertension (Stage-1)	Systolic 140-159 mmHg Diastolic 90-99 mmHg
Moderate Hypertension to Severe hypertension (Stage-2)	Systolic >160 mmHg and/or Diastolic >100 mmHg

2.9.2 Overweight and Obesity¹¹³

BMI < 18.5 Kg/m ²	Underweight
BMI ≥ 18.5 Kg/m ² to < 23.0 Kg/m ²	Normal
BMI ≥ 23.0 Kg/m ²	Overweight
BMI ≥ 25.0 Kg/m ²	Obese
BMI ≥ 27.0 Kg/m ²	Very Obese

2.9.3 Anemia¹¹⁴

Hb ≥ 12.0 g%	Normal
Hb 10.5-11.9 g%	Mild anemia
Hb 10.4-7.7 g%	Moderate anemia
Hb < 7.7 g%	Severe anemia

2.9.4 Platelet Count¹¹⁵

≥ 150 (thousand/μL)	Normal
100-150 (thousand/μL)	Low (thrombocytopenia)
< 100 (thousand/μL)	Very low (Severe thrombocytopenia)

2.10.0 Statistical Analysis

The data was processed on computer software package SPSS version 10. The numerical and categorical data was presented as mean. The Student's t test was used to evaluate mean differences in maternal serum lipid concentrations between patients and control subjects. Significance among the means of groups was expressed in term of 'P' value. 95% Confidence Interval (CI) P < 0.05 was considered as significant. To determine the relative association between

pregnancy induced hypertension and different concentrations of lipids and lipoproteins logistic regression methods were used to calculate maximal probability estimates for the coefficients and their standard errors were used to calculate odd ratio (OR) and 95% confidence interval (CI).

The patients were classified into mild and severe PIH by taking ≥ 110 mmHg for diastolic BP and ≥ 150 mmHg for systolic BP as the cut off levels. Coefficient of Correlation 'r' was also determined for different biochemical indices by using Pearson Product Moment correlation on SPSS 10 software computer package.

2.11.0 Methods

2.11.1 Determination of Serum Total Cholesterol (TC)¹¹⁶

The reagents used for the Total Cholesterol PAP, Enzymatic Colorimetric Method were of Elitech Diagnostic kits of France.

Principal

To find out total cholesterol and fatty acid by the action of cholesterol esterase, free cholesterol in the sample is oxidized to 4 Cholesten-3-one and hydrogen peroxide. The amount of hydrogen peroxide formed is directly proportional to the amount of cholesterol in the blood. Hydrogen per oxide reacts with 4-aminoantipyrine and phenol in the presence of peroxidase and produces a red colored quinone compound, which is measured at 500 nm using a Semi Automatic Chemistry Analyzer (Microlab 200 Merck).

Following is the kit composition of Total Cholesterol PAP, Enzymatic Colorimetric Method of Elitech Diagnostic (France).

Reagent 1

Pipes buffer, pH 6.90	50 mmol/L
Sodium Chlorate	0.5 mmol/L
Phenol	24 mmol/L

Reagent 2

Cholesterol esterase	≥ 200 U/L
Peroxidase	≥ 1000 U/L
Cholesterol oxidase	≥ 250 U/L
4-Aminoantipyrine	0.5 mmol/L

Standard

Cholesterol	200 mg/dL
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Reference values

Serum, plasma	150-206 mg/dL
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Samples

Serum, Heparin plasma

Procedure

Working reagent was prepared by dissolving reagent 2 in reagent 1, which is stable for three months at 2-8 °C and for 3 weeks at 20-25 °C.

Three small test tubes were labeled as standard, blank and sample. 1 mL of working reagent was added to each tube. To the standard, blank and sample test tubes 10 uL of standard solution, distilled water and sample was added respectively. The reagents were mixed and after 5 minutes incubation optical density (OD) taken. The final color is stable for one hour.

Calculation

The following relationship was used for calculation of cholesterol.

$\frac{\text{OD Sample}}{\text{OD Standard}} \times n$

Where n= standard concentration (200 mg/dL)

For this kit the linearity of curve is up to 500 mg/dL.

2.11.2 Determination of High Density Lipoprotein Cholesterol (HDL-C¹¹⁷)

Principal:

The serum is centrifuged with magnesium chloride and tungsten phosphoric acid, so that B-apoprotein is precipitated (LDL-C and VLDL-C). The supernatant thus obtained contains a-apoproteins (HDL cholesterol). HDL-C then reacts with cholesterol reagent and oxidized to cholestenone and hydrogen peroxide by the action of cholesterol oxidase. Hydrogen peroxide thus produced is directly proportional to the HDL-C in serum. Hydrogen peroxide, after reacting with 4-aminoantipyrine, gives 4-p-(benzoquinone-monoamino)-phenazone, which is a red colored compound. Its absorbance is measured at 546 nm by using Microlab 200 Merck.

Procedure:

0.2 mL of serum and 0.5 mL of reagent were taken in a tube and incubated for 10 minutes at room temperature. Afterward the contents were centrifuged for 15 minutes at 5000 rpm. 0.1 mL of supernatant was then taken, mixed with 1 mL of cholesterol reagent and incubated for 15 minutes at room temperature. The absorbance was measured at 546 nm.

2.11.3 Determination of Triglycerides (TG)¹¹⁸

The reagents used for Triglyceride enzymatic liquid colorimetric test, GPO-PAP method were obtained from Elitech Diagnostic's kits, France.

Principal:

In blood triglyceride level was determined enzymatically by the oxidation of triglycerides into glycerol and fatty acids using lipoprotein lipase. Glycerol is phosphorylated into glycerol-3 phosphate using glycerol kinase in the presence of ATP. Glycerol-3 phosphate is oxidized under the action of glycerol-3 phosphate oxidase, with immediate production of hydrogen peroxide. Hydrogen peroxide then reacts with 4-aminoantipyrine and produce a red quinone compound under the action of peroxidase. The absorbance of quinone is then measured at 546 nm using Microlab 200 Merck.

Reagents:

Reagent 1 consisted of 4-amino-antipyrine 0.7 mmol/L, ATP 0.3 mmol/L and enzymes lipoprotein lipase > 1100 U/L, glycerol kinase >800 U/L, glycerol -3-phosphate oxidase > 3000 U/L and peroxidase > 350 U/L.

Reagent 2 consisted of buffer solution of pH 7.50, 50 mmol/L.

Standard:

Consisted of triglycerides, 2.28 mmol/L or 200 mg/dL or 2.0 g/L

Preparation of working reagent:

Working reagent was prepared by dissolving reagent 2 in reagent 1 and stored in refrigerator.

Procedure:

10 uL each of distilled water, standard and sample were taken in three separate cuvettes as blank, standard and sample respectively. One mL of working reagent

was added to each cuvette. The solution was mixed and incubated for 5 minutes at 37 °C. The absorbance of the solution was measured at 546 nm on Microlab 200 against blank.

Calculation of Results:

Concentration of the sample (mg/dL) = Absorbance of Sample x Concentration of Standard / Absorbance of Standard.

2.11.4 Determination of Low Density Lipoprotein Cholesterol (LDL-C¹¹⁹)

Principle:

A direct determination of LDL-C is difficult due to technical problems. LDL-C is determined by the following formula:

$$\text{LDL cholesterol (mg/dl)} = \text{TC} - \text{HDL-cholesterol} - \text{TG}/5.$$

2.11.5 Determination of Very Low Density Lipoprotein Cholesterol (VLDL-C¹²⁰)

Principal:

VLDL-C levels were determined by derivation from the following formula:

$$\text{VLDL-C cholesterol (mg/dl)} = \text{Triglycerides}/5$$

2.11.6 Determination of Apolipoprotein-A1 (APO-A1)¹²¹

System Information

Immunoturbidimetric assay for the quantitative determination of Apolipoprotein A-1 in serum was done by using Roche Diagnostic kits on Roche Automated Clinical Chemistry Analyzer MODULAR P-800, Cobas, Japan.

Test principle

Sample is added to reagent-1 (buffer) and after the addition of reagent-2 (anti-apolipoprotein A-1 antibody) Immunoturbidimetric assay starts. Anti-apolipoprotein A-1 antibodies react with the antigen in the sample to form antigen/antibody complexes which, following agglutination and can be measured turbidimetrically.

Reagents-working solutions

R1 TRIS^a buffer: 50 mmol/L, pH8.0 PEG: 3.8% detergent; preservative
(Ready for use)

R2 Anti-human apolipoprotein A-1 antibodies (sheep): dependent on titer;
TRIS buffer: 100 mmol/L, pH 8.0; preservative. (Ready for use)

^{a)} TRIS= Tris (hydroxymethyl) aminomethane

1) Calibrator: C.f.a.s. (Calibrator to automated systems) Lipids

2) Controls: Precinorm L, Precipath L

3) Normal saline 0.9% NaCl

Calibration

Traceability: This method has been standardized against the IFCC SPI –01 reference standard (WHO-IRP October 1992)

Roche MODULAR-P Analyzers

S1: 0.9% NaCl

S2-S6: Diluted C.f.a.s .Lipids

The lot-specific C.f.a.s. Lipids values were multiplied by the factors given below to find out the standard concentrations for the 6-point calibration curve.

S2.	0.206
S3:	0.404
S4:	1.000
S5:	1.312
S6:	2.000

Quality control

For quality control the control Precinorm L and Precipath L was used. Values obtained with these controls were within mid values (means) of lower and upper limits/ranges.

Calculation

The analyzer automatically calculates the analyte concentration of each sample.

Conversion factors: $\text{mg/dL} \times 0.357 = \text{umol/L}$

$\text{mg/dL} \times 0.01 = \text{g/L}$

$\text{g/L} \times 100 = \text{mg/dL}$

Measuring range

Measuring range: 7.14-143 umol/L (0.20 –4.4.00g/L)

Expected values

The following values were obtained using serum from healthy adults:

Men (n=150): 37.1-72.1 umol/L (104-202mg/dL:1.04-2.02g/L)

Women (n=150): 38.6-80.3 umol/L (108-225 mg/dL: 1.08-2.25 g/L)

2.11.7 Determination of Apolipoprotein-B 100¹²²

Immunoturbidimetric assay for the quantitative determination of apolipoprotein A-1 in serum was done using Roche Diagnostic kits on Roche Automated Clinical Chemistry Analyzer MODULAR P-800, Cobas, Japan

Test principle

Immunoturbidimetric assay

Sample is added to R1 (buffer), and R2 (anti-apolipoprotein B antibody). Anti-apolipoprotein B antibodies react with the antigen in the sample to form antigen/antibody complexes which, following agglutination and is measured turbidimetrically.

Reagents - working solutions

R1 TRIS^a buffer: 50 mmol/L, pH 8.0; PEG: 4.2%; detergent; preservative

R2 Anti-human apolipoprotein B antibodies (sheep): dependent on titer; TRIS buffer: 100 mmol/L, pH 8.0; preservative.

Where ^a = TRIS = Tris (hydroxymethyl) aminomethane

Reagent R1 and R2 are ready for use

Calibrator: C.f.a.s. (Calibrator for automated systems) Lipids

Controls: Precinorm L, Precipath L

Serum or Plasma: Li-, Na-, NH₄⁺-heparin or Na₂-, K₂-, K₃-EDTA plasma.

Calibration

Roche MODULAR analyzers

S1: 0.9% NaCl

S2-S6: C.f.a.s. Lipids were used as calibrators.

The lot-specific C.f.a.s. Lipids values were multiplied by the factors given below to determine the standard concentrations for the 6-point calibration curve.

S2:	0.318
S3:	0.600
S4:	1.615
S5:	2.100
S6:	3.500

Quality control

For quality control the control Precinorm L and Precipath L was used. Values obtained with these controls were within mid values (means) of lower and upper limits/ranges.

Calculation

The analyzer automatically calculates the analyte concentration of each sample.

Conversion factors: $\text{mg/dL} \times 0.0195b = \mu\text{mol/L}$

$\text{mg/dL} \times 0.01 = \text{g/L}$

$\text{g/L} \times 100 = \text{mg/dL}$

Measuring range

Roche MODULAR analyzers

Measuring range: 0.39–7.8 $\mu\text{mol/L}$ (20–400 mg/dL ; 0.20–4.00 g/L)

Expected values

The following values were obtained by using serum from healthy adults:

Men (n = 150): 1.29–2.59 $\mu\text{mol/L}$ (66–133 mg/dL ; 0.66–1.33 g/L)

Women (n = 150): 1.17–2.28 $\mu\text{mol/L}$ (60–117 mg/dL ; 0.60–1.17 g/L)

2.11.8 Lipoprotein (a)¹²³

System information

Immunoturbidimetric assay for the quantitative determination of Lipoprotein (a) in serum was done by using Roche Diagnostic kits on Roche Automated Clinical Chemistry Analyzer MODULAR P-800, Cobas, Japan.

Test Principal

Immunoturbidimetric assay

Sample is added to R1 (buffer) and R2 (anti-lipoprotein (a) antibody) to start reaction. Anti-lipoprotein (a) antibodies react with antigen in the sample to form an antigen/antibody complex, which is determined turbidimetrically after agglutination.

Reagents-working solutions

R1 Phosphate buffer; 60 mmol/L, pH 7.5; NaCl 100 mmol/L

R2 Anti-human lipoprotein (a) antibodies (rabbit) dependent on titer; NaCl: 100 mmol/L; stabilizer; preservative

3 Human lipoprotein (a)

Controls: Lp (a) Control Set

R1 and R2 are ready for use

Specimen

Serum

Plasma Na:- Li-heparin or EDTA plasma.

Calibration

Traceability: This technique has been standardized against a highly purified Lp(a) preparation, which is used as an in house master calibrator.

S1 0.9% NaCl

S2-6: Calibrator

The lot specific lipoprotein (a) calibrator values were multiplied by the factors below to determine the standard concentrations for the six-point calibration curve.

S2:	0.052
S3:	0.104
S4:	0.208
S5:	0.500
S6:	1.000

Quality control

For quality control the LP (a) control set was used.

Calculation

The analyzer automatically calculates the analyte concentration of each sample.

Conversion factors: $\text{mg/dL} \times 0.01 = \text{g/L}$

$\text{g/L} \times 100 = \text{mg/dL}$

Measuring range

Roche/Hitachi 904/912/917/MODULAR P analyzers

Measuring range: 6-160 mg/dL (0.06-1.60 g/L)^a

Extended measuring range with automatic rerun: 3-320 mg/dL (0.03-3.20 g/L)

Analytical sensitivity (lower detection limit)

Detection limit: 6 mg/dl (0.06g/L)

The detection limit represents the lowest detectable analyte level that can be distinguished from zero. It is calculated as the value laying three standard deviations above that of the lowest standard (standard 1+ 3 SD, within run precision, n=21)

2.11.9 Full Blood Count

Full blood count and absolute values of both patients and control groups were measured by using three dimensional, 18 parameter, fully automated Hematology Analyzer Humacount Plus.

Reagent Solutions and Consumption

Content **HC-DILUENT**

1. (DIL} Diluents, isotonic saline solution used to dilute whole blood specimens and to rinse the fluidic system after each measurement.

Buffer	< 0.05%, pH 6.9+ 0.2
Sodium Sulphate	< 1.20%
Stabilizer	<0.30%
Detergent	< 0.01%

2. (LYSE}: **HC-Lyse CF**

Cyanide free lyses reagent was used to prepare blood hemolysate for white blood cells (WBC) and hemoglobin (Hb) measurement, which was composed of the following.

- i) Sodium Chloride < 0.15 %, pH 7.4+0.5
- ii) Organic Acid < 0.25%
- iii) Quaternary ammonium salts <7.30%
- iv) Preservatives <0.01%

3. {CLEAN}: **HC-Cleaner**

Cleaning solution was used to carry out cleaning process of the fluidics and is made of the following.

- i) Sodium Chloride <0.10%, pH 8.0+0.2
- ii) Potassium Chloride <0.03%
- iii) Proteolytic Enzymes <0.02%
- iv) Stabilizer <0.30%
- v) Detergent <0.40%

Sample Analysis

Sample preparation:

Fresh whole blood sample collected in K3-EDTA anti-coagulated vacutainer was used. prior to sampling. The sample was gently mixed by inverting it 11 times to attain a homogenous sample. Shaking the tube could damage the blood cells and was avoided. The cap of the sample tube was taken off and the aspiration needle was immersed well into the sample. The sampling bar was pushed to start measuring full blood count. During aspiration, the sampling tube was held in a stable position (for approx. 1 second). The instrument draws 25 uL of sample, and the aspirating needle is retracted while its outer surface is mechanically rinsed with diluents. When the status LED started flashing and the beeps heard indicating the end of the sampling process. The sampling tubes was removed and recapped. An external PC keyboard was connected with the instrument to get results. At the end of a measuring procedure, all measured and calculated parameters as well as the WBC, (red blood count (RBC) and platelet count (PLT) histograms were displayed on screen and a print out taken.

Of the hematological parameters, the indexes given in the table-2.1 were noted and analyzed for absolute values.

Table-2.1: Hematological parameters with normal ranges.

Test	Full name	Normal ranges
Hb	Hemoglobin	12-16 g %
RBC	Red blood count	4-6.5 $10^6/\mu\text{L}$
PCV	Packed cell volume	36-52 %
MCV	Mean cell volume	78-96 μ
MCH	Mean cell hemoglobin	27-32 pg
MCHC	Mean cell hemoglobin concentration	30-35 g/dL
WBC or TLC	Total white blood cell count	4-11 $10^3/\mu\text{L}$
GR	Granulocytes or Neutrophils & eosinophils	(45-75%)
Ly	Lymphocytes	25-55%
Mo	Monocytes	3-7%
PLT	Platelet count	150-450 $10^3/\mu\text{L}$

Blank measurement

Blank measurement was used for checking the cleanliness of the system and reagents.

Calibration

Calibration is the procedure used to standardize the instrument by applying the necessary rectification factors. Three-fold measurements of control and special calibrations material were used with known parameters. The instrument automatically calculates new factors using the following formula.

$$\text{New Factor} = \frac{\text{Assigned value stored factor}}{\text{Measured value (S) (or average of those)}}$$

Quality Control (QC)

Hum count PLUS provides six different quality control profiles (e.g. low, normal and high control blood). QC measurement results were added to the selected level and indicated at the top right corner. In the submenu, both target value and acceptable ranges for each parameter could be calculated for the different QC levels.

Patient results database management

Patient results were stored in the memory in chronological order, and they could be retrieved at any time. Memorizing capacity is 10,000 measurements including the complete parameter list, histograms, sample data dates, flags and times of the measurements.

RESULTS

This cross sectional study was conducted on the pregnant women attending the Gynecology and Obstetrics Department of tertiary care hospitals of Peshawar, North West Frontier Province (NWFP) Pakistan. A total of 402 pregnant women at gestational age of ≥ 20 weeks were registered in the study after taking informed consent. Out of these 312 women with pregnancy induced hypertension were randomly selected and compared with a control group of 90 healthy pregnant women matched for age, body mass index and socio-economic status.

The study subjects were divided into four groups of pregnant women, with three patient and one control group as under:

- Group A: Women with gestational hypertension (102)
- Group B: Women with pre-eclampsia (100)
- Group C: Toxemic women with eclampsia (110)
- Group D: Healthy women having normal uncomplicated pregnancy without Hypertension (90)

The demographic and reproductive characteristics of the three patients groups and control subjects investigated are summarized in table-3.1. All the subjects were ranging in age from 15 to 45 years with similar low socio-economic characteristics. The age of patients in the eclampsia group (C) was considerably lower (25.24 ± 0.54 years) as compared to the other groups, while lowest marriage age of 18.9 ± 0.53 years was noted in the control group

of pregnant women (Fig.3.1). Parity, number of alive birth and alive children in women of eclampsia group were noticeably lower as compared to the patients in group A, B and healthy pregnant women in group D (Fig.3.2). Mean systolic/diastolic blood pressure was gradually increasing (Fig.3.3) and platelet count was decreasing with the increase in the severity of disease as in group C (Fig.3.4). Mean weight of pregnant women in group A and B was higher as compared to patients in the eclampsia group-C and healthy pregnant women (Fig.3.5). Women in group 'A' were found to be more obese with having Body Mass Index (BMI) of $30.96 (\pm 1.08) \text{ kg/m}^2$ as compared to women in group D of control ($28.94 \pm 0.82 \text{ kg/m}^2$) pregnant women. An alarming number (59%) of women in the eclampsia group-C were primiparous as compared to 19.6% and 35% respectively among the patients of group A and B and normotensive women (23%) in the control group, D.

Table-3.1: Socio-demographic and reproductive characteristics of the study groups.

Variables	Group-A (N=102) Mean $\pm$ SEM	Group-B (N=100) Mean $\pm$ SEM	Group-C (N=110) Mean $\pm$ SEM	Group-D (N=90) Mean $\pm$ SEM
Age (years)	30.03 $\pm$ 0.66	29.54 $\pm$ 0.68	25.24 $\pm$ 0.54	30.04 $\pm$ 0.66
Marriage age (years)	21.74 $\pm$ 0.59	20.76 $\pm$ 0.57	20.39 $\pm$ 0.47	18.9 $\pm$ 0.53
Gestation age (weeks)	30.01 $\pm$ 0.49	31.39 $\pm$ 0.48	31.83 $\pm$ 0.45	29.72 $\pm$ 0.55
Parity (n)	5.08 $\pm$ 0.53	4.88 $\pm$ 0.59	2.78 $\pm$ 0.35	4.04 $\pm$ 0.27
Alive births	2.93 $\pm$ 0.26	2.36 $\pm$ 0.27	1.23 $\pm$ 0.20	2.58 $\pm$ 0.25
Still births	0.47 $\pm$ 0.13	0.39 $\pm$ 0.11	0.18 $\pm$ 0.06	0.17 $\pm$.06
No. of abortion	0.44 $\pm$ 0.08	0.31 $\pm$ 0.07	0.36 $\pm$ 0.08	0.45 $\pm$ 0.07
No. of C sections	0.12 $\pm$ 0.04	0.16 $\pm$ 0.06	0.073 $\pm$ 0.03	0.17 $\pm$.06
No. of LBB	0.15 $\pm$ 0.04	0.16 $\pm$ 0.04	0.17 $\pm$ 0.05	0.16 $\pm$.05
Alive children	2.83 $\pm$ 0.26	2.28 $\pm$ 0.28	1.21 $\pm$ 0.20	2.56 $\pm$ 0.26
Systolic BP (mm Hg)	146.49 $\pm$ 1.25	151 $\pm$ 1.79	155.58 $\pm$ 1.97	116 $\pm$ 0.91
Diastolic BP (mm Hg)	96.91 $\pm$ 0.84	99.45 $\pm$ 1.34	103.66 $\pm$ 1.53	75.28 $\pm$ 0.91
Height (cm)	157.58 $\pm$ 0.91	159.10 $\pm$ 0.91	153.0 $\pm$ 13.10	154.53 $\pm$ 1.22
Weight (kg)	75.86 $\pm$ 1.35	73.58 $\pm$ 1.27	66.66 $\pm$ 1.05	68.11 $\pm$ 1.55
BMI (kg/m ²)	30.96 $\pm$ 1.08	29.41 $\pm$ 1.04	29.27 $\pm$ 1.12	28.94 $\pm$ 0.82
Platelets count (thousand/ μ L)	233.24 $\pm$ 7.64	227.50 $\pm$ 9.35	198.60 $\pm$ 9.28	261.44 $\pm$ 8.27
Hb (g/dL)	10.29 $\pm$ 0.20	9.99 $\pm$ 0.20	10.19 $\pm$ 0.17	10.19 $\pm$ 0.18

Student's t' test was used to find level of significance at 95% confidence interval ($P < 0.05$) among the means ($\pm$ SEM) of test patients (group A, B, C as pregnancy Induced Hypertensive (PIH) women) and normotensive healthy control women of group D (Table-3.2). The difference in maternal age ($P < 0.05$), marriage age ($P < 0.001$) and weight ($P < 0.05$) of patient group was found significant when compared to the control group. As expected there was a highly significant ($P < 0.001$) difference in systolic/diastolic blood pressure and platelet count between the patient and healthy pregnant women. While frequency of still birth babies in patients group of pregnancy induced hypertension was high (0-8) vs. 0-3 still birth babies reported by the healthy pregnant women in the control group. The difference in the two groups was significant ($P < 0.05$). A highly significant ($P < 0.001$) difference was recorded in the platelet count of women with pregnancy induced hypertension and normotensive women. In the patient group 120 (38.5%) women were primiparous versus 23% in the control group. Rate of literacy was almost same in both test and control groups (8% & 8.8%) of the pregnant women. Monthly income less than Rs: 5000/- was recorded in 237 (76%) respondents from the patient group of PIH against 77 (85.6%) in the control pregnant women.

Table-3.2: Comparison of socio-demographic and reproductive characteristics among women with pregnancy induced hypertension and normotensive women.

Variables	PIH (N=312) Mean $\pm$ SEM	Control (N=90) Mean $\pm$ SEM	Student's t test P value
Age (years)	28.19 $\pm$ 0.38	30.04 $\pm$ 0.66	0.05
Marriage age (years)	20.95 $\pm$ 0.31	18.9 $\pm$ 0.53	0.001
Gestation age (weeks)	31.09 $\pm$ 0.27	29.72 $\pm$ 0.55	0.05
Parity (n)	4.21 $\pm$ 0.29	4.04 $\pm$ 0.27	NS
Alive births	2.15 $\pm$ 0.14	2.58 $\pm$ 0.25	NS
Still births	0.34 $\pm$ 0.05	0.17 $\pm$.06	0.05
No. of abortion	0.37 $\pm$ 0.04	0.45 $\pm$ 0.07	NS
No. of C sections	0.12 $\pm$ 0.03	0.17 $\pm$ 0.06	Ns
No. of LBB	0.16 $\pm$ 0.03	0.16 $\pm$ 0.05	NS
Alive children	2.20 $\pm$ 0.15	2.56 $\pm$ 0.26	NS
Systolic BP (mm Hg)	150.75 $\pm$ 0.98	116 $\pm$ 0.91	0.001
Diastolic BP (mm Hg)	99.88 $\pm$ 0.75	75.28 $\pm$ 0.91	0.001
Height (cm)	156.36 $\pm$ 0.61	154.53 $\pm$ 1.22	NS
Weight (kg)	71.89 $\pm$ 0.74	68.11 $\pm$ 1.55	0.05
BMI (kg/m ²)	29.87 $\pm$ 0.39	28.94 $\pm$ 0.82	NS
Platelets count (thousand/ μ L)	215.84 $\pm$ 5.13	261.44 $\pm$ 8.27	0.001
Hb (g/dL)	10.16 $\pm$ 0.11	10.19 $\pm$ 0.18	NS

Age wise distribution of patient and control groups is represented in figure-3.6. A maximum number (32%) of patients were recorded in age less than 20 years in eclamptic patients of group C that means eclampsia is more prevalent in younger age group. More than 19% of patients each, in group A and B were those having age more than 35 years as compared to 8.9 % in control group (Table-3.3), while the number of patients in group C of eclampsia was only 6 (5.5%).

Table-3.3: Age wise distribution among the patients and normotensive pregnant women.

Age Years	Group-A		Group-B		Group-C		Group-D	
	N	%	N	%	N	%	N	%
≤ 20	10	9.8	13	13	35	31.8	20	22.2
21-25	21	20.6	24	24	30	27.3	25	27.8
26-30	28	27.5	23	23	31	28.2	26	28.9
31-35	23	22.5	21	21	8	7.3	11	12.2
> 35	20	19.6	19	19	6	5.5	8	8.9
TOTAL	102	100	100	100	110	100	90	100

The groups (A, B, C) of patients in pregnancy induced hypertension were compared with the control group, D for different age distribution (Table-3.4). In the patient group 70% had age up to 30 years. More than 14% patients with pregnancy induced hypertension were in older age group i.e. greater than 35 years.

Table-3.4: Age wise distribution in the patients of pregnancy induced hypertension and normotensive pregnant women.

Age Years	PIH		Control	
	N	%	N	%
≤ 20	58	18.6	20	22.2
21-25	75	24.0	25	27.8
26-30	82	26.3	26	28.9
31-35	52	16.7	11	12.2
> 35	45	14.4	8	8.9
TOTAL	312	100	90	100

Of these eclamptic patients in young age group, almost 12% women in group C were those, who had got married in a teenage ≤ 15 years, i.e. at the age when the maternal reproductive organs were not fully developed. A highest percent of women (34.4%) in control group also had got married in age ≤ 15 years (Fig.3.7). Maximum number (11.8%) of patient with marriage age > 30 years were recorded in group A of pregnant women (table-3.5).

Table 3.5: Distribution of marriage age amongst the study groups.

Marriage Age (years)	Group-A		Group-B		Group-C		Group-D	
	N	%	N	%	N	%	N	%
≤ 15	10	9.8	18	18	13	11.8	31	34.4
16-20	50	49	39	39	51	46.4	33	36
21-25	20	19.6	21	21	32	29.1	18	20
26-30	10	9.8	16	16	11	10	4	4.4
> 30	12	11.8	6	6	3	2.7	4	4.4
TOTAL	102	100	100	100	110	100	90	100

The Odds ratio (OR)

To determine the probability of having acquired disease condition associated with prior exposure to a risk factor, calculation of the Odds Ratio (OR) is useful in such study design. The OR determines the probability that the disease occurred because of prior exposure to the risk factor. The odds or likelihood that the diseased person got pregnancy induced hypertension as a result of exposure to the risk factor being assessed.

The OR was determined by plotting the data in a simple contingency (2 x 2) table, so that four cells labeled as A, B, C and D are obtained. Cell 'A' contains the number of people who acquired the disease and were also exposed to the risk factors. Cell 'B' contains the number of people, who did not get disease, but were exposed to the risk factor. This indicates the probability of not getting the disease even after exposure. Some of these subjects may be in the process of acquiring the disease in future. Cell 'C' contains the number of cases who had disease, but were not exposed to the risk factor, so that some other risk factors could be attributed for their disease. Cell 'D' does not contain the number of people, who had disease nor had the risk factor. This group supports the risk effect hypothesis, as it can be said that they did not get the disease, because they were not exposed to the risk factor.

The formula for calculating the OR is: $(a / b) (d / c)$, written as $(a \times d) / (b \times c)$ as this determines the maximum probability of acquiring the disease because of presence of the risk factors, and the maximum probability of not acquiring the disease, if the risk factor was not present.

The Odds ratio will equal a value of 1.0, if there was no risk-effect association, meaning risk factor had no bearing on the outcome or disease. Values greater than 1.0 will imply increasing values of the probability that the disease was acquired as a result of the risk factor under investigation. A value of two means that there it is twice as likely that the disease was acquired due to the risk factor rather than not due to it.

When the Odd ratio formula was applied to the data from the present study, a strong and linear positive association was found between maternal age at marriage and pregnancy induced hypertension (table 3.6). The odds ratio for women marriage age less than 15 years was 3.07 (95% confidence interval (1.45 to 6.53), χ^2 10.36 & $P < 0.001$) when compared with women with marriage age 21-25 years as referent. This means that a women, if married in younger age of less than 15 years will be three times more prone to develop pregnancy induced hypertension.

Table-3.6: Comparison of marriage age among women with pregnancy induced hypertension and normotensive pregnant women.

Marriage Age (years)	PIH		Control		Odd ratio		
	N	%	N	%	OR (95%CI)	χ^2	P
≤ 15	41	13.1	31	34.4	3.07 (1.45—6.53)	10.36	0.001
16-20	140	44.9	33	36	0.96 (0.48-1.91)	0.02	0.89
21-25	73	23.4	18	20	Referent		
26-30	37	11.9	4	4.4	0.44 (0.12-1.52)	2.04	0.15
> 30	21	6.7	4	4.4	0.77 (0.2-2.80)	0.18	0.66
Total	312	100	90	100			

This condition is getting more worsen in primiparous women, where 59% of patients were recorded to be eclamptic, that is consider to be most severe form of disease (Fig.3.8). A large number of patients in group B of pre-eclampsia had parity > 7 (table-3.7).

Table-3.7: Comparison of parity in women with pregnancy induced hypertension and normotensive pregnant women.

Parity	Group-A		Group-B		Group-C		Group-D	
	N	%	N	%	N	%	N	%
Primi	20	19.6	35	35	65	59.1	21	23.1
2-4	41	40.2	24	24	23	20.9	31	35.2
5-7	24	23.5	18	18	13	11.8	27	29.7
> 7	17	16.7	23	23	9	8.2	11	12.1
Total	102	100	100	100	110	100	90	100

Overall 38.5% patients were primiparous in three patient groups of pregnancy induced hypertension vs. 23% in the control group. Primiparous women were twice as likely to be eclamptic (OR 2.08, CI (1.08 - 4.03), χ^2 5.55, $P < 0.01$) when compared to women having parity 2-4, while women with parity greater than 7 were 1.6 times (CI 0.71-3.76) more at risk to develop pre-eclampsia (table-3.8).

Table- 3.8: Comparison in parity among women with pregnancy induced hypertension and healthy pregnant women.

Parity	PIH		Control		Odd ratio				
	N	%	N	%	OR	95% CI		χ^2	P
Primi	120	38.5	21	23.1	2.08	1.08	4.03	5.55	0.01
2-4	88	28.2	32	35.2	Referent				
5-7	55	17.6	27	29.7	0.71	0.37	1.38	1.16	0.28
> 7	49	15.7	11	12.1	1.62	0.71	3.76	1.53	0.21

A crude relationship between hypertension in pregnancy and the history of perinatal outcome has been summarized in Table-3.9. There was an increased risk of still birth among infants born to women with any hypertensive disorder (OR 1.87, 95% CI 0.85-4.26, χ^2 2.76, $P < 0.09$) as compared with infants born to women with normotensive pregnancies. There was an increased risk of C-section among infants born to women with hypertension (OR 1.29, 95% CI 0.49-3.63, χ^2 0.30, $P < 0.58$) as compared to the healthy pregnant women.

Table-3.9: History of still birth, abortion, C-section and low birth baby (LBB) given by the women with pregnancy induced hypertension and normotensive pregnant women.

Perinatal Out come	PIH		Control		Odd ratio			
	Yes	No	Yes	No	OR	95% CI	χ^2	P
Still birth	53	259	9	81	1.87	0.85-4.26	2.76	0.09
Abortion	70	242	29	61	0.62	0.36-1.06	3.44	0.06
C-section	26	286	6	84	1.29	0.49-3.63	0.30	0.58
LBB	33	279	10	80	0.96	0.43-2.18	0.01	0.91

Different risk factors/medical history of maternal associated with PIH are represented in table-3.10. Previous history of pregnancy induced hypertension was given by 9% patients. Women who had complications in previous pregnancy had more than 4 times the risk of pre-eclampsia in the present pregnancy (OR 4.58, CI (1.32–19), P 0.006), when compared to normotensive pregnant women. In the patient group 5.8% women reported to be diabetic vs. 2.2% in the control group. The likelihood of pre-eclampsia nearly became triple if diabetes was present before pregnancy (OR 2.72 CI (0.59-17.28). One of the known risk factor for developing pre-eclampsia is multiple pregnancy with expecting twin or triplet by the women. In the present study 2.9% women were expecting multiple pregnancy in the patient group vs. none in the normotensive women. Pregnancy induced hypertension is highly preventable. Its signs and symptoms are very clear and can be diagnosed in early antenatal checkup by simply recording blood pressure and screening for proteinuria. In this study, those patients who had visited antenatal clinics less than two times were more than three times susceptible to develop PIH when compared to those patients, who had paid more than two visits to such clinics for routine antenatal checkups (OR 3.24, CI (1.43-7.63), $P < 0.001$, χ^2 9.68). Literacy rate and socioeconomic condition seems not to affect pregnancy induced hypertension in this study. Overweight and obese women with BMI $\geq 23.0 \text{ kg/m}^2$ had a two fold higher risk of pregnancy induced hypertension than women with normal body mass index $< 23.0 \text{ kg/m}^2$ (OR 1.95, CI 1.02-3.71, $P < 0.02$). Primi para women were found two times more expose to develop PIH as compared to multi para women (OR 2.22, CI 1.26-3.96, $P < 0.003$). Similarly women in the age more than 30 years was 1.7 times more at risk to be eclamptic, as compared to women less than 30 years (OR 1.69 CI (0.93-3.07) $P < 0.06$).

Family history of hypertension was given by 62.3% patient and 19.8% control subjects. Women with a family history of hypertension were seven times more at risk to develop pre-eclampsia as compared to those having no history of hypertension in the family (OR 6.70, CI (3.69-12.28) $P < 0.0001$). A woman with a family history of PIH was five times more at risk to develop pregnancy induced hypertension (OR 4.73, CI 1.07-29.24, $P < 0.02$) as compared to those having no such family history.

Table-3.10: Comparison of risk factors among the women with pregnancy induced hypertension and healthy pregnant women.

Risk Factors	PIH N = 312	Control N = 90	Crude odd ratio		
	Yes (%)	Yes (%)	OR	(95% CI)	P value
Prior PIH	8.9	0	-	-	-
Complication in previous Pregnancy	13.4	3.3	4.58	1.32-19	0.006
Diabetes	5.8	2.2	2.72	0.59-17.28	0.26
Heart diseases	2.2	0	-	-	-
Renal diseases	0.6	1.0	0.58	0.04-16.31	0.65
Expecting twins	2.9	0	-	-	-
No. of antenatal visits < 2	69.9	87.9	3.24	1.43-7.63	0.001
Literate	8.0	8.8	1.11	0.44-2.69	0.81
Monthly income < Rs: 5000	75.7	84.6	0.53	0.27-1.05	0.05
BMI < 23.0 kg/m ²	12.1	21.9	1.95	1.02-3.71	0.02
Primiparous	38.3	23.1	2.22	1.26-3.96	0.003
Age > 30 yrs	31.0	20.8	1.69	0.93-3.07	0.06
Family Hx of hypertension	62.3	19.8	6.70	3.69-12.28	0.0001
Family Hx of PIH	9.5	2.2	4.73	1.07-29.24	0.02

Figure-3.9 represents comparison between body mass indexes among the study groups. A high number (22.2%) of pregnant women had normal level of BMI less than 23 Kg/m² as compared to three patient groups. A large number 56 (57.1%) of pregnant women in the group 'A' of gestational hypertension were obese (table-3.11).

Table-3.11: Distribution of Body Mass Index among the four study groups.

BMI	Group-A		Group-B		Group-C		Group-D	
	N	%	N	%	n	%	N	%
< 23	12	12.2	10	10.4	15	14.4	20	22.2
≥ 23	10	10.2	14	14.6	12	11.5	13	14.4
≥ 25	05	25.1	12	12.5	15	14.4	09	10.0
≥ 27	15	15.3	16	16.7	22	21.2	12	13.3
≥ 30	56	57.1	44	45.8	40	38.5	36	40.0

Table-3.12 illustrates a univariate regression analysis of body mass index among the patient and control groups. Body mass index less than 23 Kg/m² was used as reference and the other groups were compared with it. It was observed that with the increase of body mass index, the risk of developing pregnancy induced hypertension also increased. Pregnant women with body obesity greater than 27 Kg/m² and 30 Kg/m² were found to be 2.32 times (95% CI (0.94-5.79), χ^2 4.09, P 0.04) and 2.03 times (95% CI (1.0-4.11), χ^2 4.62, P 0.03) respectively at higher risk to develop eclampsia as compared to women with BMI < 23.0 Kg/m².

Table-3.12: Comparison of body mass index among women with pregnancy induced hypertension and control subjects.

BMI	PIH		Control		Odd Ratio		
	N	%	N	%	OR (95% CI)	χ^2	P
< 23	38	12.8	20	22.2	Referent		
≥ 23	36	12.1	13	14.4	1.46 (0.59-3.65)	0.79	0.37
≥ 25	32	10.7	09	10.0	1.87 (0.69-5.19)	1.82	0.17
≥ 27	53	17.8	12	13.3	2.32 (0.94-5.79)	4.09	0.04
≥ 30	139	46.6	36	40.0	2.03 (1.0-4.11)	4.62	0.03

Different sign and symptoms in the patients of pregnancy induced hypertension are represented in (Table-3.13). Common signs and symptoms of PIH were swelling in face (59.6%), swelling in feet (71.1%), severe headache (80.1%) and dizziness (78.5%). In the most severe patients of eclampsia seizures were noted in 35.9% of patients, while 16.3% of these patients were in coma.

Table-3.13: Frequency of Sign and Symptoms in women with Pregnancy induced Hypertension

Sign & symptoms	PIH (N=312)	
	N	%
Swelling In face	186	59.6
Swelling in feet	225	71.1
Abdominal pain	150	48.1
Severe headache	250	80.1
Change in reflexes	48	15.4
↓ urine	105	33.6
No urine	73	23.4
Blood in urine	26	8.3
Seizures	112	35.9
Dizziness	245	78.5
Coma	51	16.3

Table-3.14 shows different complications developed in the patients of Pregnancy induced hypertension. The most common complications of pregnancy induced hypertension were pulmonary edema observed in 35.5%, visual in 31% and renal complication in 10.5% of patients.

Table-3.14: Frequency of complications in women with Pregnancy induced Hypertension.

Complications	PIH (N = 312)	
	N	%
Visual	97	31
Cerebrovascular	8	2.6
Cardiovascular	6	1.9
Pulmonary	8	2.6
LRT Infection	10	3.2
Pulmonary edema	111	35.5
Bronchospasm	4	1.3
Pulmo embolism	4	1.3
Asp pneumonia	5	1.6
Hepatic	9	2.9
Renal	33	10.5
Haemostatic	1	0.3
Obstetrical	7	2.2

Table-3.15 compares mean ($\pm$ SEM) lipoprotein concentration among the study groups. Statistically highly significant ($P < 0.001$) differences were noted in most of maternal serum lipid and lipoprotein concentrations in the three individual patients groups when compared with the control subjects of normotensive pregnant women, except changes in LDL-cholesterol ($P > 0.05$). Changes in the total cholesterol were non significant in group A and B, while difference in group

C of eclampsia were significant ($P < 0.05$) when compared with the normotensive women (Fig 3.10). Similarly APO-A1 was non significant ($P > 0.05$), markedly significant ($P < 0.01$) and highly significant ($P < 0.001$) in group A, B & C respectively when compared with the healthy pregnant women. Mean concentrations of APO-B100 were non significant in group B, while it was significant ($P < 0.05$) in group A and C when compared with group D of healthy pregnant women. Changes in the mean values of lipoprotein (a) were non significant in group A and B, while it was highly significant ($P < 0.001$) in group C of eclampsia as compared to normal healthy pregnant women (Fig 3.11).

Table -3.15: Lipoprotein concentrations among the normotensive and pregnancy induced hypertensive women.

Lipoprotein Conc.	Group-A Mean ± SEM	P value	Group-B Mean ± SEM	P value	Group-C Mean ± SEM	P value	Group-D Mean ± SEM
Total Cholesterol (mg/dL)	209.76 ± 5.59	NS	212.88 ±5.64	NS	216.63 ±5.17	0.05	202.23 ±4.6
HDL-Cholesterol (mg/dL)	45.98 ±1.08	0.05	43.98 ±0.96	0.001	40.83 ±0.92	0.001	52.20 ±1.14
LDL-Cholesterol (mg/dL)	111.30 ±5.26	NS	111.68 ±5.14	NS	110.54 ±4.79	NS	107.42 ±4.07
VLDL-Cholesterol (mg/dL)	52.05 ±1.99	0.001	56.11 ±2.19	0.001	66.93 ±2.84	0.001	42.22 ±1.46
Triglyceride (mg/dL)	259.05 ±10.0	0.001	280.63 ±10.94	0.001	337.71 ±14.34	0.001	212.30 ±7.28
APO-A1-1 (mg/dL)	177.86 ±5.67	NS	168.0 ±5.52	0.01	144.43 ±4.50	0.001	190.14 ±5.31
APO-B100 (mg/dL)	112.24 ±4.29	0.05	124.60 ±4.31	NS	120.06 ±4.32	0.05	128.33 ±5.50
LPA (mg/dL)	63.78 ±2.96	NS	75.89 ±10.82	NS	81.62 ±5.61	0.001	58.3 ±4.94

Table-3.16 compares different lipoprotein ratios between the four study groups. Amongst the different lipoprotein ratio TC: HDL-C, LDL-C: HDL-C, TG: HDL-C and HDL-C: VLDL-C ratio were found highly significant ($P < 0.001$) in patient groups of A, B and C, as compared with normotensive pregnant women (Fig.3.12). The importance of HDL: APO-B100 ratio and LDL: APO-A1 ratio could not be established. Both of these lipoprotein ratios were found non significant in group B of patients as compared to healthy pregnant women (Fig.3.13).

Table-3.16: Comparison of lipoprotein ratio among the four study groups.

Lipoprotein Ratio	Group-A Mean ± SEM	P value	Group-B Mean ± SEM	P value	Group-C Mean ± SEM	P value	Group-D Mean ± SEM
TC:HDL-C	4.72 ±0.15	0.001	5.08 ±0.18	0.001	5.49 ±0.15	0.001	3.87 ±0.11
LDL-C: HDL-C	2.50 ±0.13	0.01	2.69 ±0.14	0.001	2.77 ±0.12	0.001	2.05 ±0.09
TG:HDL-C	6.06 ±0.29	0.001	6.77 ±0.33	0.001	8.70 ±0.45	0.001	4.35 ±0.19
HDL-C: VLDL-C	1.02 ±0.05	0.001	0.91 ±0.04	0.001	0.71 ±0.03	0.001	1.36 ±0.06
LDL: APO-B100	1.003 ±0.062	0.05	0.93 ±0.05	NS	1.02 ±0.06	0.01	0.81 ±0.05
HDL: APO-A1	0.26 ±0.009	NS	0.27 ±0.01	NS	0.31 ±0.01	0.05	0.28 ±0.012

Difference in the mean and standard error of mean in blood lipids of patient and control subjects is represented in table-3.17. Women who developed hypertension after 20 weeks of gestation had 5.45%, 3.5%, 39%, 38.6% and 26.98% higher concentrations of total cholesterol, LDL cholesterol, VLDL cholesterol, triglycerides and lipoprotein (a) levels respectively, than control subjects

(Fig.3.14). A significant decrease of (16.76%) and (18.5%) was respectively noted in HDL-Cholesterol and APO-A1 of patient group when compared with normotensive control pregnant women, while no significant change in APO-B100 levels was seen among the groups (Fig.3.15).

Table -3.17: Blood Lipids in Normal Pregnancy and patients of pregnancy induced hypertension.

Lipoprotein (mg/dL)	PIH Mean ± SEM	Control Mean ± SEM	% change	P Value
Total Cholesterol	213.25 ± 3.14	188.23 ± 4.6	5.5	NS
HDL-Cholesterol (mg/dL)	43.45 ± 0.58	52.20 ± 1.14	16.8	0.001
LDL-Cholesterol (mg/dL)	111.15 ± 2.91	93.42 ± 4.07	3.5	NS
VLDL-Cholesterol (mg/dL)	58.74 ± 1.44	42.22 ± 1.46	39.1	0.001
Triglyceride (mg/dL)	294.25 ± 7.24	212.30 ± 7.28	38.6	0.001
APO-A1 (mg/dL)	160.45 ± 3.11	190.14 ± 5.31	18.5	0.001
APO-B100 (mg/dL)	119.64 ± 2.55	128.33 ± 5.50	7.3	NS
LPA (mg/dL)	74.03 ± 4.17	58.3 ± 4.94	26.9	0.05

Comparison of lipoprotein ratio among the groups is given in Table-3.18. Total cholesterol: HDL ratios, LDL-C: HDL-C ratio and TG: HDL-C ratios were higher (32.3%, 29.8% & 66.4% respectively) among women with pregnancy induced hypertension and were found highly significant (P 0.001) as compared to normotensive women. In the PIH group LDL/APO-B100 was raised to the marked

significant level of $P < 0.01$, while the difference between the two groups was found non significant for LDL: APO-B100 ratio ($P > 0.05$). HDL-C: VLDL-C ratio were decreased by 38.23% in the patients and were highly significant as compared with control subjects ($P < 0.001$) (Fig.3.16)

Table -3.18: Comparison of lipoprotein ratios in normal and pregnancy induced hypertension.

Parameters	PIH Mean $\pm$ SEM	Control Mean $\pm$ SEM	% change	P Value
TC : HDL-C ratio	5.12 $\pm$ 0.09	3.74 $\pm$ 0.11	32.29	0.001
LDL-C: HDL-C ratio	2.66 $\pm$ 0.07	1.86 $\pm$ 0.09	29.76	0.001
TG : HDL-C ratio	7.24 $\pm$ 0.22	4.35 $\pm$ 0.19	66.44	0.001
HDL-C : VLDL-C ratio	0.87 $\pm$ 0.02	1.36 $\pm$ 0.06	38.23	0.001
LDL: APO-B100	0.98 $\pm$ 0.03	0.81 $\pm$ 0.05	20.98	0.01
HDL: APO-A1	0.28 $\pm$ 0.007	0.28 $\pm$ 0.01	-	NS

The severities of hypertension in the patients of PIH are expressed in terms of systolic and diastolic blood pressures. Systolic blood pressure ≥ 150 mm Hg and diastolic blood pressure ≥ 110 mm Hg is considered as severe hypertension. Lipid and lipoprotein levels of PIH patients were compared for systolic blood pressure less than and greater than 150 mmHg (Table-13.19). A significant difference was found in maternal triglycerides levels, VLDL-C, cholesterol/HDL, TG/HDL and HDL/VLDL ratio, when the two groups of patients with systolic blood pressure less than and greater than 150 mmHg were compared. In the two groups, changes were also observed in total cholesterol, HDL-C and LDL-cholesterol; however no

significant difference could be established among the groups. Changes found in LDL-C: HDL-C ratio, APO-A1, APO-B100, lipoprotein (a) and LDL/APO-B100 ratio did not reach the level of significance.

Mean concentration of these lipoproteins in the group of patients with systolic blood pressure less than and greater than 150 mmHg were also compared individually with the healthy pregnant women. In all the lipoprotein fractions some level of significance was established, except in total cholesterol, LDL-C, LDL/APO-B100 ratio and HDL/APO-A1 ratio, where changes among the groups were found non significant ($P > 0.05$).

Table-3.19: Comparison between lipoprotein of patients with systolic blood pressure < 150 mmHg and $\geq$ 150 mmHg.

Lipoprotein Concentration	Systolic BP < 150 mm Hg Mean $\pm$ SEM N= 160	Systolic BP $\geq$ 150 mm Hg Mean $\pm$ SEM N= 152	P Value
Total cholesterol (mg/dL)	211 $\pm$ 4.71	216.13 $\pm$ 4.36	NS
HDL-Cholesterol (mg/dL)	44.71 ^d $\pm$ 0.85	42.35 ^c $\pm$ 0.78	NS
LDL-Cholesterol (mg/dL)	111.71 $\pm$ 4.44	111.0 $\pm$ 3.97	NS
VLDL-Cholesterol (mg/dL)	53.96 ^d $\pm$ 1.53	63.89 ^d $\pm$ 2.46	< 0.001
Triglyceride (mg/dL)	270.77 ^d $\pm$ 7.84	319.53 ^c $\pm$ 12.29	< 0.001
TC : HDL-C ratio	4.89 ^b $\pm$ 0.13	5.32 ^d $\pm$ 0.13	< 0.05
LDL-C: HDL-C ratio	2.60 ^c $\pm$ 0.11	2.71 ^c $\pm$ 0.10	NS
TG : HDL-C ratio	6.45 ^c $\pm$ 0.24	8.04 ^d $\pm$ 0.38	< 0.001
HDL-C : VLDL-C ratio	0.95 ^c $\pm$ 0.04	0.79 ^d $\pm$ 0.03	< 0.01
APO-A1 (mg/dL)	161.68 ^b $\pm$ 4.44	159.4 ^c $\pm$ 4.54	NS
APO-B100 (mg/dL)	118.15 ^d $\pm$ 3.67	121.42 $\pm$ 3.67	NS
LPA (mg/dL)	71.10 ^a $\pm$ 5.86	77.06 ^a $\pm$ 5.98	NS
LDL: APO-B100	1.01 $\pm$ 0.05	0.94 $\pm$ 0.04	NS
HDL: APO-A1	0.29 $\pm$ 0.01	0.27 $\pm$ 0.008	NS

- a P < 0.05 (values compared with control)
b P < 0.01 (values compared with control)
c P < 0.001 (values compared with control)
d P < 0.0001 (values compared with control)

Similarly PIH patients had significantly elevated serum HDL cholesterol, VLDL cholesterol, triglycerides, TC/HDL, TG/HDL, HDL/VLDL and LDL/APO-B100 ratio when patients with diastolic blood pressure less than 110 were compared with diastolic blood pressure greater than 110 mmHg (Table-3.20). Difference in

mean value of total cholesterol, LDL cholesterol, APO-B100 levels and HDL/APO-A1-1 remained non significant at the two cutoff of diastolic blood pressure. At comparison of each group of patients with diastolic blood pressure less than and greater than 110 mmHg with healthy pregnant women, some level of significance was established among all the sub fractions and ratios of lipoprotein, except in total cholesterol, APO-B100 and HDL: APO-A1 ratios, where the difference in the means of two groups of test and control was found non significant ($P > 0.05$).

Table-3.20: Comparison between lipoprotein of patients with diastolic blood pressure < 110 mmHg and $\geq$ 110 mmHg.

Parameters	Diastolic BP < 110 mm Hg Mean $\pm$ SEM N = 237	Diastolic BP $\geq$ 110 mm Hg Mean $\pm$ SEM N = 75	P Value
Total cholesterol (mg/dL)	214.11 $\pm$ 3.72	211.98 $\pm$ 6.40	NS
HDL-Cholesterol (mg/dL)	44.51 ^c $\pm$ 0.68	40.39 ^c $\pm$ 1.02	0.001
LDL-Cholesterol (mg/dL)	114.0 ^c $\pm$ 3.46	102.32 $\pm$ 5.78	NS
VLDL-Cholesterol (mg/dL)	55.39 ^c $\pm$ 1.44	70.30 ^a $\pm$ 3.84	0.001
Triglyceride (mg/dL)	277.66 ^c $\pm$ 7.28	351.54 ^c $\pm$ 19.23	0.001
TC : HDL-C ratio	5.00 ^d $\pm$ 0.10	5.44 ^d $\pm$ 0.18	0.05
LDL-C: HDL-C ratio	2.67 ^c $\pm$ 0.09	2.60 ^c $\pm$ 0.15	NS
TG : HDL-C ratio	6.63 ^d $\pm$ 0.23	9.19 ^d $\pm$ 0.54	0.001
HDL-C : VLDL-C ratio	0.93 ^d $\pm$ 0.03	0.69 ^d $\pm$ 0.04	0.001
APO-A1 (mg/dL)	160.01 ^c $\pm$ 3.68	162 ^c $\pm$ 6.28	NS
APO-B100 (mg/dL)	117.75 $\pm$ 3.04	125.44 $\pm$ 4.92	NS
LPA (mg/dL)	72.77 ^a $\pm$ 4.88	78.07 ^a $\pm$ 8.13	NS
LDD: APO-B100	1.02 ^a $\pm$ 0.04	0.86 ^a $\pm$ 0.06	0.05
HDL: APO-A1	0.29 $\pm$ 0.009	0.26 $\pm$ 0.01	NS

- a P < 0.05 (values compared with control)
b P < 0.01 (values compared with control)
c P < 0.001 (values compared with control)
d P < 0.0001 (values compared with control)

Table-3.21 represents comparison between different categories of lipid concentrations as desirable, acceptable and undesirable among the four study groups. Highest concentration of cholesterol (Fig.3.17) greater than 240 mg/dl (undesirable) was noted in 35.8% patients of eclampsia group 'C', while in more than 50% of the patients in

the eclampsia group had HDL cholesterol which is considered to be undesirable(F.g.3.18). Borderline high concentration of LDL (23.6%) (Fig.3.19), high concentrations of triglycerides (73.2%) (Fig.3.20), undesirable cholesterol ratio > 5.2 in 52.3% (Fig.3.21), undesirable LDL ratio > 1.6 were noted all in the patients of eclampsia (Fig.3.22).

Table-3.21: Comparison in different categories of lipoprotein concentrations among the study groups.

Lipid Concentration (mg/dL)		Group-A	Group-B	Group-C	Group-D
		%	%	%	%
Cholesterol	Category				
< 200	Desirable	51.1	47.5	41.3	53.8
200-239	Acceptable	23.4	26.3	22.9	23.1
> 240	Undesirable	25.5	26.3	35.8	23.1
HDL-C					
> 60	Desirable	12.2	4.1	4.7	18.9
40-60	Acceptable	52.2	60.2	44.9	67.8
< 40	Undesirable	35.6	35.7	50.5	13.3
LDL-C					
< 100	Optimal	43.3	43.9	41.5	51.1
100-129	Near optimal	27.8	31.6	21.7	22.2
130-159	Borderline high	15.6	6.1	23.6	11.1
160-189	High	10	9.2	6.6	7.8
≥ 190	Very high	3.3	9.2	6.6	7.8
VLDL-C					
< 129	Optimal	100	99	95.4	100
130-159	Borderline high	-	1	3.7	-
> 160	High	-	-	0.9	-
Triglyceride					
0-149	Normal	6.4	7	4.6	14.6
150-199	Borderline high	22.3	16	6.5	34.8
200-499	High	67	72	73.2	49.4
> 500	Very high	4.3	4	15.7	1.1
Cholesterol ratio					
≤ 5.1	Desirable	67.8	60.2	47.7	85.6
> 5.1	Undesirable	32.2	39.8	52.3	14.4
LDL ratio					
< 1.21	Desirable	1.1	94.9	9.4	18.9
1.21-1.6	Acceptable	16.7	-	8.5	21.1
> 1.6	Undesirable	67.8	5.1	82.1	60.0
HDL ratio					
< 3.3	Desirable	98.9	100	100	98.9
> 3.3	Undesirable	1.1	-	-	1.1

For estimating the relative association between PIH and varying concentrations of lipids and lipoproteins, each subject was categorized according to tertiles determined by the distribution of each analyte among normotensive control subjects. Using the lowest lipid category as the referent group (for all lipid variables except HDL), odds ratios (OR) and their 95% confidence intervals (CI) were estimated. The results from logistic regression analyses in which the relative risk (OR) of PIH associated with varying concentrations of maternal lipids and lipoproteins are estimated is given in the Table-3.22. A 1.5-fold increase in risk of PIH among women with total cholesterol >240 mg/dl (upper tertile), as compared with women whose total cholesterol concentrations were < 200 mg/dl (95% CI (0.80-2.75) χ^2 1.81, P 0.17) was noted. In univariate analyses a strong inverse relationship between plasma concentrations of HDL cholesterol and risk of PIH (P < 0.00001) was noted. The OR for PIH increased across increasing tertiles of HDL cholesterol concentration. Women in the lowest tertile experienced an 8.6-fold increased risk of PIH as compared with women in the highest tertile (95% CI (3.28-22.71) χ^2 27.9) as referent.

The OR for PIH increased across increasing LDL cholesterol concentration up to certain extent. The women in the tertile of 130-159 mg/dl experienced a 1.5-fold increased risk of PIH as compared with women in the lowest tertile (95% CI (0.67-3.40), though the difference did not reached the significant level (P > 0.28).

Finally, a strong positive relationship between plasma triglyceride concentrations and risk of PIH was noted. Women in the triglyceride tertile concentrations (200-499 mg/dl) experienced a 3.5-fold increased risk of PIH as compared with those

women in the lowest tertile as referent (95% CI (1.50 to 8.22) χ^2 10.82, $P < 0.001$). The risk of PIH increased significantly with higher tertiles of triglycerides concentration ($P < 0.0008$, OR 18.06, CI (12.09-403), χ^2 11.07).

In order to evaluate the significance of TC: HDL-C ratio, two groups of patients and control were compared at two cut off values of HDL-C ratio ≤ 5.1 and > 5.1 . It was noted that the risk of pregnancy induced hypertension increased 4.5 times as the ratio increased (95% CI (2.-8.87) χ^2 24.39, $P < 0.0001$). For the same purpose HDL/LDL ratio was compared for cut off less than and greater than 3.3. No significance difference was noted for this ratio in the two groups ($P > 0.57$).

Next PIH risk in relation to maternal LDL/HDL cholesterol ratio was evaluated. Here, it was noted that the risk of PIH increased as the ratio increased ($P < .007$). Women with the highest ratio values, experienced an almost 2.4-fold increased risk of PIH (OR 2.43, 95% CI 1.18 to 4.98, χ^2 7.09, P 0.007) against women whose ratio values were < 1.21 (lower tertile).

Table-3.22: Odds ratios (OR) and 95% confidence intervals (CI) of the association between pregnancy induced hypertension risk and maternal lipoprotein concentrations.

Lipoprotein (mg/dL)	PIH Patients	Control Women	Odd Ratio		
	%	%	OR (95%CI)	χ^2	P
Total cholesterol					
<200	46.4	53.8	Referent		
200–239	24.2	23.1	1.22 (0.65-2.28)	0.43	0.51
>240	29.5	23.1	1.48 (0.80-2.75)	1.81	0.17
HDL-C					
>60	6.8	18.9	Referent		
40-60	52.2	67.8	2.15 (0.99-4.63)	4.56	0.03
<40	41	13.3	8.57 (3.28-22.71)	27.89	0.00001
LDL-C					
<100	44.7	51.1	Referent		
100-129	25.7	22.2	1.32(0.71-2.47)	0.9	0.3
130-159	14.5	11.1	1.50(0.67-3.40)	1.13	0.28
≥160	8.6	15.6	0.63(0.3-1.36)	1.60	0.19
Triglycerides					
<150	6.0	14.6	Referent		
150–199	14.6	34.8	1.03(0.4-2.6)	0.00	0.95
200-499	71.1	49.4	3.51(1.5-8.22)	10.82	0.001
≥ 500	8.31	1.1	18.06(2.09-403.53)	11.07	0.0008
TC: HDL-C					
≤ 5.1	56.9	85.6	Referent		
> 5.1	43.1	14.4	4.48(2.3-8.87)	24.39	0.0001
HDL-C:LDL-C					
< 3.3	99.7	98.9	Referent		
≥ 3.3	0.3	1.1	0.46(0.01-16.98)	0.32	0.57
LDL: HDL					
< 1.21	9.9	18.9	Referent		
1.21 – 1.60	13.9	21.1	1.26(0.52-3.07)	0.32	0.56
> 1.60	76.2	60.0	2.43(1.18-4.98)	7.09	0.007

Table-3.23 represents gestation age of normotensive pregnant women and women with pregnancy induced hypertension in weeks. In both of the groups maximum numbers of women were in gestation age of 25-28 weeks (43.2% in PIH women versus 42.9% in the control group, Fig.3.23).

Table-3.23: Comparison of gestation age in women with PIH and healthy pregnant women without hypertension.

Gestation Age (weeks)	PIH Women		Normotensive Women	
	N	%	N	%
< 25	21	6.8	15	16.5
25-28	133	43.2	39	42.9
29-32	42	13.6	10	11
33-36	58	18.8	16	17.6
> 36	54	17.5	11	12.1

Table-3.24 characterize mean $\pm$ SEM of lipoproteins concentration at different gestation ages of women with Pregnancy Induced Hypertension. A linear trend has been observed in all the fractions of lipoprotein concentration and progress in the pregnancy, except in the high density lipoproteins-cholesterol concentration which had decreased with increase in the gestation weeks (Fig.3.24). A similar direct relationship has also been observed for APO-B100 concentration and progress in pregnancy, while APO-A1 concentrations remained almost constant for gestation week of up to 32 weeks, beyond which a sharp increase has been noted in its concentration. On the other hand lipoprotein-a concentration had

shown an increasing trend with the period of gestation up to 32 weeks and with the further progress of pregnancy, it started decreasing (Fig.3.25).

Table-3.24: Mean lipoprotein concentrations at different gestational weeks of women with pregnancy induced hypertension.

Lipoprotein Mean $\pm$ SEM	Gestation Week (N=312)				
	< 25	25-28	29-32	33-36	> 36
Total Cholesterol (mg/dL)	211.81 $\pm$ 9.75	219.73 $\pm$ 4.68	195.32 $\pm$ 8.73	206.29 $\pm$ 7.721	220.03 $\pm$ 8.03
HDL-C (mg/dL)	47.62 $\pm$ 2.6	44.15 $\pm$ 0.81	43.97 $\pm$ 1.96	41.92 $\pm$ 1.39	41.42 $\pm$ 1.24
LDL-C (mg/dL)	111.44 $\pm$ 9.16	122.64 $\pm$ 4.54	97.29 $\pm$ 7.45	93.09 $\pm$ 6.74	112.38 $\pm$ 7.13
VLDL-C (mg/dL)	54.79 $\pm$ 4.85	52.88 $\pm$ 1.35	56.29 $\pm$ 4.16	67.16 $\pm$ 4.36	66.16 $\pm$ 4.09
Triglycerides (mg/dL)	273.95 $\pm$ 24.28	264.46 $\pm$ 6.77	281.58 $\pm$ 20.82	339.55 $\pm$ 22.40	330.83 $\pm$ 20.45
APO-A1 (mg/dL)	157.7 $\pm$ 13.29	153.97 $\pm$ 4.36	153.0 $\pm$ 7.58	166.18 $\pm$ 7.49	171.95 $\pm$ 7.73
APO-B100 (mg/dL)	107.3 $\pm$ 9.23	112.5 $\pm$ 3.39	118.13 $\pm$ 7.86	124.28 $\pm$ 5.26	161 $\pm$ 6.57
LPA (mg/dL)	64.7 $\pm$ 3.41	70.13 $\pm$ 6.03	91.0 $\pm$ 12.83	74.28 $\pm$ 10.93	79.1 $\pm$ 14.93

Changes in hemoglobin concentration, platelet count, systolic and diastolic blood pressure were compared at different gestational weeks in women of pregnancy induced hypertension (Table-3.25). No prominent change could be seen in the platelet count (Fig.3.26) and hemoglobin concentration of women at different

period of gestation; however an increasing trend has been noted in systolic and diastolic blood pressure (Fig.3.27) with progression of pregnancy.

Table-3.25: Changes in hemoglobin concentration, platelet count, systolic and diastolic blood pressure at different gestational weeks of women with PIH.

Mean $\pm$ SEM	Gestation Week (N=312)				
	< 25	25-28	29-32	33-36	> 36
Hb (g%)	10.25 $\pm$ 0.44	9.99 $\pm$ 0.16	10.14 $\pm$ 0.30	10.47 $\pm$ 0.25	10.21 $\pm$ 0.30
Platelet Count (thousands/uL)	215.61 $\pm$ 14.57	203.94 $\pm$ 7.98	218.82 $\pm$ 11.52	235.35 $\pm$ 12.39	225.98 $\pm$ 13.9
Systolic BP (mmHg)	144.28 $\pm$ 4.38	149.17 $\pm$ 1.28	151.11 $\pm$ 2.01	151.48 $\pm$ 2.28	159.21 $\pm$ 3.12
Diastolic BP (mmHg)	95.81 $\pm$ 3.62	97.58 $\pm$ 1.03	99.92 $\pm$ 1.40	102.05 $\pm$ 1.36	107.03 $\pm$ 2.06

The number of women with PIH were 54 (17.3%) in the second trimester versus 24 (26.7%) in the control group, while rest 258 (82.7%) of PIH women were in their third trimester as compared to 66 (73.3%) in the group of normotensive healthy pregnant women (table-3.26).

Table-3.26: Number of normotensive and pregnancy induced hypertensive women in the second and third trimester of pregnancy.

Gestation Weeks	IIrd Trimester < 27 Weeks		IIIrd Trimester ≥ 27 Weeks	
	N	%	N	%
PIH Women	54	17.3	258	82.7
Normotensive Women	24	26.7	66	73.3

Mean lipoprotein concentrations in second and third trimester of normotensive and pregnancy induced hypertensive women are compared in table-3.27. A change was observed in the lipoprotein concentrations with the progress of pregnancy. A significant change was also seen in the concentration of HDL-C ($P < 0.01$), VLDL-C ($P < 0.05$), triglycerides ($P < 0.05$), APO-B100 ($P < 0.05$) and LPA ($P < 0.05$), when PIH women in the second trimester were compared with those in their third trimester. In the control group of normotensive pregnant women, significant changes could only be noted for total cholesterol ($P < 0.01$) and LDL-C ($P < 0.001$) when women in two groups of second and third trimester were compared. Lipoprotein concentrations of PIH women in the second and third trimester were also compared with its corresponding counterpart healthy pregnant women. A significant change was recorded in the total cholesterol ($P < 0.001$), LDL-C ($P < 0.01$), VLDL-C ($P < 0.001$), triglycerides ($P < 0.01$) and APO-A1 ($P < 0.05$), when PIH patients in second trimester were compared with the corresponding control women in the second trimester. When two groups of patient and control in the third trimester of pregnancy were compared for any difference in their lipoprotein concentration, it was noted that the difference in HDL-C ($P < 0.001$),

VLDL-C ($P < 0.001$), triglycerides ($P < 0.001$), APO-A11 ($P < 0.001$) and LPA ($P < 0.05$) were highly significant.

Table-3.27: Comparison of lipoprotein concentrations in second and third trimester of normotensive and pregnancy induced hypertensive women.

Lipoprotein Mean $\pm$ SEM	PIH Women			Control Women		
	IInd Trimester N=54	IIIrd Trimester N=258	Student t' test (P value)	IInd Trimester N=24	IIIrd Trimester N=66	Student t' test (P value)
Total Cholesterol (mg/dL)	218.56 ^{***} $\pm$ 6.39	212.25 $\pm$ 3.62	NS	175.41 $\pm$ 10.3	211.68 $\pm$ 7.88	< 0.01
HDL-C (mg/dL)	47.82 $\pm$ 1.48	42.56 ^{***} $\pm$ 0.62	< 0.01	50.12 $\pm$ 2.21	52.89 $\pm$ 1.31	NS
LDL-C (mg/dL)	118 ^{**} $\pm$ 6.41	109.94 $\pm$ 3.33	NS	85.2 $\pm$ 9.36	114.44 $\pm$ 6.91	< 0.001
VLDL-C (mg/dL)	53.58 ^{***} $\pm$ 2.46	59.64 ^{***} $\pm$ 1.67	< 0.05	40.09 $\pm$ 3.19	43.87 $\pm$ 1.81	NS
Triglycerides (mg/dL)	268 ^{**} $\pm$ 12.32	298.92 ^{***} $\pm$ 8.42	< 0.05	204.56 $\pm$ 16.14	219.36 $\pm$ 9.07	NS
APO-A1 (mg/dL)	156.25 [*] $\pm$ 8.25	161 ^{***} $\pm$ 3.41	NS	182.66 $\pm$ 9.46	192.78 $\pm$ 6.38	NS
APO-B100 (mg/dL)	107.69 $\pm$ 5.95	121.14 $\pm$ 2.81	< 0.05	118.55 $\pm$ 7.97	131.78 $\pm$ 6.87	NS
LPA (mg/dL)	63.08 $\pm$ 3.26	77.45 [*] $\pm$ 5.17	< 0.05	55.5 $\pm$ 5.82	59.5 $\pm$ 6.70	NS

Values compared with the corresponding control group of pregnant women

* $P < 0.05$

** $P < 0.01$

*** $P < 0.001$

Mean hemoglobin, platelet count, systolic and diastolic blood pressure of PIH women in its second and third trimester were compared with the healthy pregnant women without hypertension (Table-3.28). The only significant changes observed were in the systolic ($P < 0.05$) and diastolic blood pressure ($P < 0.01$) of PIH women, when two trimesters were compared together. No significant changes were noted in any entity of the control group of pregnant women, when their second and third trimesters were compared with each other. Women with PIH in its second and third trimester were also compared with its corresponding control group. In the second trimester a significant ($P < 0.05$) decrease in the platelet count and a highly significant ($P < 0.001$) rise in systolic and diastolic blood pressure was seen when comparison were made with the control group of women. In the third trimester of PIH women, a highly significant decrease in platelet count ($P < 0.001$) and increase in both systolic and diastolic blood pressure ($P < 0.001$) were seen, when compared with the control women.

Table-3.28: Comparison of hemoglobin, platelet count and blood pressure in second and third trimester of normotensive and pregnancy induced hypertensive women.

Mean $\pm$ SEM	PIH Women			Control Women		
	IInd Trimester N=54	IIIRD Trimester N=258	Student's t' test (P value)	IInd Trimester N=24	IIIRD Trimester N=66	Student's t' test (P value)
Hb (g %)	10.12 $\pm$ 0.27	10.16 $\pm$ 0.12	NS	9.55 $\pm$ 0.37	10.41 $\pm$ 0.20	NS
Platelet Count (thousands/uL)	202.84* $\pm$ 8.89	218.85*** $\pm$ 5.99	NS	263.17 $\pm$ 22.63	260.83 $\pm$ 8.03	NS
Systolic BP (mmHg)	146.94*** $\pm$ 2.20	152.17*** $\pm$ 1.10	< 0.05	115.62 $\pm$ 2.0	116.67 $\pm$ 1.02	NS
Diastolic BP (mmHg)	96.03*** $\pm$ 1.66	101.14*** $\pm$ 0.79	< 0.01	75.70 $\pm$ 1.45	75.13 $\pm$ 0.79	NS

Values compared with the corresponding control group of pregnant women

* P < 0.05

*** P < 0.001

One of the risk factor for developing pregnancy induced hypertension is giving birth to first child (primiparous) by the affected women. In the present study 120 (30%) women were primiparous against 21 (23%) women in the control group of pregnant women (table-3.29). Highest levels of mean systolic blood pressure (158.8 mmHg) and diastolic blood pressure (105.6 mmHg) were recorded in the patients of eclampsia, when compared with the remaining patient and control groups of pregnant women. On comparison of platelet estimation between control and study groups, a significant decrease in platelet number was also observed in eclampsia group of patients.

Table-3.29: Socio-demographic and medical characteristics of primiparous pregnant women in the study groups.

Variables	Group-A Mean ± SEM N=19	Group-B Mean ± SEM N=35	Group-C Mean ± SEM N=65	Group-D Mean ± SEM N=21
Age (years)	24.78 ± 1.18	24.28 ± 0.86	23.15 ± 0.52	23.90 ± 1.16
Marriage age (years)	21.42 ± 0.95	20.65 ± 0.72	20.5 ± 0.62	20.42 ± 1.07
Gestation age (weeks)	29 ± 0.95	31.6 ± 0.83	31.64 ± 0.58	28.81 ± 1.03
Systolic BP (mmHg)	149.73 ± 2.63	149.68 ± 2.27	158.79 ± 2.82	115.23 ± 2.05
Diastolic BP (mmHg)	97.89 ± 1.63	99.88 ± 1.86	105.59 ± 2.02	76.04 ± 1.54
Height (cm)	160.32 ± 1.82	154.22 ± 1.82	151.48 ± 1.52	150.26 ± 3.04
Weight (kg)	75.55 ± 2.31	69.0 ± 2.07	66.61 ± 1.49	67.85 ± 3.37
BMI (kg/m ²)	29.59 ± 1.21	29.45 ± 1.22	30.00 ± 1.00	30.90 ± 2.22
Mean Platelets count (thousand/ μ L)	199.72 ± 15.25	235.41 ± 17.37	178.15 ± 9.83	268.80 ± 19.42
Hb (g/dL)	9.50 ± 0.57	9.37 ± 0.45	10.4 ± 0.21	10.12 ± 0.36

In order to find any level of significant difference between the patient and control groups of primiparous pregnant women, three groups of patient were combined and presented as a group of pregnancy induced hypertension. On comparing the two groups of patient and control pregnant women (Table-3.30), it was found that no significant difference was present in the mean age, marriage age, weight, body mass index and hemoglobin between the groups ($P > 0.05$). However the difference in systolic/diastolic blood pressure and platelet count were highly significant ($P < 0.001$).

Table-3.30: Comparison of different variables among 120 primiparous women with pregnancy induced hypertension against 21 normotensive primiparous pregnant women.

Variables	PIH Mean $\pm$ SEM (N=120)	Control Mean $\pm$ SEM (N=21)	Student's t test P
Age (years)	23.74 $\pm$ 0.42	23.90 $\pm$ 1.16	NS
Marriage age (years)	20.69 $\pm$ 0.43	20.42 $\pm$ 1.07	NS
Gestation age (weeks)	31.21 $\pm$ 0.43	28.81 $\pm$ 1.03	NS
Systolic BP (mmHg)	154.56 $\pm$ 1.75	115.23 $\pm$ 2.05	0.001
Diastolic BP (mmHg)	102.61 $\pm$ 1.27	76.04 $\pm$ 1.54	0.001
Height (cm)	156.97 $\pm$ 1.21	150.26 $\pm$ 3.04	NS
Weight (kg)	68.72 $\pm$ 1.11	67.85 $\pm$ 3.37	NS
BMI (kg/m ²)	29.76 $\pm$ 0.67	30.90 $\pm$ 2.22	NS
Platelets count (thousand/ μ L)	197.46 $\pm$ 8.02	268.80 $\pm$ 19.42	0.001
Hb (g/dL)	9.97 $\pm$ 0.20	10.12 $\pm$ 0.36	NS

Table-3.31 shows mean $\pm$ SEM of blood lipid levels in normal pregnancy and in primiparous women of pregnancy induced hypertension. The difference in the total cholesterol, HDL-C, VLDL-C, TC: HDL ratio and TG: HDL-C ratio of eclampsia group was more prominent as compared to control pregnant women. No large difference was noted in the mean values of APO-B100, HDL/APO-A1 and LDL/APO-B100 ratio among the test and control groups of women.

Table -3.31: Lipoprotein concentrations in primiparous women with normal pregnancy and three groups of pregnancy induced hypertension.

Parameters	Group-A Mean $\pm$ SEM N=19	Group-B Mean $\pm$ SEM N=35	Group-C Mean $\pm$ SEM N=65	Group-D Mean $\pm$ SEM N=21
Total Chol. (mg/dL)	198.26 $\pm$ 10.26	207.82 $\pm$ 8.43	213.61 $\pm$ 6.84	206.28 $\pm$ 16.47
HDL-Chol. (mg/dL)	42.78 $\pm$ 2.06	43.87 $\pm$ 1.79	40.72 $\pm$ 1.16	53.20 $\pm$ 2.36
LDL-Chol. (mg/dL)	103.68 $\pm$ 10.53	117.83 $\pm$ 7.99	109.55 $\pm$ 6.37	106.55 $\pm$ 14.37
VLDL-Chol. (mg/dL)	48.08 $\pm$ 4.28	47.31 $\pm$ 2.14	65.12 $\pm$ 3.51	44.7 $\pm$ 3.57
Triglyceride (mg/dL)	240.46 $\pm$ 21.43	236.74 $\pm$ 10.67	327.98 $\pm$ 17.78	223.4 $\pm$ 17.87
TC:HDL-C ratio	4.63 $\pm$ 0.25	5.01 $\pm$ 0.29	5.38 $\pm$ 0.19	3.95 $\pm$ 0.36
LDL-C:HDL-C ratio	2.47 $\pm$ 0.25	2.85 $\pm$ 0.24	2.76 $\pm$ 0.16	2.07 $\pm$ 0.29
TG:HDL-C ratio	5.79 $\pm$ 0.59	5.77 $\pm$ 0.38	8.38 $\pm$ 0.50	4.41 $\pm$ 0.43
HDL-C: : VLDL-C ratio	0.94 $\pm$ 0.06	0.99 $\pm$ 0.03	0.72 $\pm$ 0.03	1.30 $\pm$ 0.09
APO-A1 (mg/dL)	169.25 $\pm$ 14.05	151.82 $\pm$ 9.35	143.59 $\pm$ 5.85	189 $\pm$ 11.31
APO-B100 (mg/dL)	119.25 $\pm$ 6.29	114.69 $\pm$ 8.17	118.98 $\pm$ 4.96	126.18 $\pm$ 13.25
LDL: APO- B100	0.90 $\pm$ 0.10	1.08 $\pm$ 0.12	0.99 $\pm$ 0.06	0.95 $\pm$ 0.14
HDL: APO-A1	0.25 $\pm$ 0.01	0.29 $\pm$ 0.01	0.31 $\pm$ 0.02	0.28 $\pm$ 0.03

Comparison of the mean of lipoprotein fractions among the groups is given in Table-3.32. It is evident that no significant difference could be established in total cholesterol of women with pregnancy induced hypertension and normotensive pregnant women. Similarly a non significant difference ($P > 0.05$) was noted in LDL-cholesterol, APO-B100, HDL/APO-A1 ratio and LDL/APO-B100 ratio. However highly significant difference were established in HDL-cholesterol ($P <$

0.001), total cholesterol/HDL-C ratio ($P < 0.001$), TG/HDL-C ratio ($P < 0.0001$), HDL-C/VLDL-C ratio ($P < 0.0001$) and APO-A1 level ($P < 0.001$).

Table -3.32: Lipoprotein concentrations in primiparous women with normal pregnancy and pregnancy induced hypertension.

Parameters (mg/dL)	PIH Mean $\pm$ SEM N=120	Control Mean $\pm$ SEM N=21	% change	P Value
Total cholesterol	209.86 $\pm$ 4.82	206.28 $\pm$ 16.47	1.7	NS
HDL-Cholesterol	41.91 $\pm$ 0.90	53.20 $\pm$ 2.36	26.9	0.001
LDL-Cholesterol	111.28 $\pm$ 4.55	106.55 $\pm$ 14.37	4.4	NS
VLDL-Cholesterol	57.57 $\pm$ 2.31	44.7 $\pm$ 3.57	28.8	0.05
Triglyceride	289.25 $\pm$ 11.71	223.4 $\pm$ 17.87	29.5	0.01
TC : HDL-C ratio	5.18 $\pm$ 0.14	3.95 $\pm$ 0.36	31.1	0.001
LDL-C: HDL-C ratio	2.75 $\pm$ 0.12	2.07 $\pm$ 0.29	32.9	0.05
TG : HDL-C ratio	7.29 $\pm$ 0.34	4.41 $\pm$ 0.43	65.3	0.0001
HDL-C : VLDL-C ratio	0.83 $\pm$ 0.03	1.30 $\pm$ 0.09	56.6	0.0001
APO-A1	147.88 $\pm$ 4.71	189 $\pm$ 11.31	27.9	0.001
APO-B100	117.93 $\pm$ 3.88	126.18 $\pm$ 13.25	6.9	NS
LDH: APO-B100	1.0 $\pm$ 0.05	0.95 $\pm$ 0.14	5.3	NS
HDL: APO-A1	0.30 $\pm$ 0.01	0.28 $\pm$ 0.03	7.1	NS

Comparing primiparous women among various groups on the basis of normal, low and very low platelet count, it was found that the number of women with very low count is more (18.5%) prevalent in women with eclampsia (Table-3.33). In the control group 95.2% of pregnant women had normal platelet count > 151 (thousand/ μ L) against 60% in the group of eclamptic patients.

Table-3.33: Distribution of patients based on severity of PIH and estimated platelet counts among the primiparous pregnant women.

Platelet count (thousand/ μ L)	Group-A		Group-B		Group-C		Group-D	
	N	%	N	%	N	%	N	%
< 100 Very low	2	10	5	14.3	12	18.5	0	-
100-150 Low	2	10	3	8.6	14	21.5	1	4.8
> 151 Normal	16	80	27	77.1	39	60	20	95.2

Linear regression analysis for odds of normal, low and very low platelet count in Pregnancy Induced Hypertension and normal pregnant women is compared in Table-3.34. Normal values of platelet count greater than 151 thousand/ μ L was used as reference and compared with low platelet count 100-150 thousand/ μ L. It was evaluated that patients with pregnancy induced hypertension were 4 times more exposed to have low platelet count as compared to normotensive pregnant women (OR 4.40, 95% CI 0.56-93.6).

Table-3.34: Odd ratio and 95% CI for very low, low and normal platelet count for primiparous PIH and control group of pregnant women.

Platelet count (thousand/ μ L)	PIH		Control		Odd Ratio			
	N	%	N	%	OR	95% CI	χ^2	P
< 100 (very low)	19	15.8	0	-	-		4.25	0.04
100-150 (low)	19	15.8	1	4.8	4.40	0.56-93.6	2.3	19
> 151 (normal)	82	68.3	19	95.2	Referent			

A comparison of different hematological parameters, like White Blood Count (WBC), Lymphocytes, Monocytes, Neutrophils, Basophils, Red Blood cell Count (RBC), Hemoglobin, PCV, MCV, MCH, MCHC and platelet count in the four study group is given in the Table-3.35. A remarkable increase in WBC, lymphocytes, monocytes, GRA and a notable decrease in platelet count in group C of eclampsia was noted among the patient groups when compared with the control group of normotensive pregnant women. It could also be observed that there is an inverse relationship between the severity of PIH and platelet numbers.

Table-3.35: Comparison between different hematological changes among the four groups of pregnant women.

Parameters	Group-A Mean ± SEM	Group-B Mean ± SEM	Group-C Mean ± SEM	Group-D Mean ± SEM
WBC (10 ³ µL)	10.104 ± 0.45	10.424 ± 0.41	12.477 ± 0.47	9.166 ± 0.38
Lym 10 ^{9/l}	2.04 ± 0.09	1.94 ± 0.07	2.02 ± 0.113	1.84 ± 0.08
Mono 10 ^{9/l}	0.67 ± 0.06	0.63 ± 0.06	0.89 ± 0.08	0.68 ± 0.04
GRA 10 ^{9/l}	7.39 ± 0.429	7.85 ± 0.41	9.58 ± 0.45	6.65 ± 0.35
Ly (%)	22.51 ± 1.17	20.97 ± 1.13	17.41 ± 0.95	21.15 ± 0.79
MO (%)	7.20 ± 0.67	6.83 ± 0.66	7.84 ± 0.69	0.68 ± 0.04
GR (%)	70.27 ± 1.42	72.19 ± 1.42	74.74 ± 1.37	70.57 ± 1.04
RBC (10 ⁶ /µL)	3.71 ± 0.08	3.69 ± 0.07	3.70 ± 0.075	3.83 ± 0.06
Hb (g %)	10.29 ± 0.20	9.99 ± 0.20	10.19 ± 0.17	10.19 ± 0.18
HCT (%)	30.23 ± 0.67	29.83 ± 0.61	30.33 ± 0.54	30.49 ± 0.51
MCV (µ)	82.36 ± 1.01	81.35 ± 0.97	82.83 ± 0.89	80.47 ± 1.18
MCH (pg)	28.50 ± 0.59	27.32 ± 0.42	27.89 ± 0.38	26.99 ± 0.52
MCHC (g/dL)	34.44 ± 0.39	33.47 ± 0.19	33.89 ± 0.31	33.38 ± 0.24
RDWC (fL)	16.69 ± 0.34	16.41 ± 0.24	16.81 ± 0.25	16.14 ± 0.26
PLT (10 ³ /µL)	223.24 ± 7.64	227.50 ± 9.35	198.60 ± 9.28	261.44 ± 8.27
PCT (%)	0.22 ± 0.00	0.23 ± 0.00	0.20 ± 0.00	0.26 ± 0.00
MPV (fL)	10.02 ± 0.12	10.11 ± 0.12	10.21 ± 0.12	10.23 ± 0.13
PDWC (%)	40.75 ± 0.19	41.18 ± 0.20	41.00 ± 0.25	41.26 ± 0.20

The student's t' test was used to evaluate mean differences in hematological parameters between patients and control subjects and the findings are presented in table-3.36. A highly significant difference ($P < 0.001$) was recorded in white blood cell count, neutrophils, PCT and platelet count, while changes in hemoglobin and other entities was non significant ($P > 0.05$) among the two groups. Out of all the hematological changes that occur in pre-eclampsia and eclampsia, thrombocytopenia is the most common hematological abnormality found.

Table-3.36: Comparison between different hematological changes among the women with pregnancy induced hypertension and healthy pregnant women.

Parameters	PIH (N=312) Mean $\pm$ SEM	Control (N=90) Mean $\pm$ SEM	% Change	P-Value
WBC ($10^3/\mu\text{L}$)	11.05 $\pm$ 0.26	9.166 $\pm$ 0.38	20.55	0.001
Lym $10^9/l$	2.00 $\pm$ 0.05	1.84 $\pm$ 0.08	8.69	NS
Mono $10^9/l$	0.74 $\pm$ 0.04	0.68 $\pm$ 0.04	8.82	NS
GRA $10^9/l$	8.32 $\pm$ 0.25	6.65 $\pm$ 0.35	25.11	0.001
Ly (%)	20.20 $\pm$ 0.63	21.15 $\pm$ 0.79	4.49	NS
MO (%)	7.31 $\pm$ 0.39	0.68 $\pm$ 0.04	11.50	NS
GR (%)	72.47 $\pm$ 0.81	70.57 $\pm$ 1.04	2.69	NS
RBC ($10^6/\mu\text{L}$)	3.70 $\pm$ 0.04	3.83 $\pm$ 0.06	3.39	NS
Hb (g %)	10.16 $\pm$ 0.11	10.19 $\pm$ 0.18	0.29	NS
HCT (%)	30.14 $\pm$ 0.34	30.49 $\pm$ 0.51	1.15	NS
MCV (μ)	82.21 $\pm$ 0.55	80.47 $\pm$ 1.18	2.16	NS
MCH (pg)	27.91 $\pm$ 0.27	26.99 $\pm$ 0.52	3.41	NS
MCHC (g/dL)	33.93 $\pm$ 0.18	33.38 $\pm$ 0.24	1.65	NS
RDWC	16.65 $\pm$ 0.16	16.14 $\pm$ 0.26	3.16	NS
PLT ($10^3/\mu\text{L}$)	215.84 $\pm$ 5.13	261.44 $\pm$ 8.27	17.44	0.001
PCT	0.21 $\pm$ 0.0	0.26 $\pm$ 0.00	19.23	0.001
MPV	10.12 $\pm$ 0.07	10.23 $\pm$ 0.13	9.09	NS

The anemia status in the four study groups of pregnant women is reported in table-3.37. It has been observed that majority of women with severe anemia (Hb < 7.7 g %) were present in the three patient groups as compared to the normal pregnant women (Fig.3.28).

Table-3.37: Anemia status among the four study groups of pregnant women.

Hb g%	Group-A		Group-B		Group-C		Group-D	
	N	%	N	%	N	%	N	%
> 12.00 (normal)	16	15.7	11	11	18	16.4	14	15.5
10.5-11.9 (mild anemia)	39	38.2	36	36	33	30	26	28.9
10.4-7.7 (moderate anemia)	35	34.3	43	43	50	45.4	44	48.9
< 7.7 (severe anemia)	12	11.8	10	10	09	8.2	6	6.7
Total	102	100	100	100	110	100	90	100

The relative association between Pregnancy Induced Hypertension and varying concentrations of hemoglobin were represented with the help of odd ratio (table-3.38). It has been observed that the patient group was 1.3 times (OR 1.3 (CI 0.58-2.9) and 1.6 times (OR 1.6(CI 0.5-5.41)) more prone to mild and severe anemia respectively, though the difference at various cut off to anemia status among the groups were non significant ($P > 0.05$).

Table-3.38: Anemia status among the women with pregnancy induced hypertension and healthy pregnant women.

Hb (Status) (g%)	PIH		Control		Un adjusted Odd Ratio		
	N	%	N	%	OR	χ^2	P
> 12.00 (normal)	45	14.4	14	15.5	Referent		
10.5-11.9 (mild anemia)	108	34.6	26	28.9	1.30 (0.58-2.90)	0.49	0.48
10.4-7.7 (moderate anemia)	128	41.0	44	48.9	0.93 (0.44-1.96)	0.04	0.84
< 7.7 (severe anemia)	31	10.0	6	6.7	1.63(0.5-5.41)	0.81	0.36
Total	312	100	90	100			

It was also observed that out of all the hematological changes that occur in pre-eclampsia and eclampsia, thrombocytopenia is the most common hematological abnormality found. Table-3.39 describes different ranges of platelet count in four study groups as very low (< 100), low (100-150) and normal platelet count > 150 thousand/ μ l. In comparison of women among various groups with normal, very low platelet number, it was observed that the number of women with very low count is more in women with eclampsia (13.6%) versus 1.1% in the control women. Normal platelet count > 150 thousand/ μ L was recorded in 86 (95.5%) of control pregnant women against 72 (65.4%) in the group of eclampsia patients. Severity of PIH and thrombocytopenia observed are closely co-related which indicates that thrombocytopenia is directly proportional to the severity of PIH (Fig.3.29).

Table-3.39: Status of platelet count as very low, low and normal among the four study groups of pregnant women.

Platelet count (thousand/ μ L)	Group-A		Group-B		Group-C		Group-D	
	N	%	N	%	N	%	N	%
< 100 (very low)	6	5.8	6	6	15	13.6	1	1.1
100-150 (low)	9	8.8	9	9	23	21.0	3	3.4
> 151 (Normal)	87	85.4	85	85	72	65.4	86	95.5
Total	102	100	100	100	110	100	90	100

When the value of platelet count was compared between control and study groups (PIH), a significant decrease in platelet number was observed (Table-3.40). In the patient group 8.7% of pregnant women had severe thrombocytopenia as compared to 1.1% in the control group. These patients were nine times more likely to have severe eclampsia as compared to those having platelet count of greater than 151 thousand/ μ l (OR 9.41, CI (1.33-188.8) P 0.008, χ^2 6.99. Severity of PIH and thrombocytopenia observed are closely co-related which indicates that thrombocytopenia is directly proportional to the severity of PIH.

Table-3.40: Status of platelet count as very low, low and normal among the women with PIH and healthy pregnant women.

Platelet count (thousand/ μ L)	PIH		Control		Odd Ratio			
	N	%	N	%	OR	95% CI	P	χ^2
< 100 (very low)	27	8.7	1	1.1	9.41	1.33-188.85	0.008	6.99
100-150 (low)	41	13	3	3.4	4.76	1.37-19.80	0.005	7.79
> 151 (Normal)	244	78.3	86	95.5	Referent			

The platelet count in the present study was compared with the results obtained from other studies. Like other studies²³⁹⁻²⁴³ the number of platelet count was inversely proportional to the severity of disease and lowest count was observed in the patients of eclampsia (Table-3.41).

Table-3.41: Comparison of platelet counts reported by various authors in relation to severity of PIH.

Pregnant women	Present study Mean platelet count (thousand/ μ L)	Platelet value reported by different authors (thousand/ μ L)				
		Mohapatra et al ²³⁸	Vrunda et al ²³⁹	Kulkarni et al ²⁴⁰	Giles et al ²⁴¹	Dube et al ²⁴²
Normal	261	238	220	250	280	230
Gestational hypertension	223	223	200	184	240	190
Pre-eclampsia	227	182	140	119	210	190
Eclampsia	198	121	130	118	115	180

The pre-eclamptic/eclamptic patients were diagnosed by the presence of persistent hypertension (more than 140/90 mmHg), gross proteinuria and pathological edema. The severity of PIH is directly proportional to the quantity of protein present in the urine. Figure-3.30 represents a comparison of urinary protein between the study groups. Most severe form of proteinuria was seen in the eclampsia group, wherein 32.7% and 18.2% patients were excreting 3.0 g/L and 20 g/L protein respectively (Table-3.42). In the control group 86.7% normal pregnant women had no excretion of protein, while 12.2% had only traces of protein in their urine.

Table-3.42: Urinary protein concentration among the four groups of pregnant women.

Urinary Protein(g/l)	Group-A		Group-B		Group-C		Group-D	
	N	%	N	%	N	%	N	%
0 (Not detectable)	91	89.2	-	-	-	-	78	86.7
0.15 (trace)	11	10.8	-	-	-	-	11	12.2
0.3 (+)	-	-	69	69	23	20.9	1	1.1
1.0 (++)	-	-	15	15	31	28.2	-	-
3.0 (+++)	-	-	10	10	36	32.7	-	-
20 (++++)	-	-	6	6	20	18.2	-	-

Coefficient of Correlation

Coefficient of Correlation 'r' was determined between different biochemical indices by using Pearson Product Moment correlation on SPSS 10 software computer package.

Table-3.43 defines biochemical tests that tends to correlate and are likely to be altered as groups during the disease process. The magnitude of alteration of one value by changes in the other is determined by the value of 'r'. P values of 'r' < 0.05 indicated that the correlations shown are significant.

Different variables were correlated with each other and presented in figures 3.31- 3.66. A mild positive and statistically significant correlation was found between Systolic BP & VLDL-C ($r=.203$ and p value of 'r' 0.001, Fig. 3.34), Systolic BP & Triglycerides ($r=.199$ and p value of 'r' 0.001, Fig. 3.35), Diastolic BP & VLDL-C ($r=.214$ and p value of 'r' 0.001, Fig. 3.42), Diastolic BP &

Triglycerides ($r = .210$ and p value of ' r ' 0.001 , Fig. 3.43) and Total Cholesterol & HDL-C ($r = .181$ and p value of ' r ' 0.002 , Fig. 3.47). A positive strong and highly significant correlation was seen between Total Cholesterol & LDL-C ($r = .870$ and p value of ' r ' 0.001 , Fig. 3.48). Similarly a positive moderate and significant correlation was observed in Total Cholesterol & VLDL-Cholesterol ($r = .342$ and p value of ' r ' 0.001 , Fig. 3.49) and Total Cholesterol & Triglycerides ($r = .341$ and p value of ' r ' 0.001 , Fig. 3.50).

A negative weak but statistically significant correlation was developed between Systolic BP & HDL-C ($r = -.123$ and p value of ' r ' $.036$, Fig. 3.32), Diastolic BP & HDL-C ($r = -.153$ and p value of ' r ' $.009$, Fig. 3.40), HDL-C & VLDL-C ($r = -.157$ and p value of ' r ' $.007$, Fig. 3.52) and HDL-C & Triglycerides ($r = -.157$ and p value of ' r ' $.007$, Fig. 3.53).

Table-3.43: Correlation and significance levels of various biochemical indices in patients of PIH.

X-axis	VS	Y-axis	Coefficient of Correlation 'r'	P value of 'r'
Systolic BP		Total Cholesterol	0.071	.221
Systolic BP		HDL-C	-.123**	.036
Systolic BP		LDL-C	.014	.814
Systolic BP		VLDL-C	.203**	.001
Systolic BP		Triglycerides	.199**	.001
Systolic BP		APO-A1	-.091	.175
Systolic BP		APO-B100	.004	.943
Systolic BP		Platelet Count	-.066	.260
Diastolic BP		Total Cholesterol	.037	.528
Diastolic BP		HDL-C	-.153**	.009
Diastolic BP		LDL-C	-.030	.613
Diastolic BP		VLDL-C	.214**	.001
Diastolic BP		Triglycerides	.210**	.001
Diastolic BP		APO-A1	-.091	.172
Diastolic BP		APO-B100	.093	.164
Diastolic BP		Platelet Count	-.055	.348
Total Cholesterol		HDL-C	.181**	.002
Total Cholesterol		LDL-C	.870**	.001
Total Cholesterol		VLDL-C	.342**	.001
Total Cholesterol		Triglycerides	.341**	.001
HDL-C		LDL-C	.076	.194
HDL-C		VLDL-C	-.157**	.007
HDL-C		Triglycerides	-.157**	.007
LDL-C		VLDL-C	-.081	.166
LDL-C		Triglycerides	-.082	.162
VLDL-C		Triglycerides	.996**	.001
Platelet Count		Total Cholesterol	.090	.124
Platelet Count		HDL-C	.117	.046
Platelet Count		LDL-C	.080	.175
Platelet Count		VLDL-C	-.023	.698
Platelet Count		Triglycerides	-.021	.719
Platelet Count		APO-A1	-.050	.449
Platelet Count		APO-B100	.073	.270

** = Significant value

An attempt has been made to correlate different variables with gestation age of pregnant women and presented in figures 3.64-3.75 and table-3.44. A mild positive and statistically significant correlation was found between HDL-C & gestation week ($r=.169$ and p value of 'r' 0.004, Fig. 3.65), APO-A1 & gestation week ($r=.114$ and p value of 'r' 0.046, Fig. 3.69), Systolic BP & gestation period ($r=.212$ and p value of 'r' 0.01, Fig. 3.74), Diastolic BP & gestation period ($r=.249$ and p value of 'r' 0.01, Fig. 3.75) and between platelet count and gestation period ($r=.101$ and p value of 'r' .083, Fig. 3.71). A negative weak but statistically significant correlation was found between gestational week & VLDL-C ($r=-.133$ and p value of 'r' .021, Fig. 3.67) and gestational week & triglycerides ($r=-.132$ and p value of 'r' .022, Fig. 3.68).

Table-3.44: Correlation and significance levels of various biochemical indices with gestation week in patients of pregnancy induced hypertension.

X-axis	VS Y-axis	Coefficient of Correlation 'r'	P value of 'r'
Gestational week	TC	-.075	.197
Gestational week	HDL-C	.169(**)	.004
Gestational week	LDL-C	-.051	.389
Gestational week	VLDL-C	-.133(*)	.021
Gestational week	Triglycerides	-.132(*)	.022
Gestational week	APO-A1	.114(*)	.046
Gestational week	APO-B100	-.023	.683
Gestational week	Lipoprotein-a	-.166	.144
Gestational week	Platelet Count	.101	.083
Gestational week	Hemoglobin	.027	.645
Gestational week	Weight	.074	.203
Gestational week	Systolic BP	.212(**)	.01
Gestational week	Diastolic BP	.249(**)	.01

* = Significant value

** = More significant value

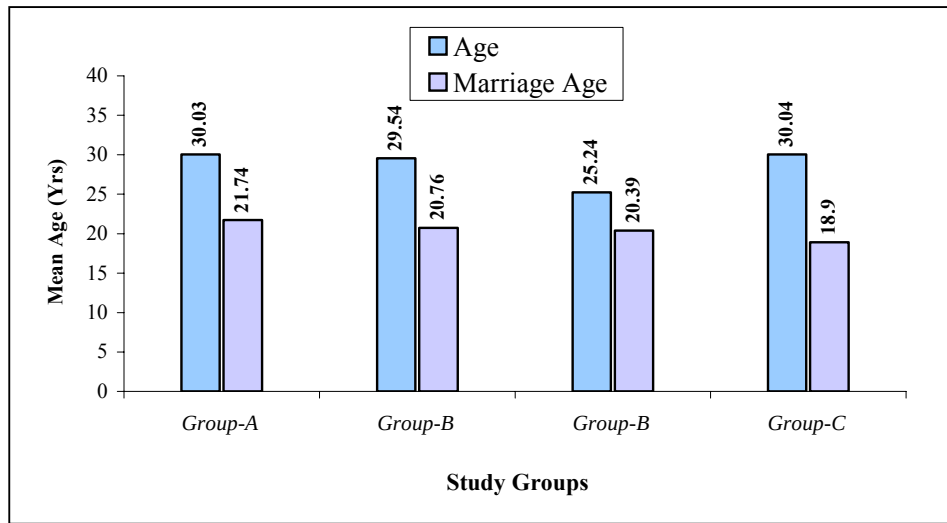


Figure-3.1: Comparison between maternal age and marriage age among the study groups.

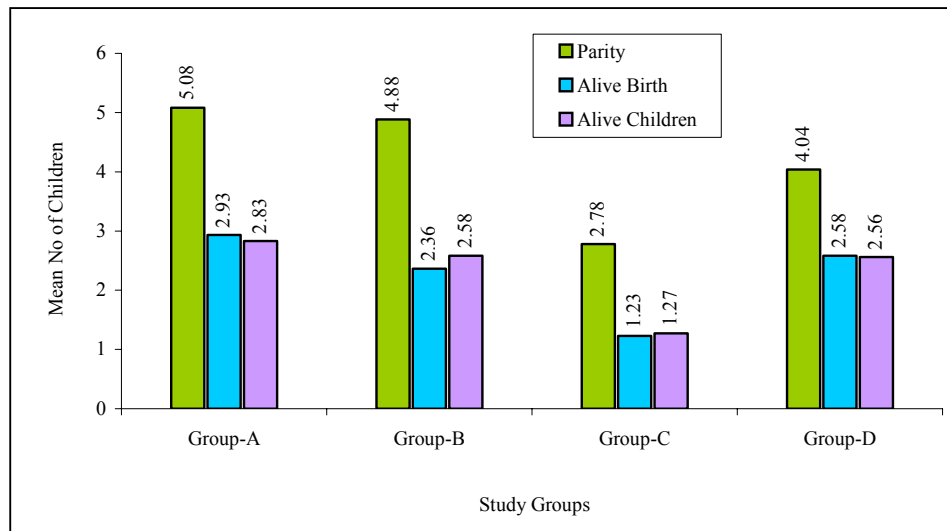


Figure-3.2: Comparison between maternal parity, alive births and alive children among the study groups.

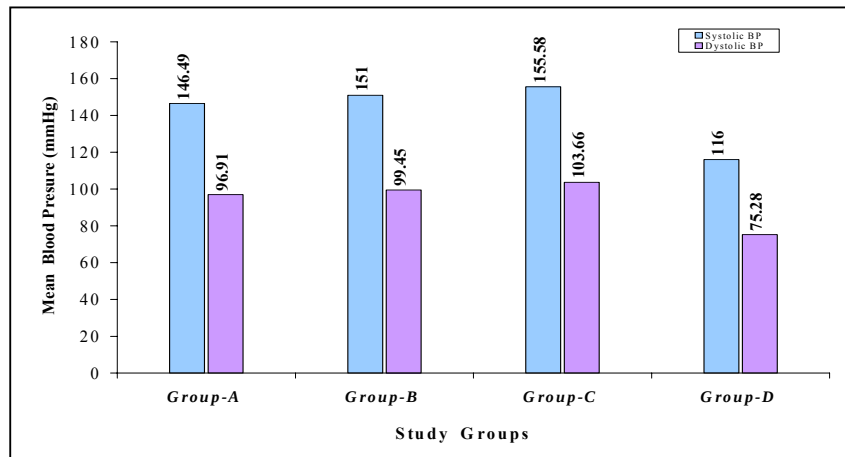


Figure-3.3: Comparison between maternal systolic and diastolic blood pressure among the study groups.

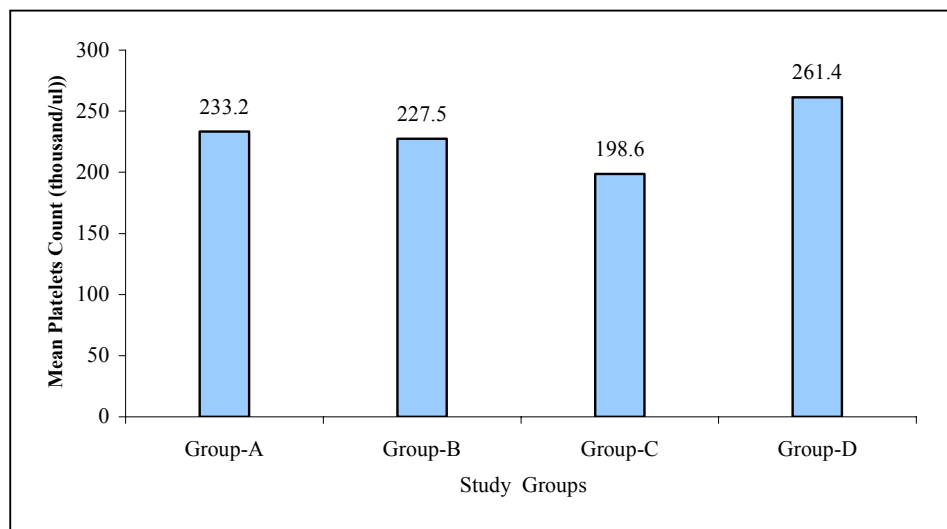


Figure 3.4: Comparison between platelet counts among the four study groups.

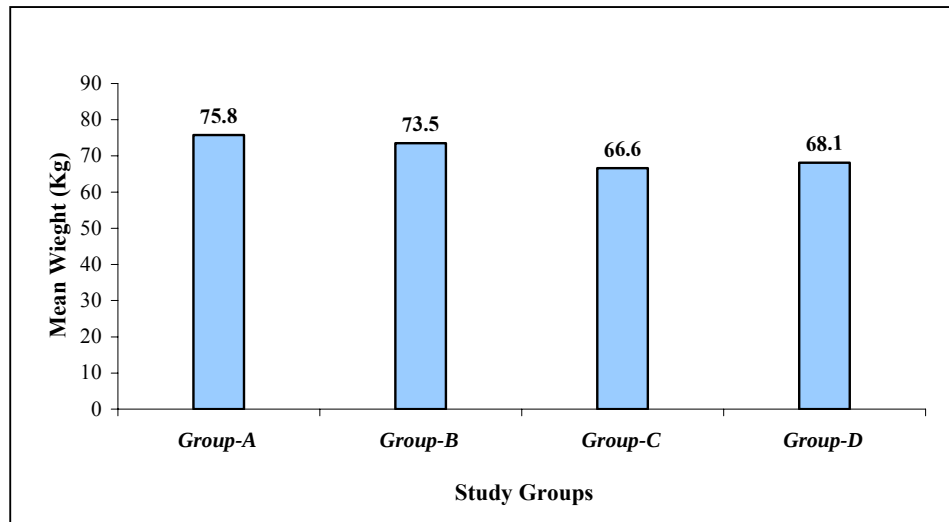


Figure-3.5: Comparison between maternal weights among the four study groups.

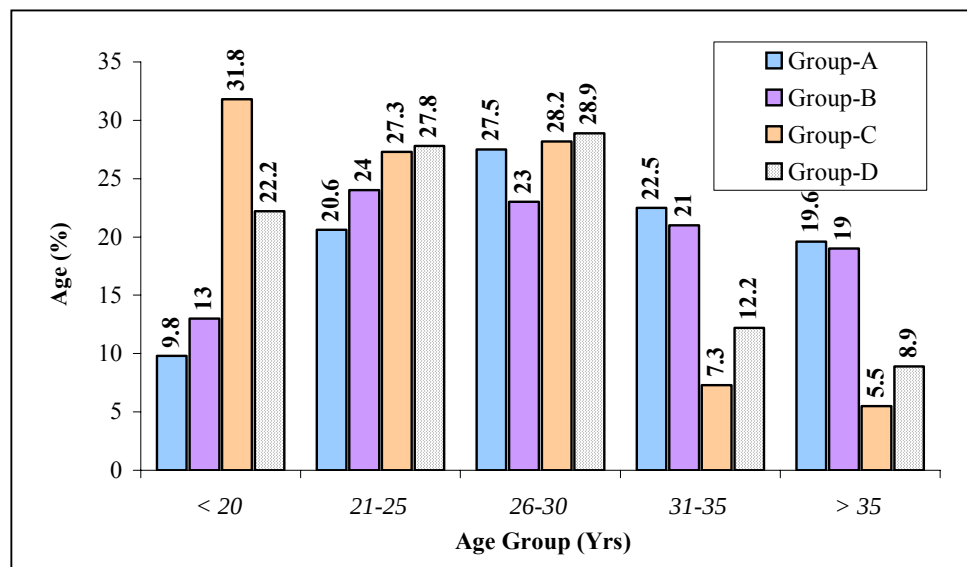


Figure-3.6: Comparison of age distribution among the pregnant women of four study groups.

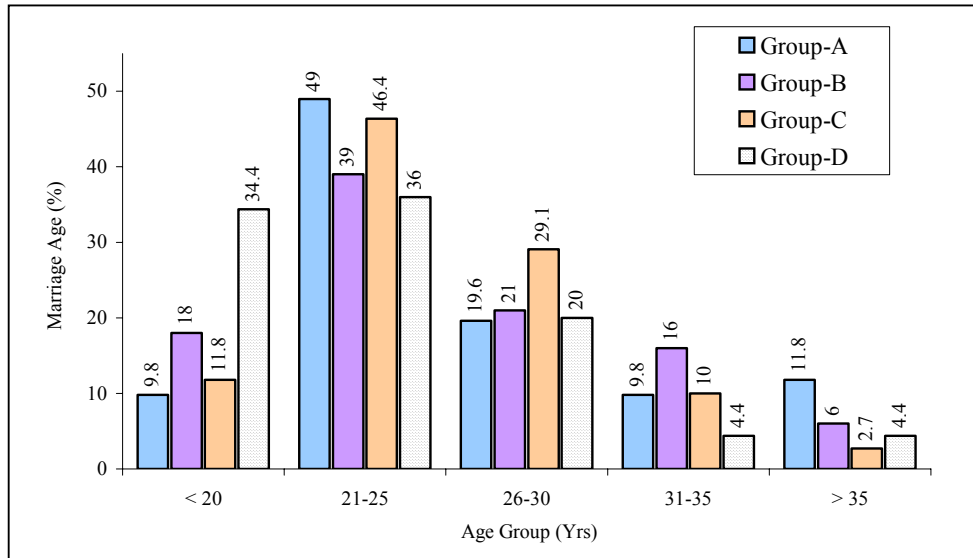


Figure-3.7: Distribution of marriage age among the pregnant women of four study groups.

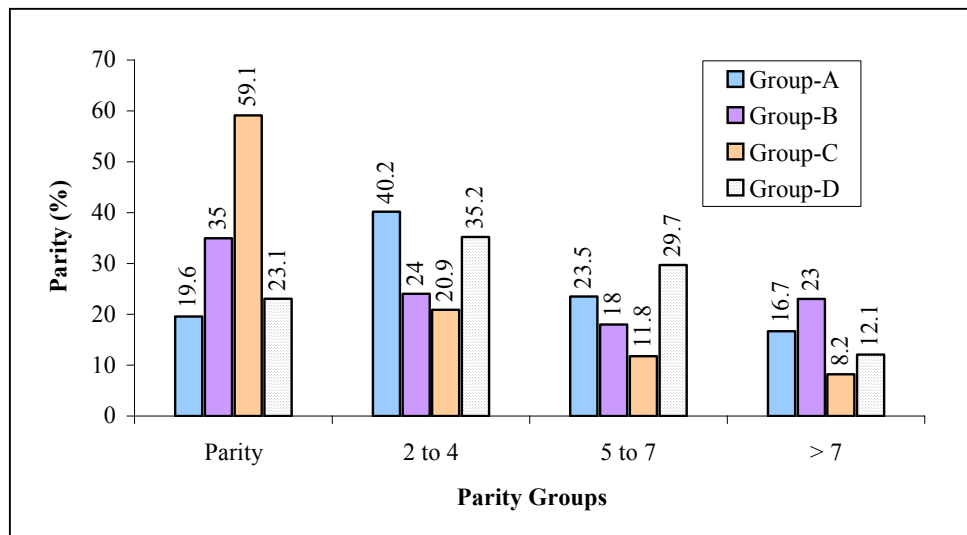


Figure-3.8: Distribution of parity among the pregnant women of four study groups

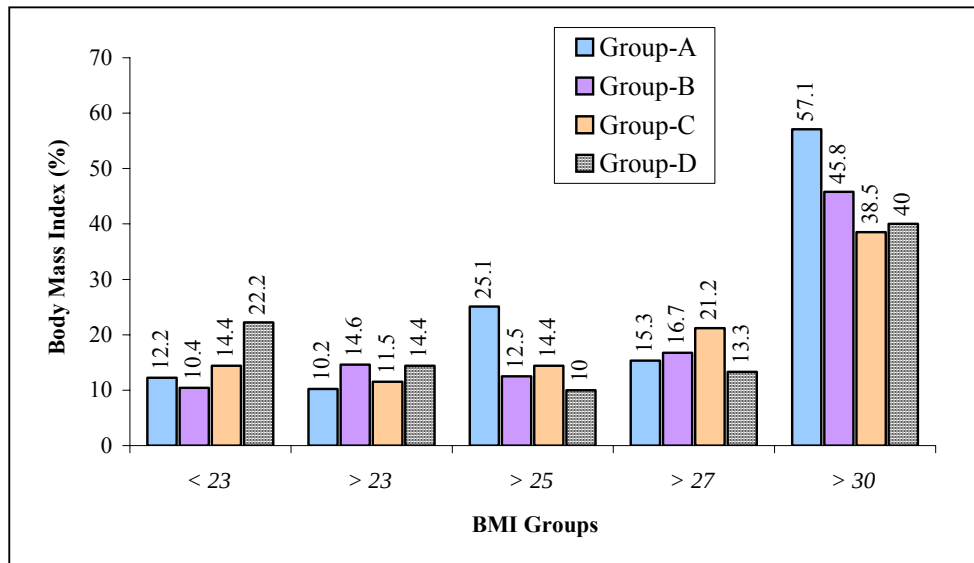


Figure-3.9: Distribution of Body Mass Index among the pregnant women of four study groups.

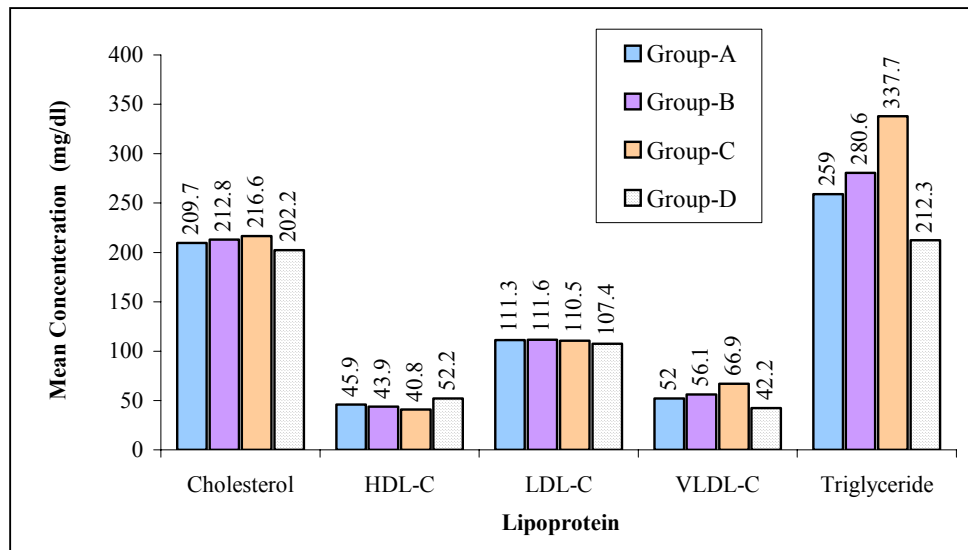


Figure-3.10: Comparison between mean lipoprotein concentrations among the pregnant women of four study groups.

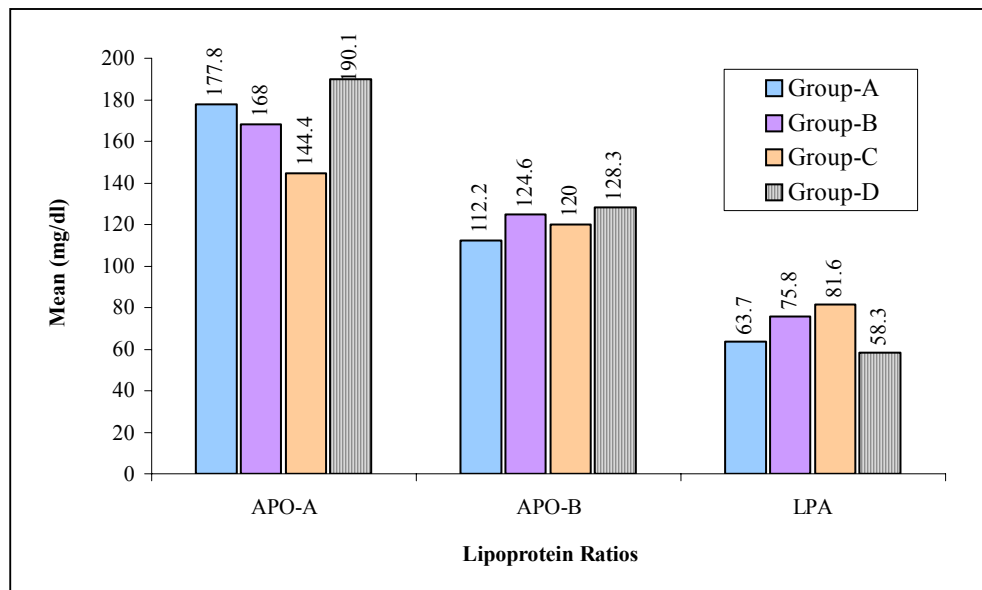


Figure-3.11: Comparison between mean Apo-lipoproteins and lipoprotein-a concentration among the pregnant women of four study groups

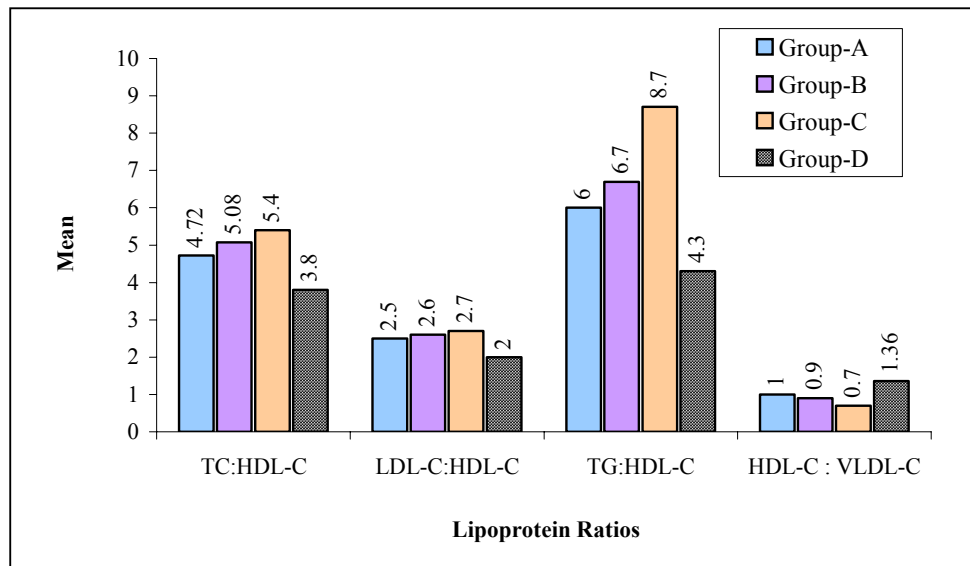


Figure-3.12: Comparison between mean Lipoprotein ratio among the pregnant women of four study groups

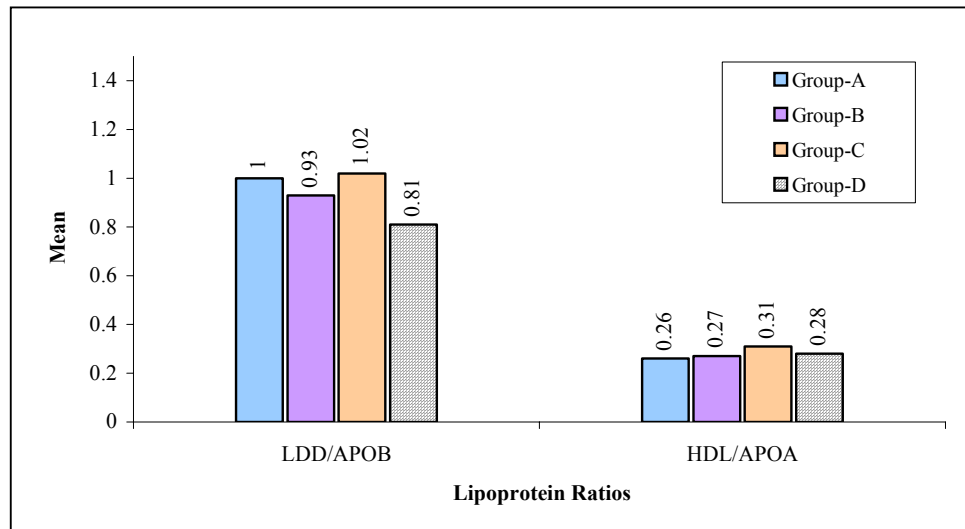


Figure-3.13: Comparison between mean Apo Lipoproteins ratio among the pregnant women of four study groups

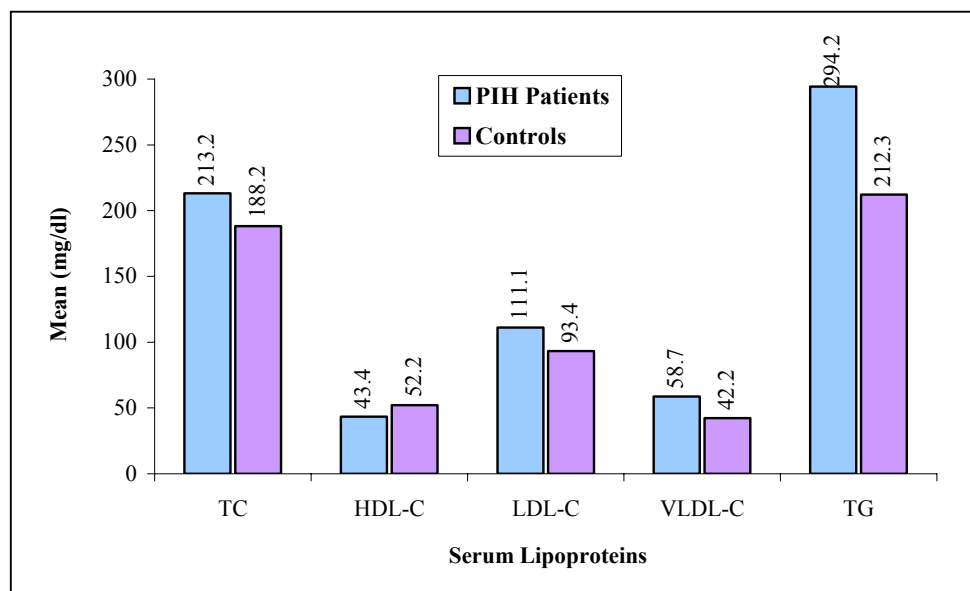


Figure-3.14: Comparison between mean lipoprotein concentrations among the PIH women and healthy pregnant women without hypertension.

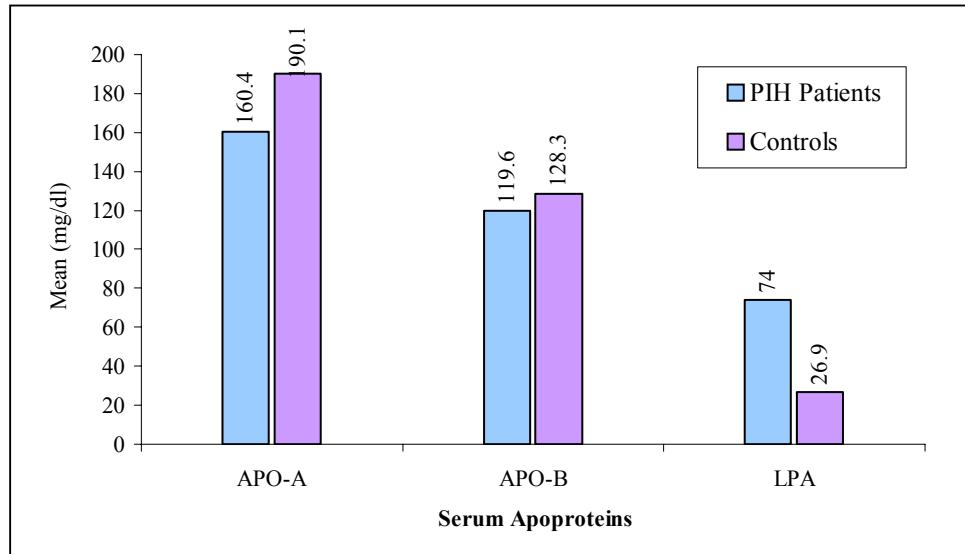


Figure-3.15: Comparison between mean Apo-lipoproteins and lipoprotein-a concentration among the PIH women and healthy pregnant women without hypertension.

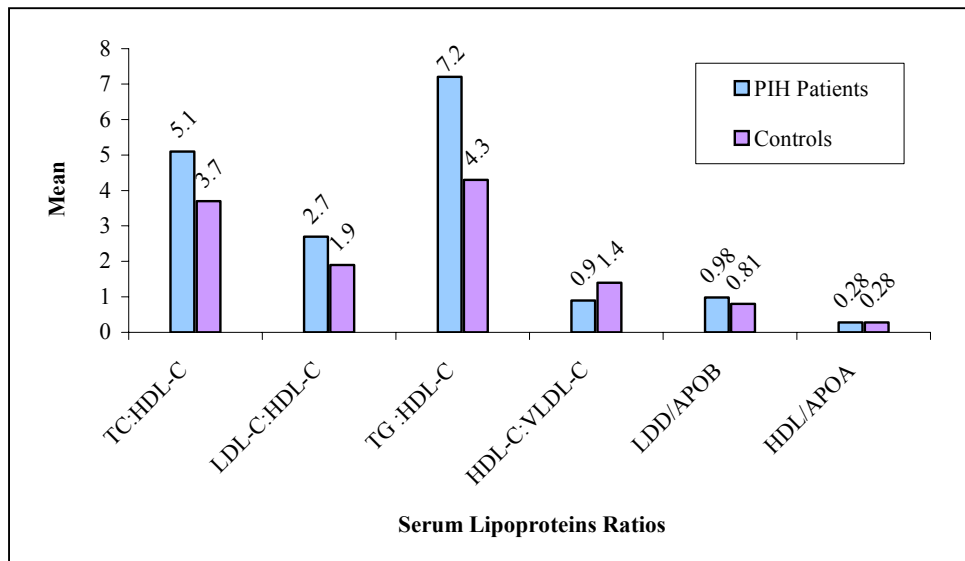


Figure-3.16: Comparison between mean lipoprotein ratio among the PIH and healthy pregnant women without hypertension.

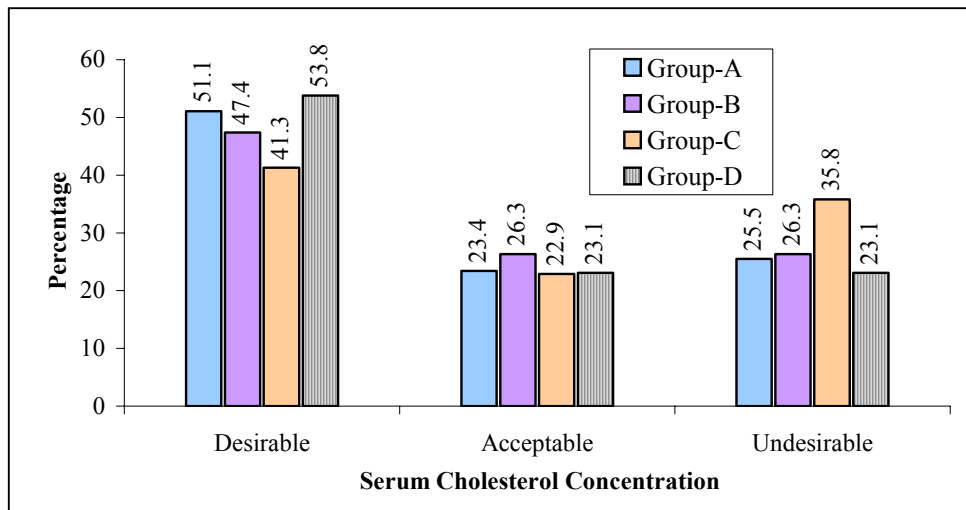


Figure-3.17: Serum Cholesterol concentrations as desirable, acceptable and undesirable among the four study groups of patients and control.

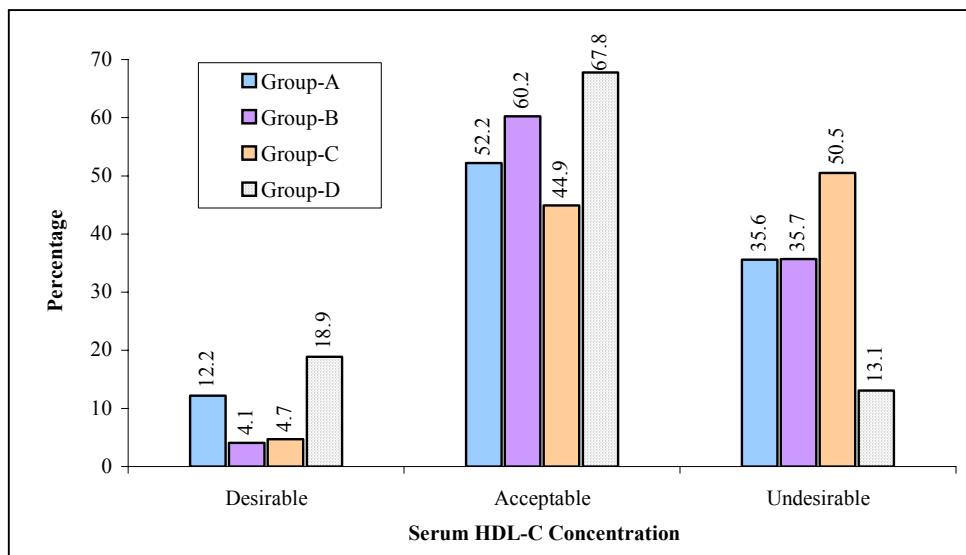


Figure-3.18: Serum high density lipoprotein concentrations as desirable, acceptable and undesirable among the four study groups of patients and control.

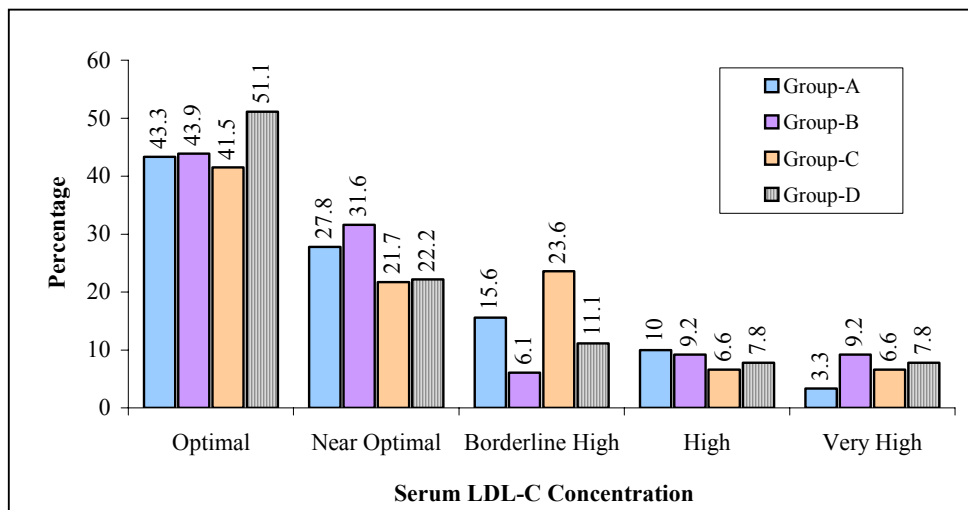


Figure-3.19: Serum low density lipoprotein concentrations among the four study groups of patients and control.

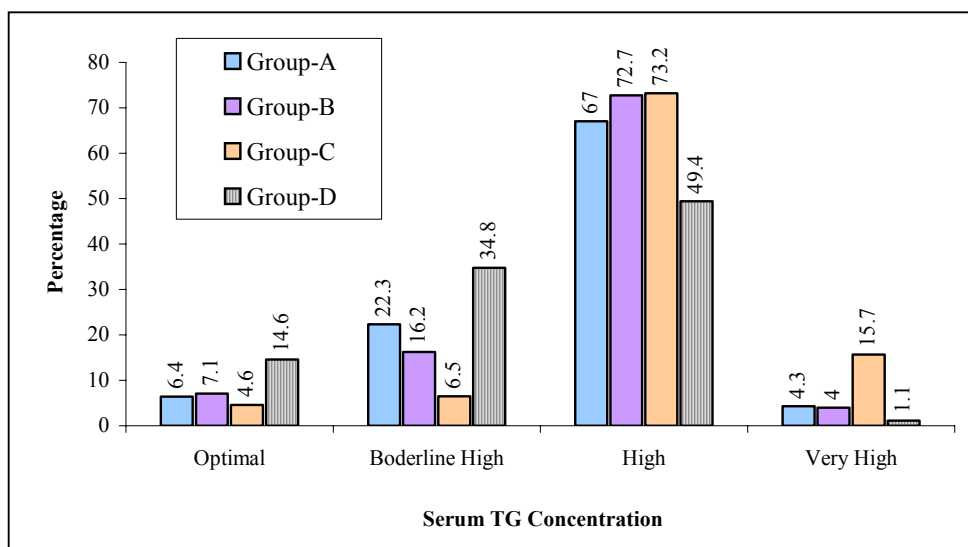


Figure-3.20: Serum triglyceride concentrations as optimal, borderline high, high and very high among the four study groups of patients and control.

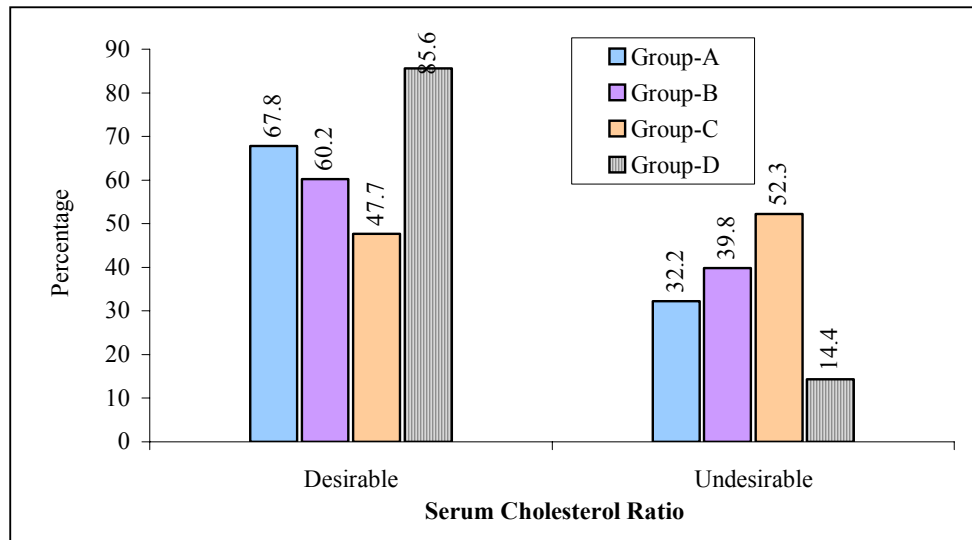


Figure-3.21: Serum cholesterol ratio as desirable and undesirable among the four study groups of patients and control.

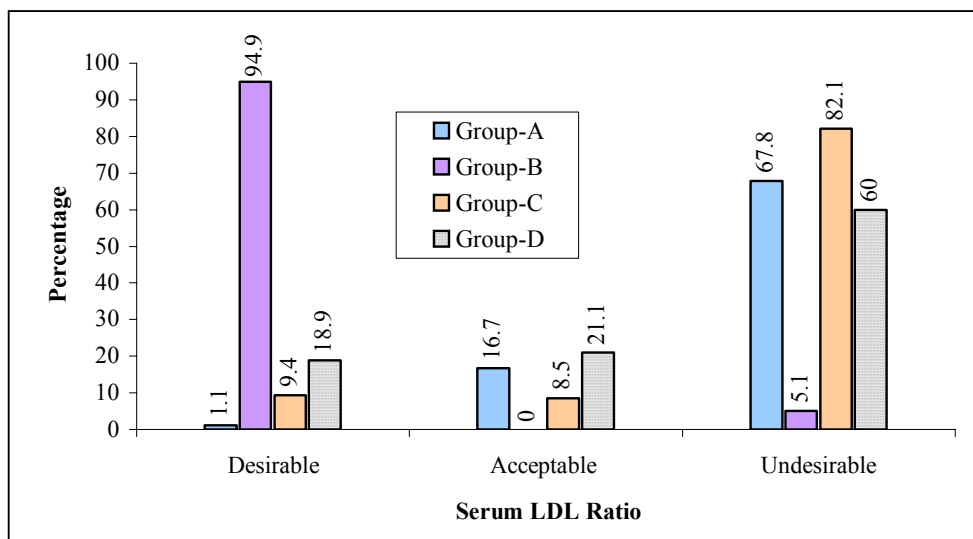


Figure-3.22: Serum low density lipoprotein ratio as desirable, acceptable and undesirable among the four study groups of patients and control.

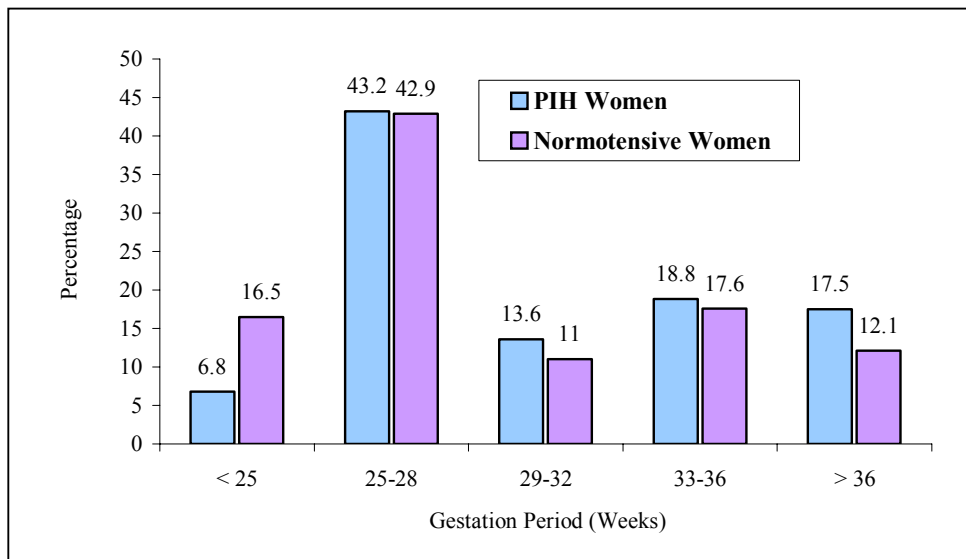


Figure-3.23: Comparison of gestation age in women with pregnancy induced hypertension and healthy pregnant women without hypertension.

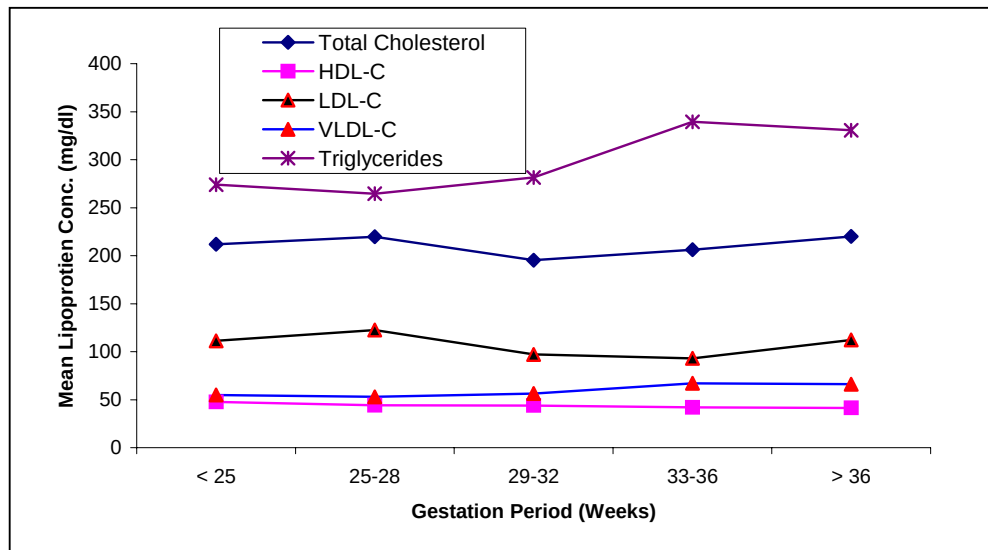


Figure-3.24: Changes in lipoprotein concentration at different gestational weeks of women with pregnancy induced hypertension.

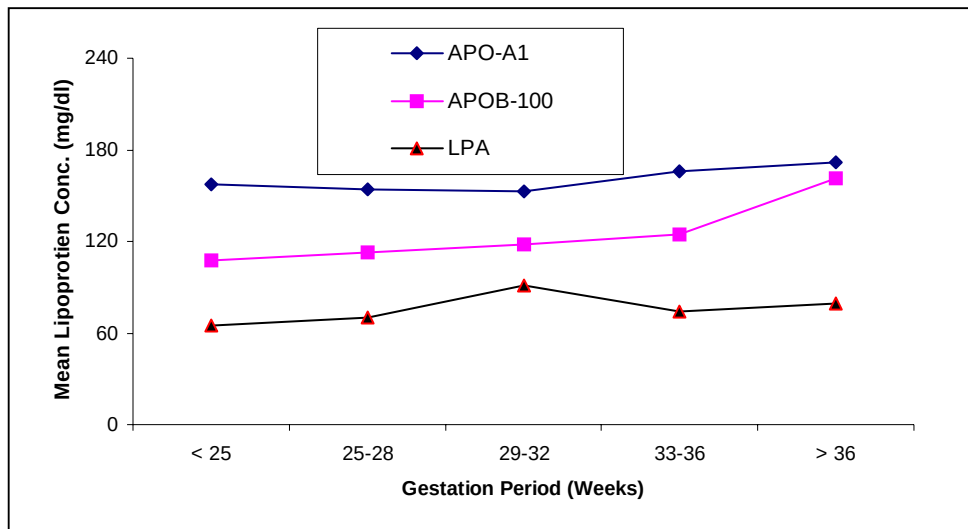


Figure-3.25: Changes in Apo-lipoproteins and lipoprotein-a concentration at different gestational weeks of women with pregnancy induced hypertension.

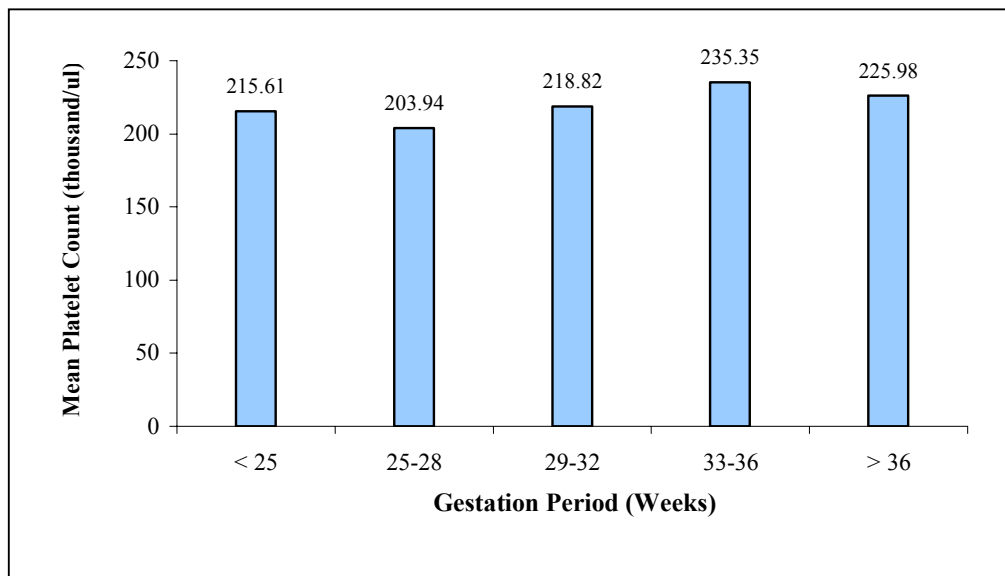


Figure-3.26: Changes in mean platelet count at different gestational weeks of women with pregnancy induced hypertension.

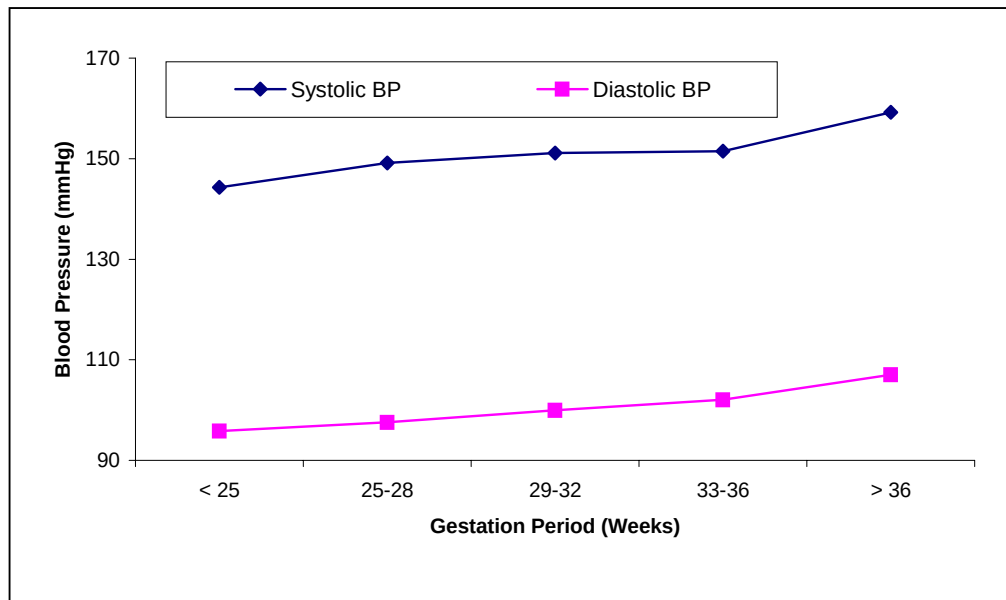


Figure-3.27: Changes in systolic and diastolic blood pressure at different gestational weeks of women with pregnancy induced hypertension.

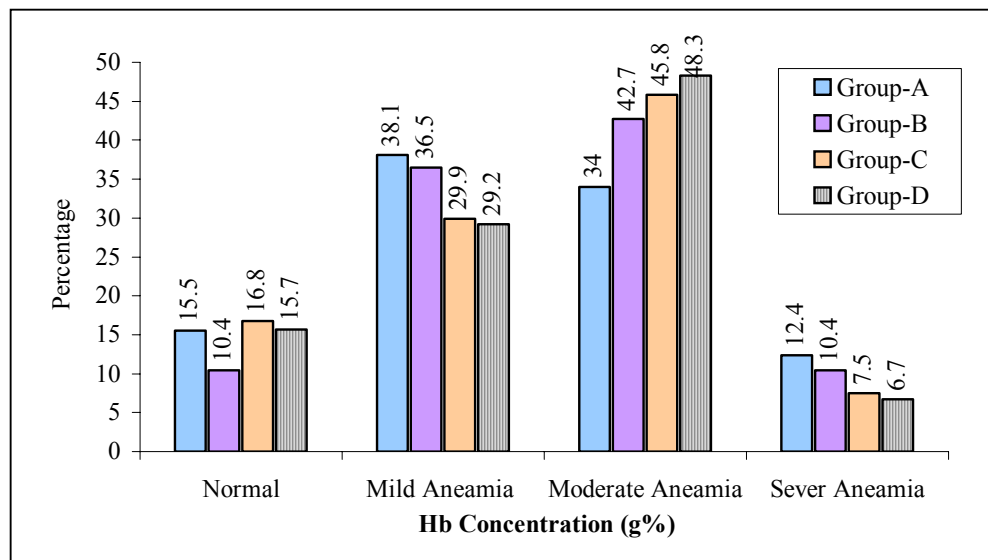


Figure-3.28: Comparison of normal, mild, moderate and severe anemia among the four study groups of patients and control.

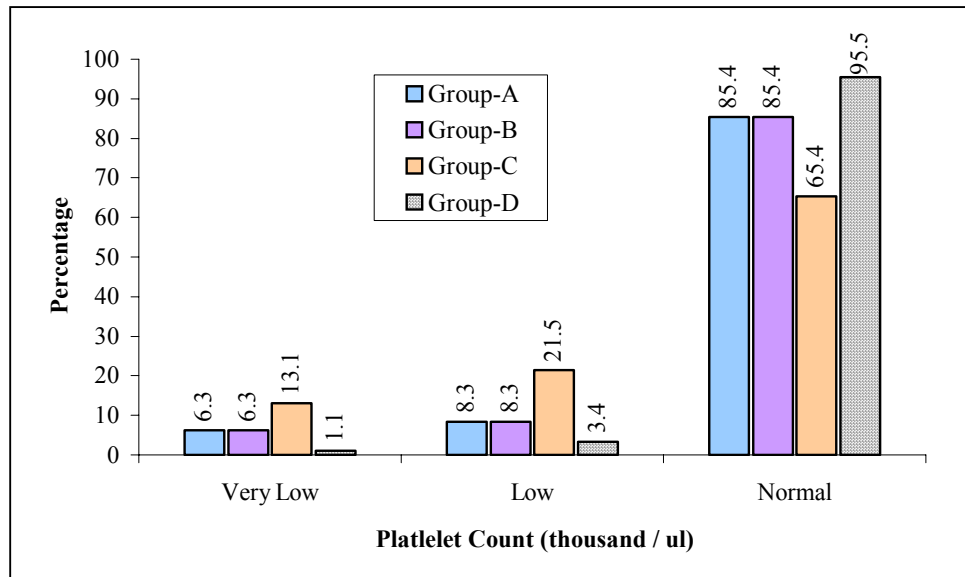


Figure-3.29: Comparison of normal, low and very low platelet count among the four study groups of patients and control.

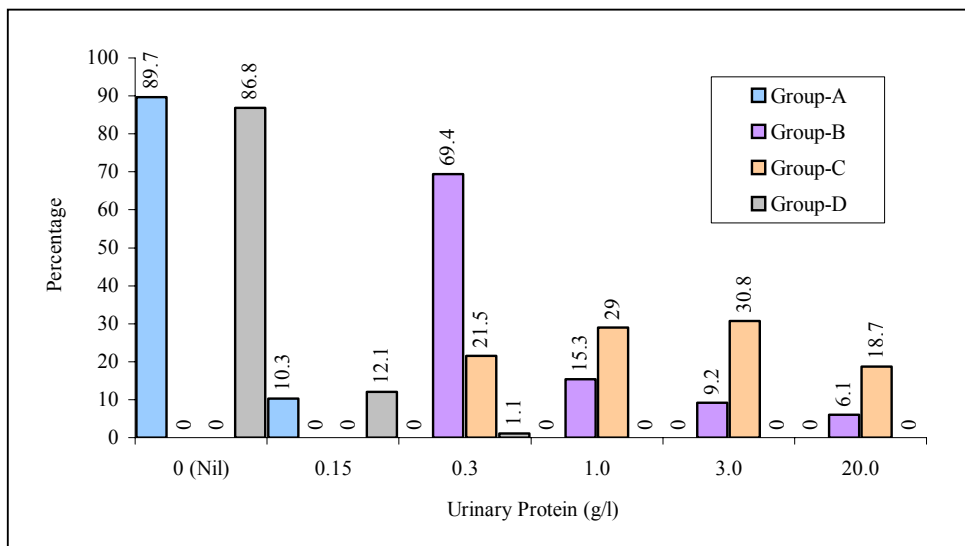


Figure-3.30: Comparison of urinary proteins as nil, traces, +1, +2, +3 and +4 among the four study groups of patients and control.

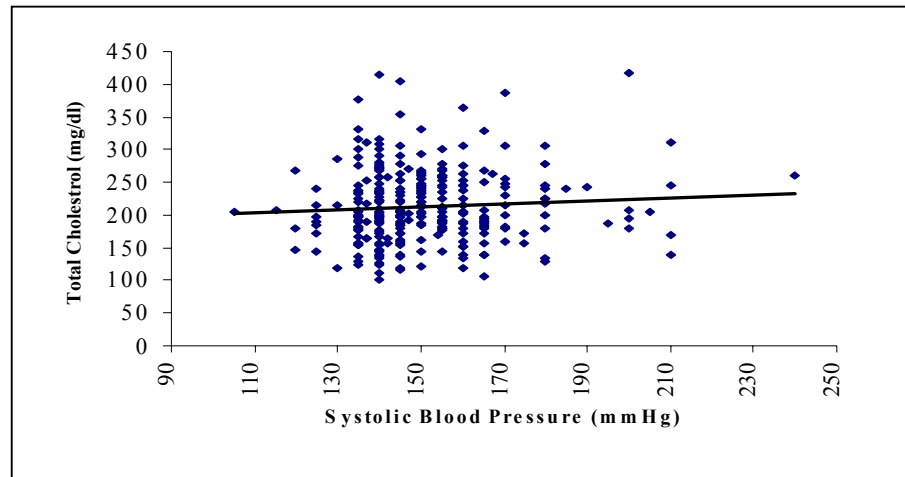


Figure-3.31: Correlation between total cholesterol and systolic blood pressure in the patients of Pregnancy Induced Hypertension

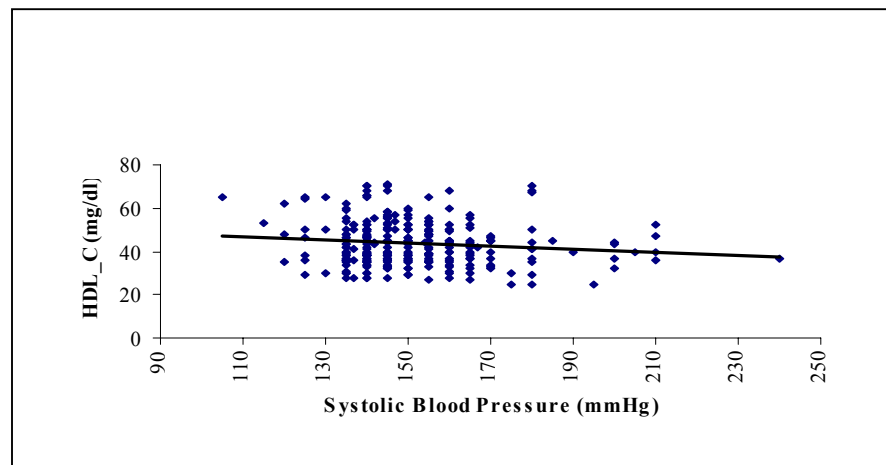


Figure-3.32: Correlation between HDL-C and systolic blood pressure in the patients of Pregnancy Induced Hypertension.

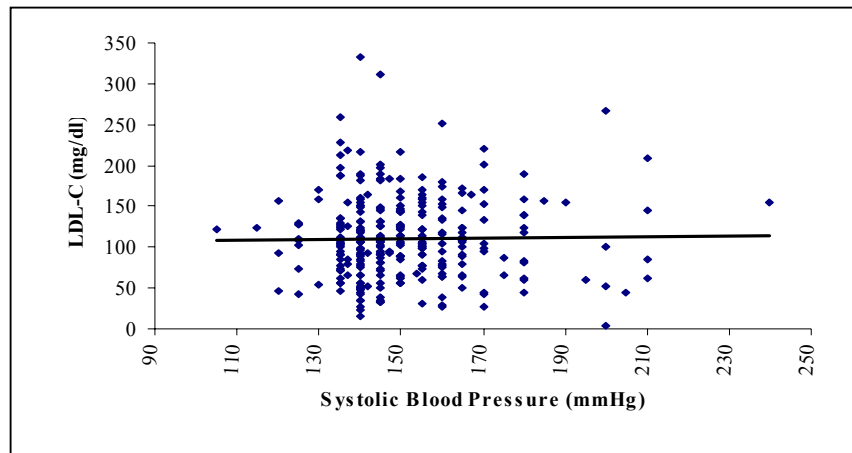


Figure-3.33: Correlation between LDL-C and systolic blood pressure in the patients of Pregnancy Induced Hypertension

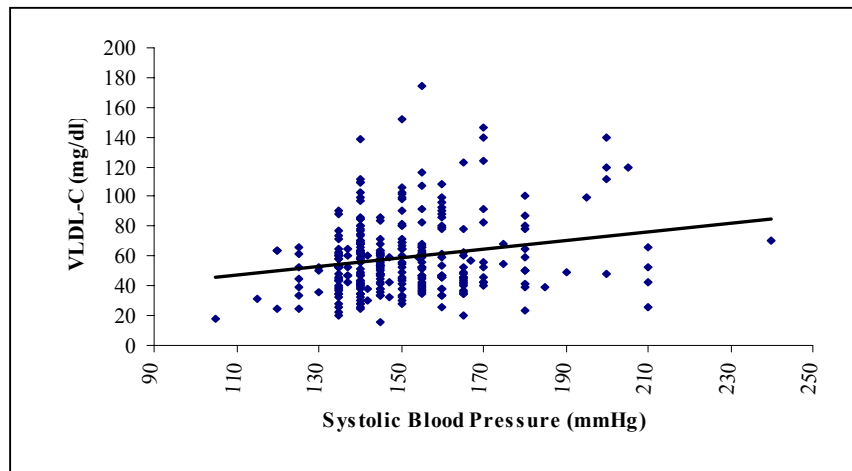


Figure-3.34: Correlation between Very High Density Lipoprotein cholesterol and systolic blood pressure in the patients of Pregnancy Induced Hypertension.

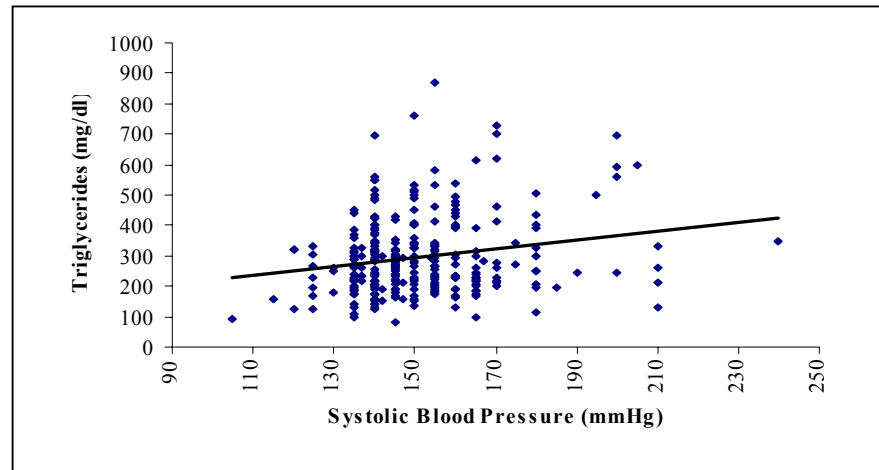


Figure-3.35: Correlation between Triglycerides and systolic blood pressure in the patients of Pregnancy Induced Hypertension.

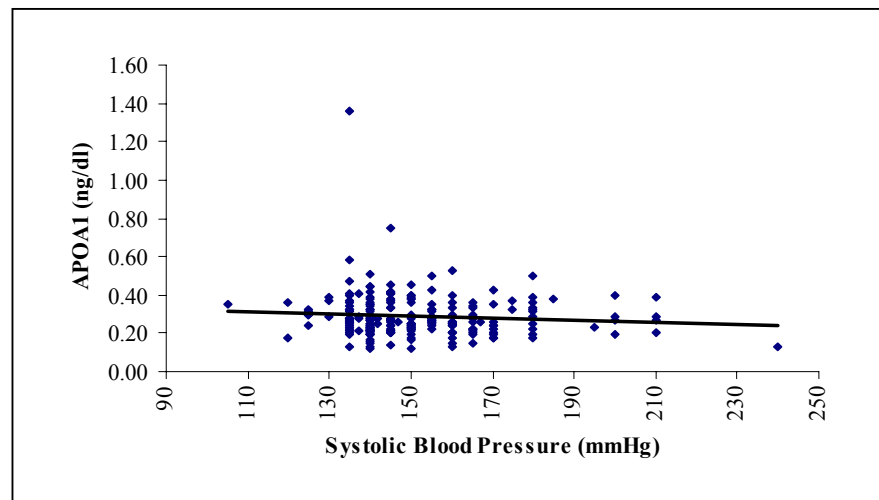


Figure-3.36: Correlation between APO-A1 and systolic blood pressure in the patients of Pregnancy Induced Hypertension.

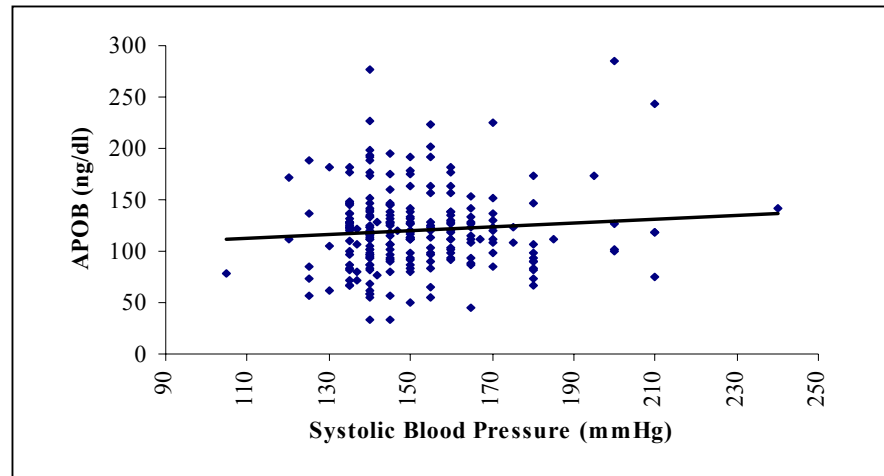


Figure-3.37: Correlation between APOB and systolic blood pressure in the patients of Pregnancy Induced Hypertension.

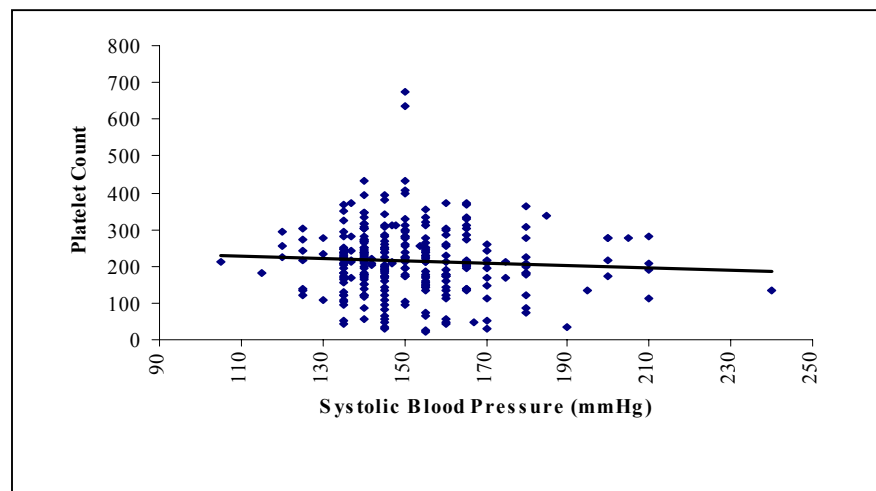


Figure-3.38: Correlation between platelet count and systolic blood pressure in the patients of Pregnancy Induced Hypertension.

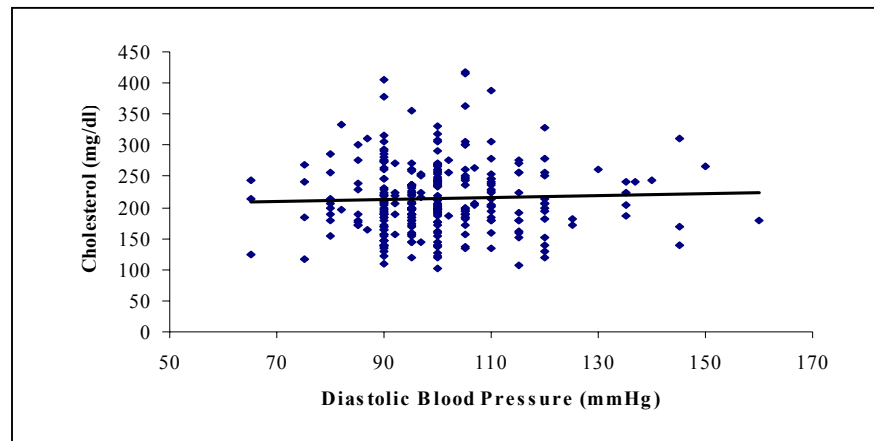


Figure-3.39: Correlation between cholesterol and diastolic blood pressure in the patients of Pregnancy Induced Hypertension.

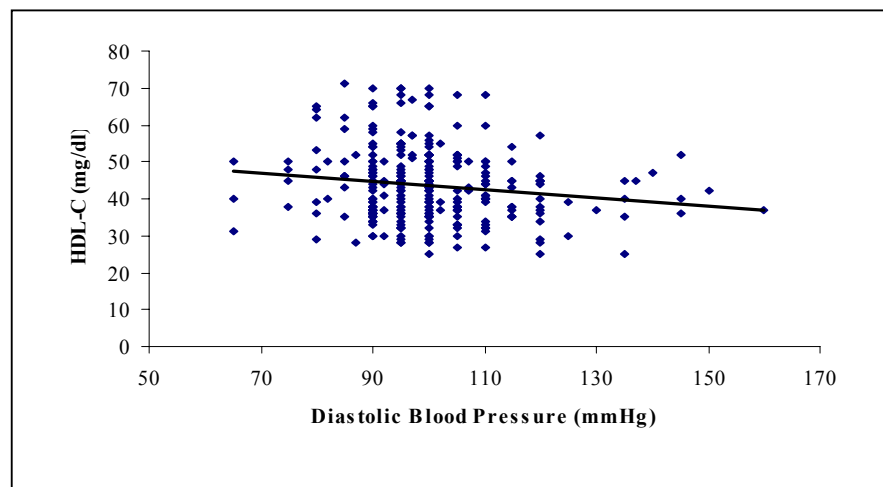


Figure-3.40: Correlation between HDL-C and diastolic blood pressure in the patients of Pregnancy Induced Hypertension.

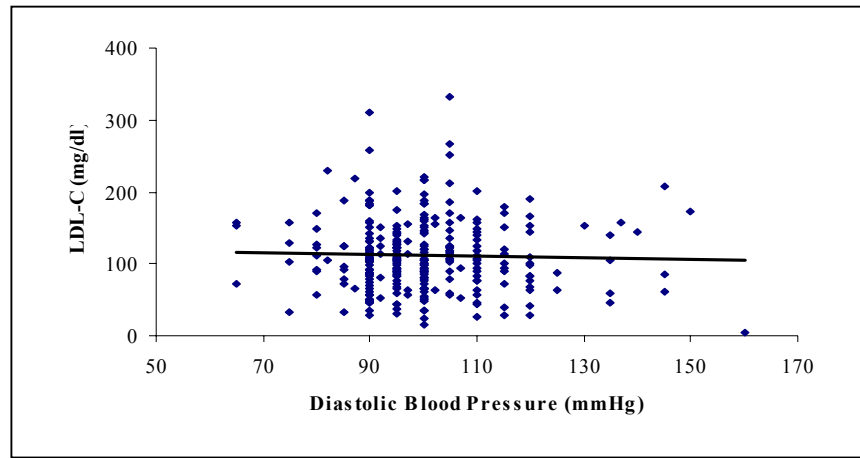


Figure-3.41: Correlation between LDL-C and diastolic blood pressure in the patients of Pregnancy Induced Hypertension.

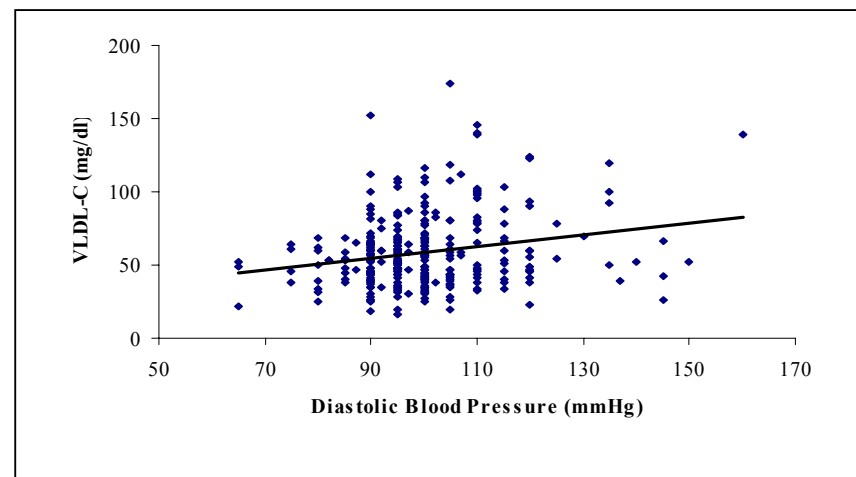


Figure-3.42: Correlation between VLDL-C and diastolic blood pressure in the patients of Pregnancy Induced Hypertension.

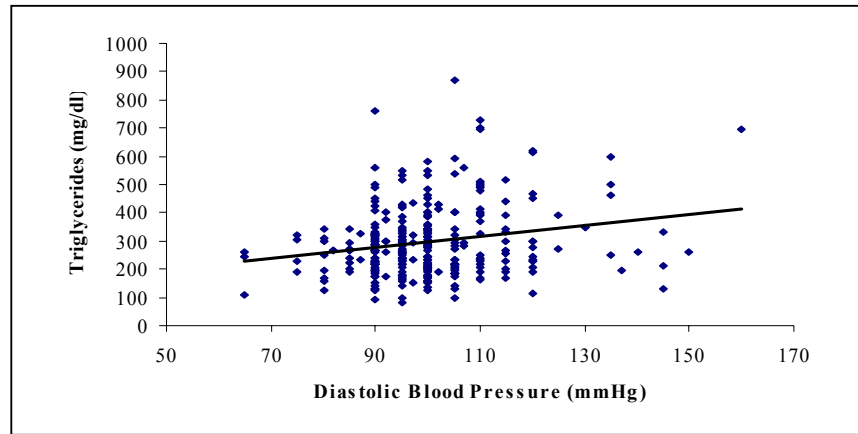


Figure-3.43: Correlation between triglycerides and diastolic blood pressure in the patients of Pregnancy Induced Hypertension.

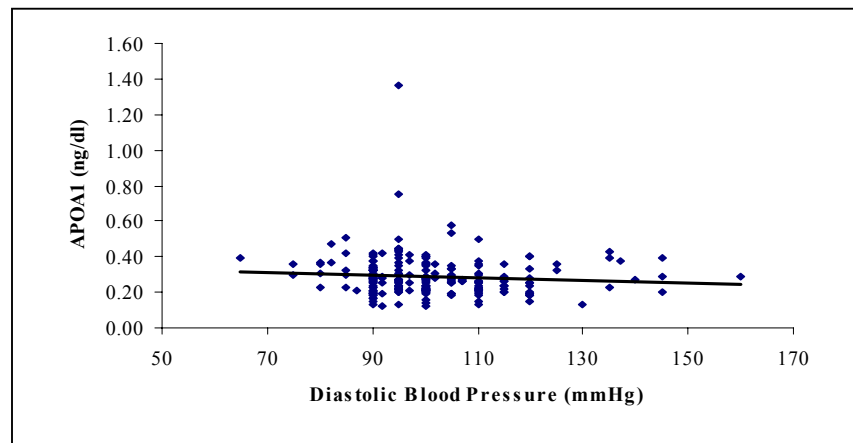


Figure-3.44: Correlation between APOA1 and diastolic blood pressure in the patients of Pregnancy Induced Hypertension.

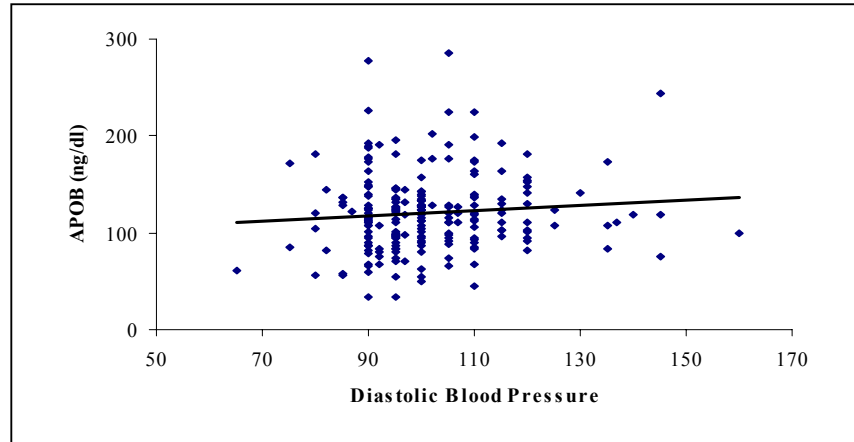


Figure-3.45: Correlation between APOB and diastolic blood pressure in the patients of Pregnancy Induced Hypertension.

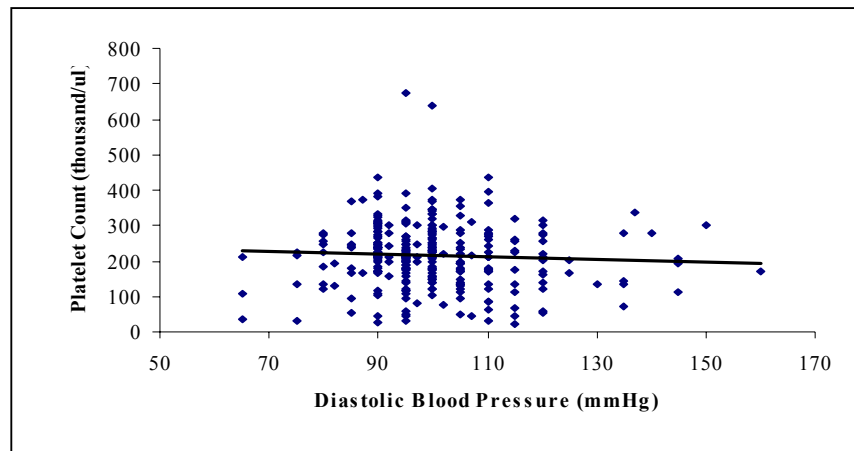


Figure-3.46: Correlation between platelet count and diastolic blood pressure in the patients of Pregnancy Induced Hypertension.

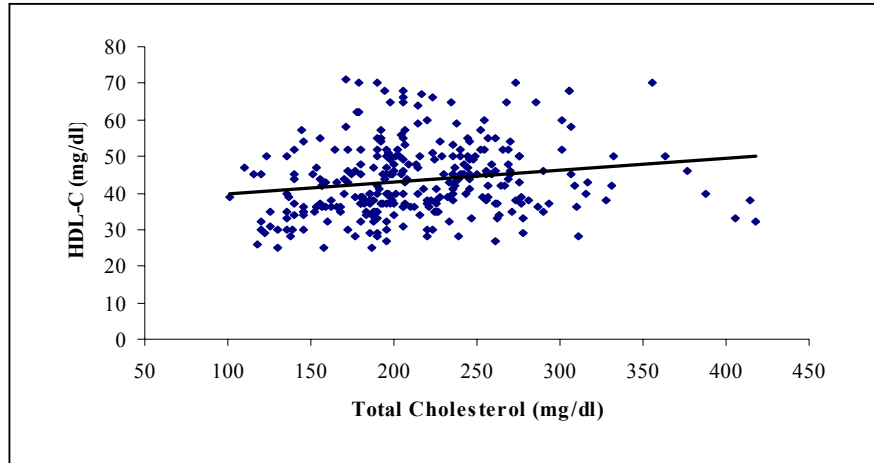


Figure-3.47: Correlation between HDL-C and Total cholesterol in the patients of Pregnancy Induced Hypertension.

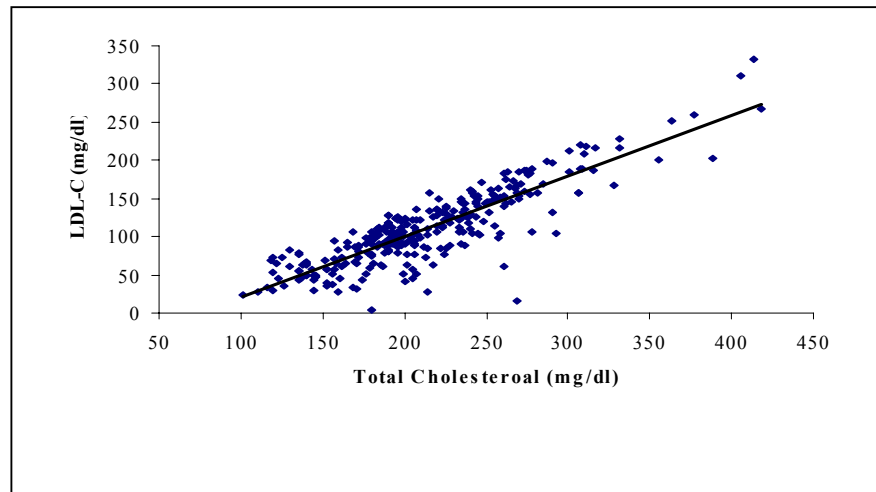


Figure-3.48: Correlation between LDL-C and Total Cholesterol in the patients of Pregnancy Induced Hypertension.

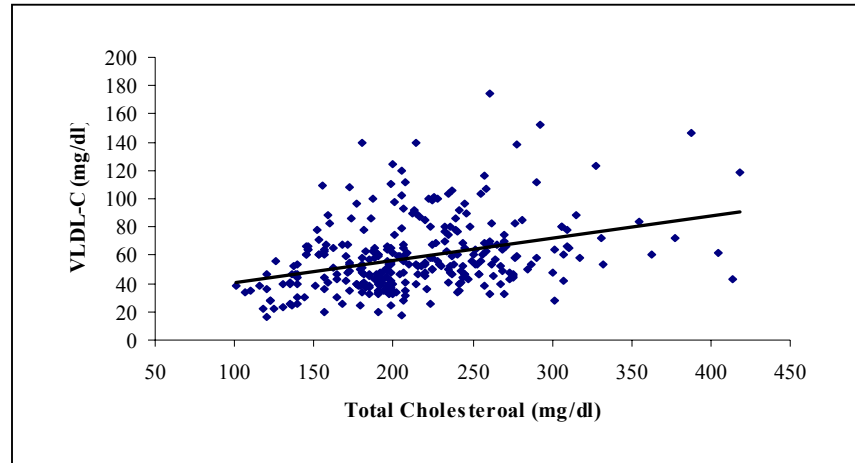


Figure-3.49: Correlation between VLDL-C and Total cholesterol in the patients of Pregnancy Induced Hypertension.

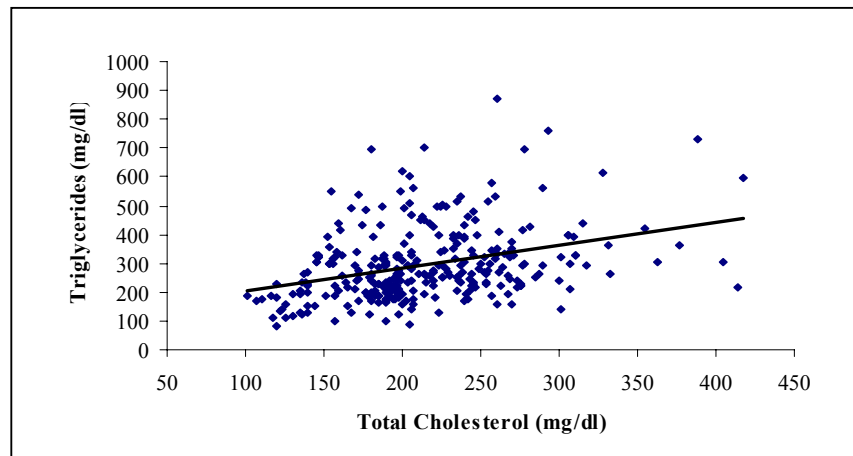


Figure-3.50: Correlation between Triglycerides and Total cholesterol in the patients of Pregnancy Induced Hypertension.

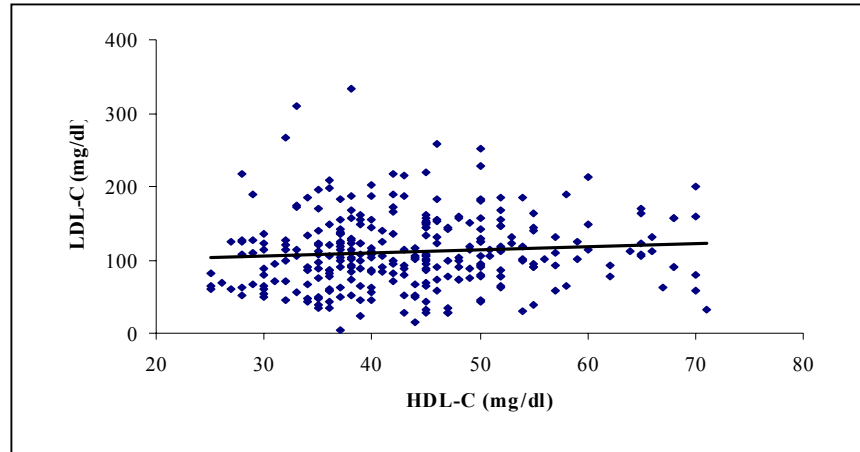


Figure-3.51: Correlation between LDL-C and HDL-C in the patients of Pregnancy Induced Hypertension.

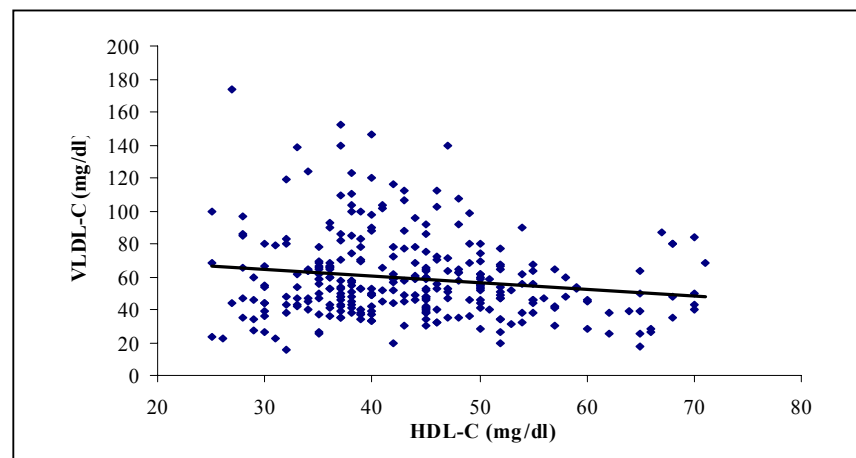


Figure-3.52: Correlation between VLDL-C and HDL-C in the patients of Pregnancy Induced Hypertension.

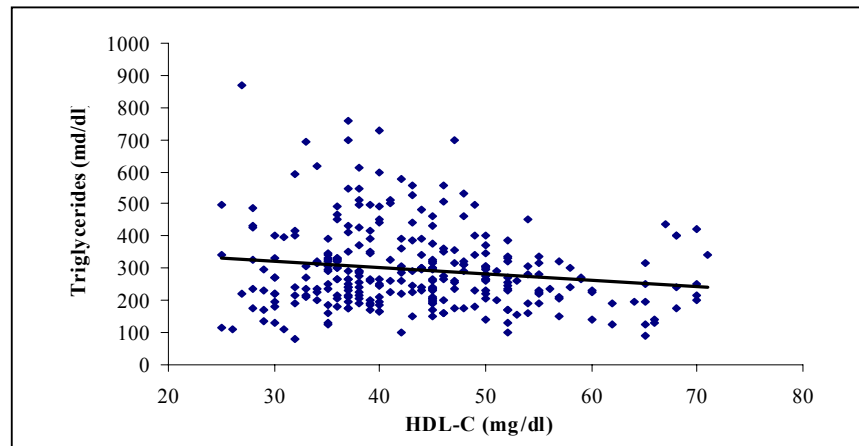


Figure-3.53: Correlation between Triglycerides and HDL-C in the patients of Pregnancy Induced Hypertension.

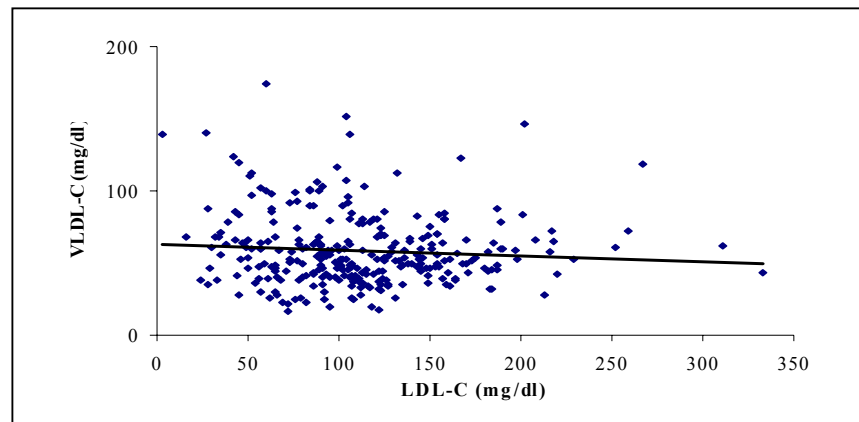


Figure-3.54: Correlation between VLDL-C and LDL-C in the patients of Pregnancy Induced Hypertension.

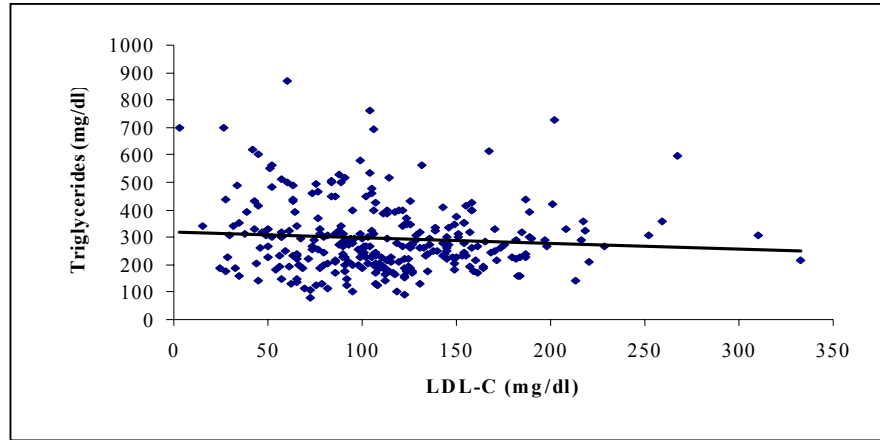


Figure-3.55: Correlation between Triglycerides and LDL-C in the patients of Pregnancy Induced Hypertension.

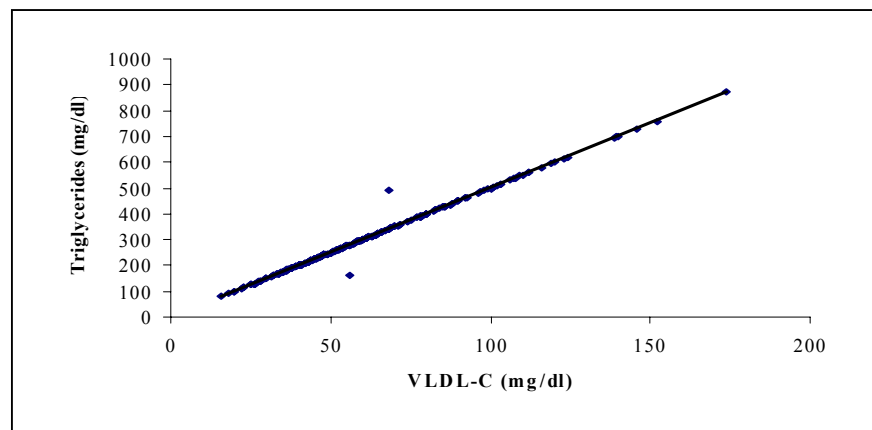


Figure-3.56: Correlation between Triglycerides and VLDL-C in the patients of Pregnancy Induced Hypertension.

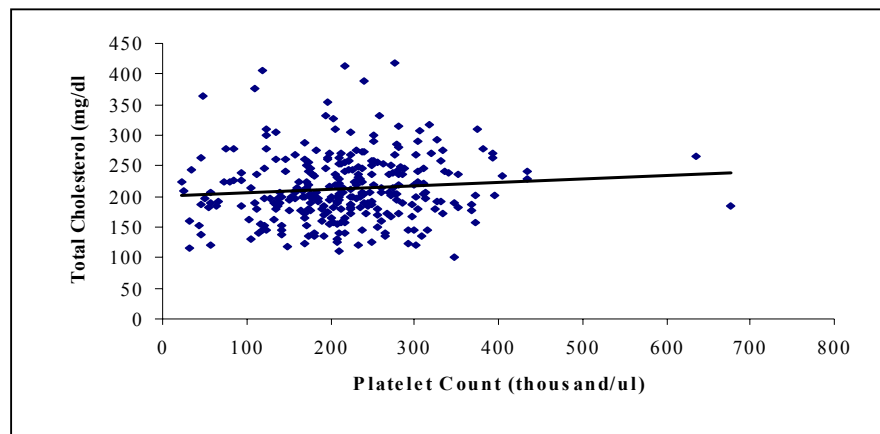


Figure-3.57: Correlation between Triglycerides and Total cholesterol in the patients of Pregnancy Induced Hypertension.

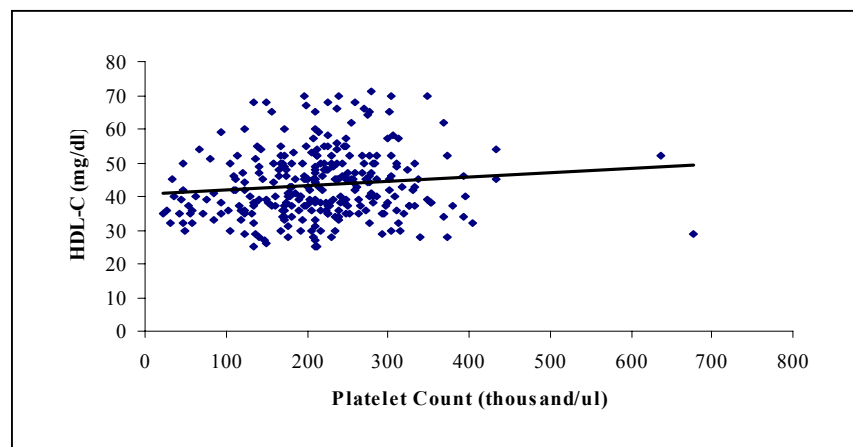


Figure-3.58: Correlation between HDL-C and Platelet count in the patients of Pregnancy Induced Hypertension.

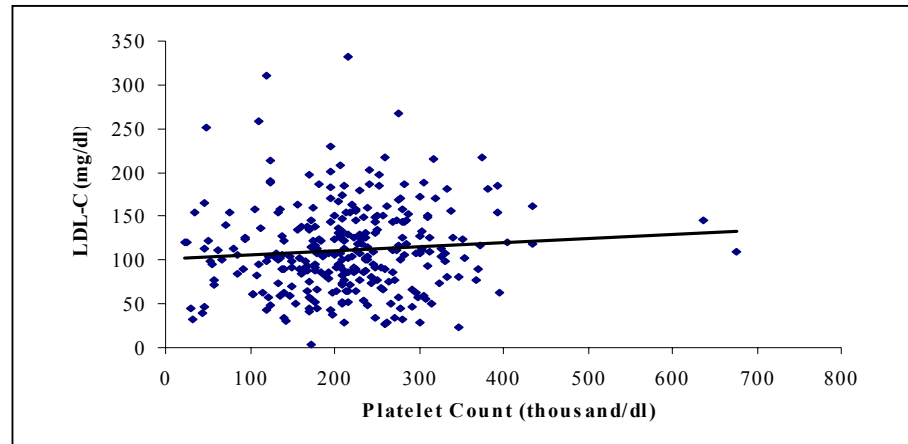


Figure-3.59: Correlation between LDL-C and Platelet count in the patients of Pregnancy Induced Hypertension.

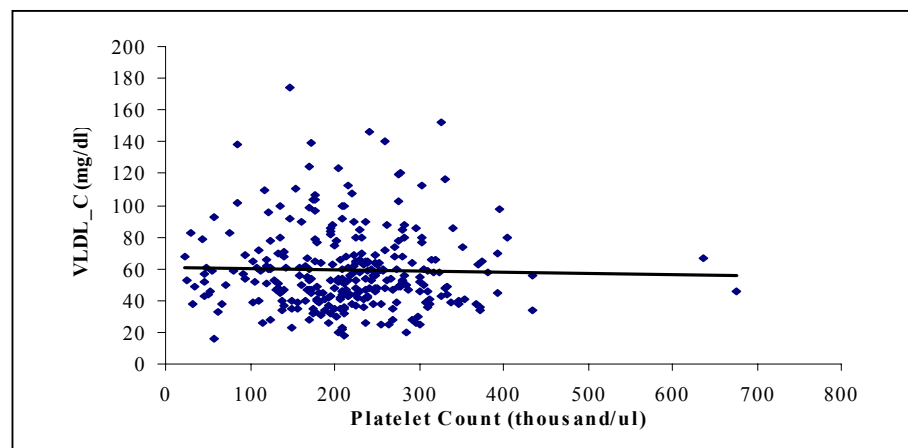


Figure-3.60: Correlation between VLDL-C and Platelet count in the patients of Pregnancy Induced Hypertension.

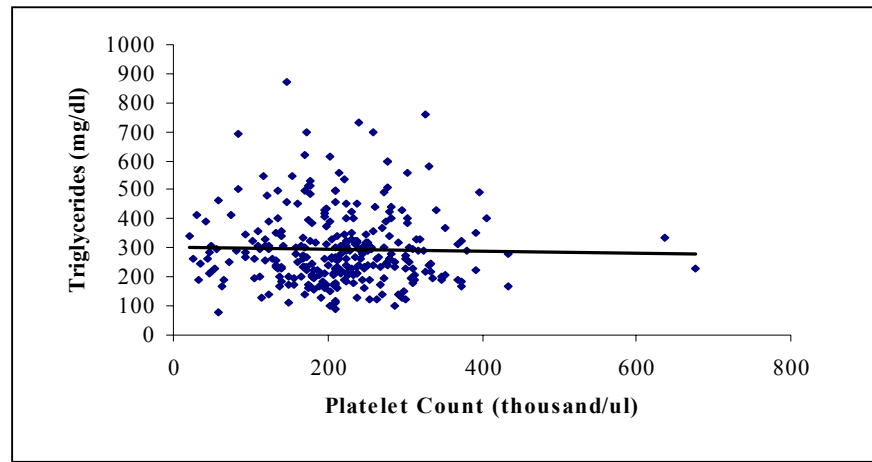


Figure-3.61: Correlation between Triglycerides and Platelet count in the patients of Pregnancy Induced Hypertension.

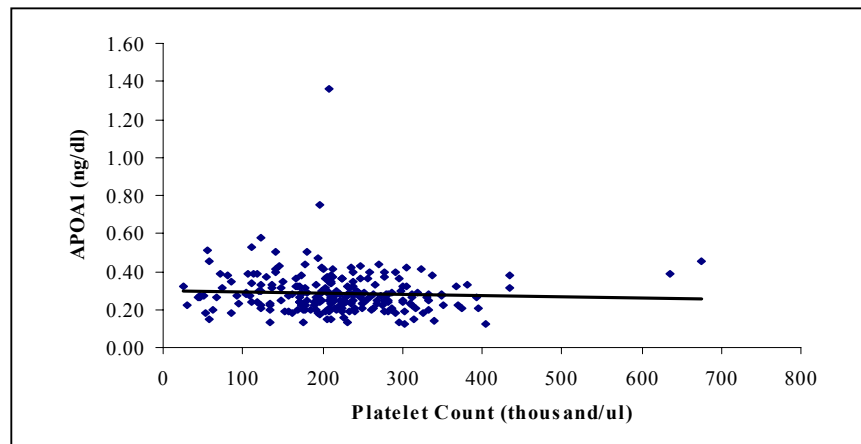


Figure-3.62: Correlation between APOA1 and Platelet count in the patients of Pregnancy Induced Hypertension.

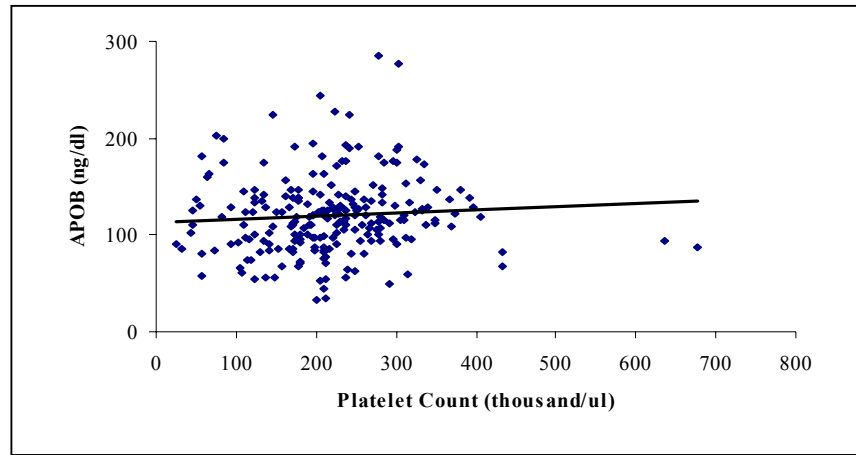


Figure-3.63: Correlation between APOB and Platelet count in the patients of Pregnancy Induced Hypertension.

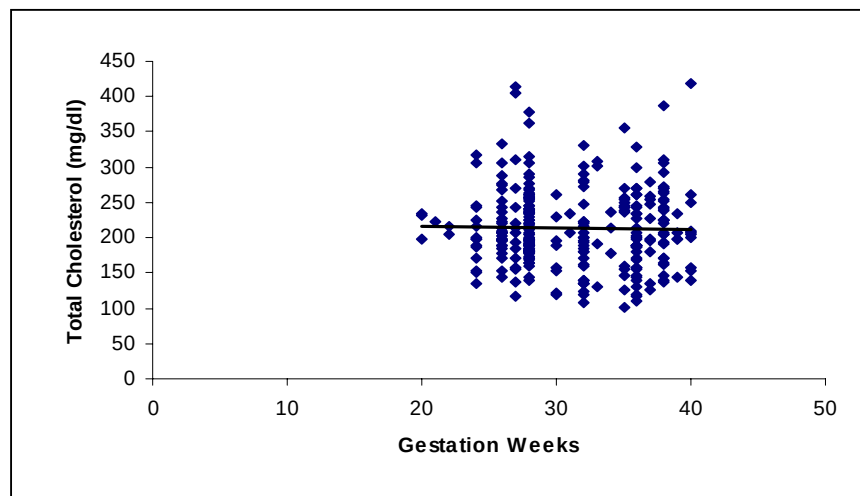


Figure-3.64: Correlation between Gestation weeks and total cholesterol concentration in the patients of Pregnancy Induced Hypertension.

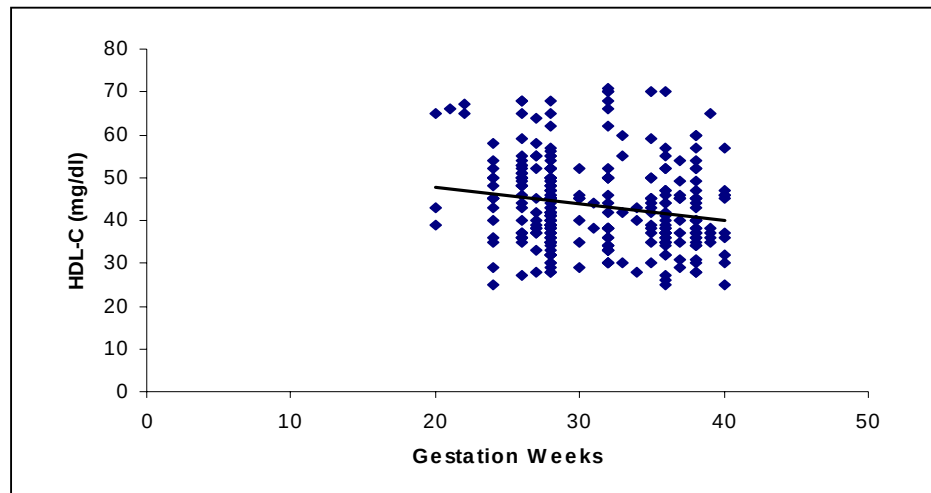


Figure-3.65: Correlation between Gestation weeks and HDL-C in the patients of Pregnancy Induced Hypertension.

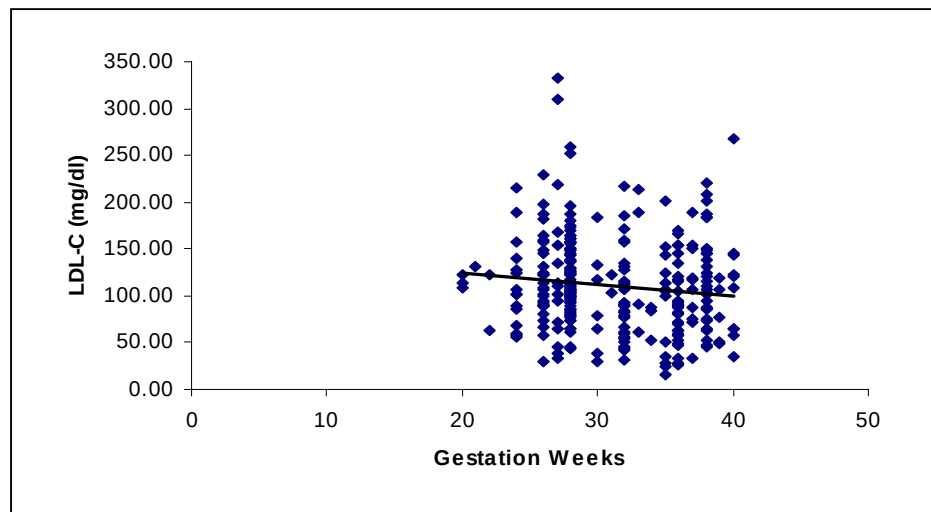


Figure-3.66: Correlation between Gestation weeks and LDL-C in the patients of Pregnancy Induced Hypertension.

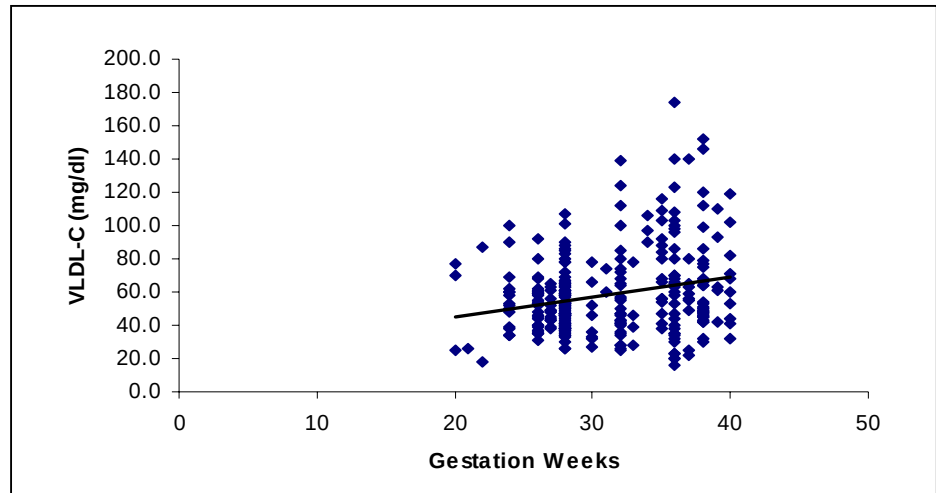


Figure-3.67: Correlation between Gestation weeks and VLDL-C in the patients of Pregnancy Induced Hypertension.

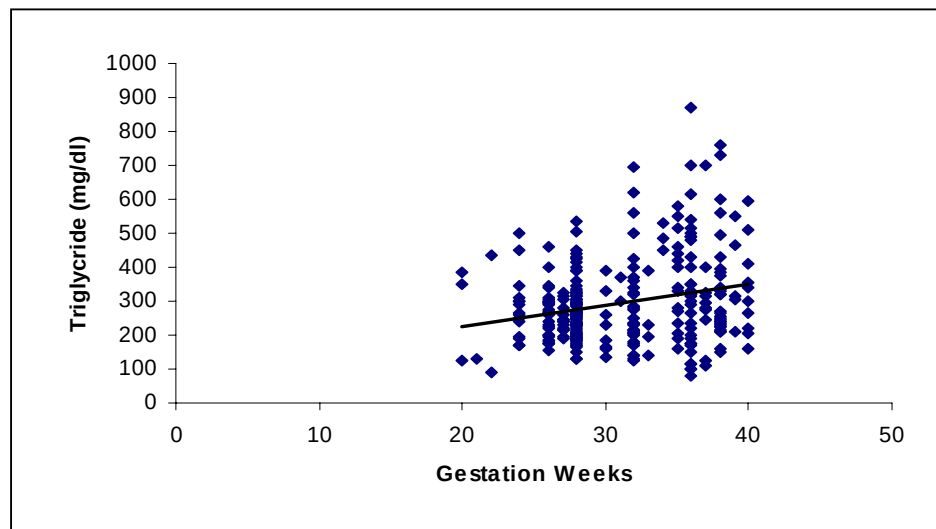


Figure-3.68: Correlation between Gestation weeks and Triglycerides in the patients of Pregnancy Induced Hypertension.

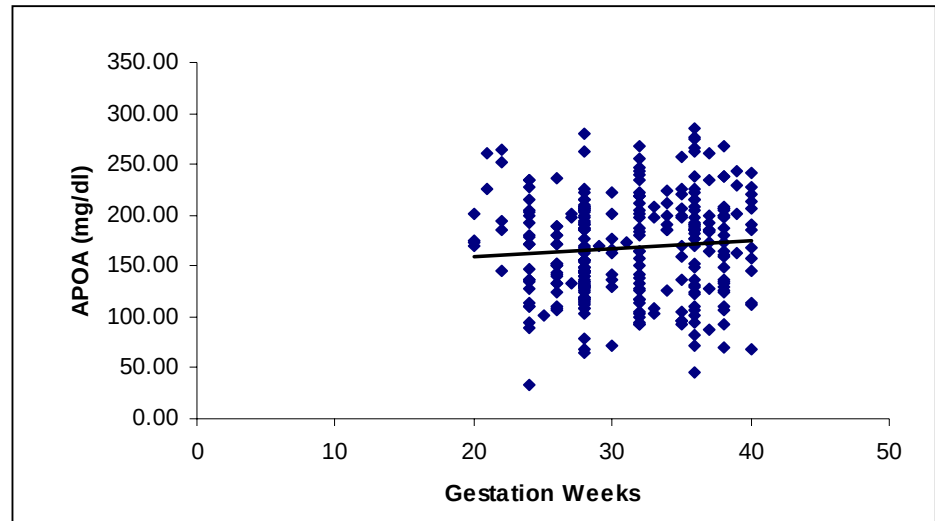


Figure-3.69: Correlation between Gestation weeks and APOA in the patients of Pregnancy Induced Hypertension.

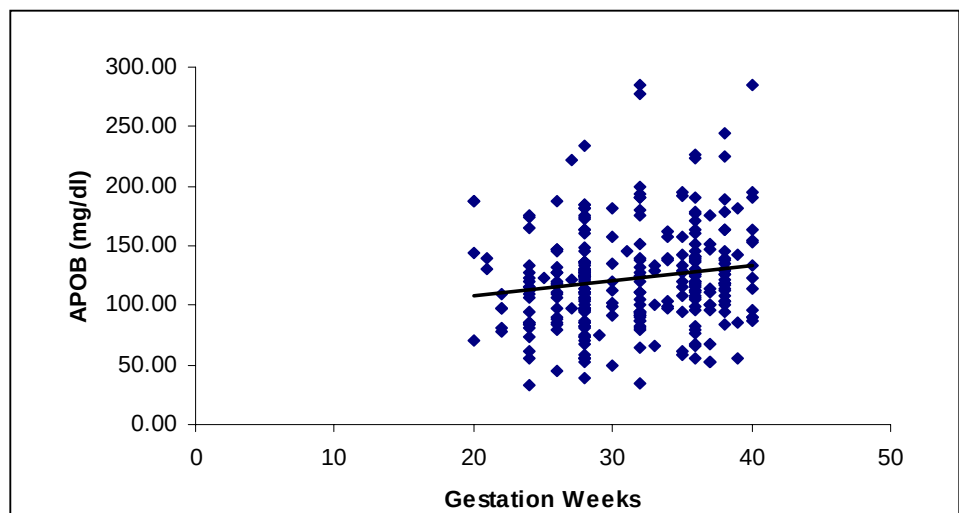


Figure-3.70: Correlation between Gestation weeks and APOB in the patients of Pregnancy Induced Hypertension.

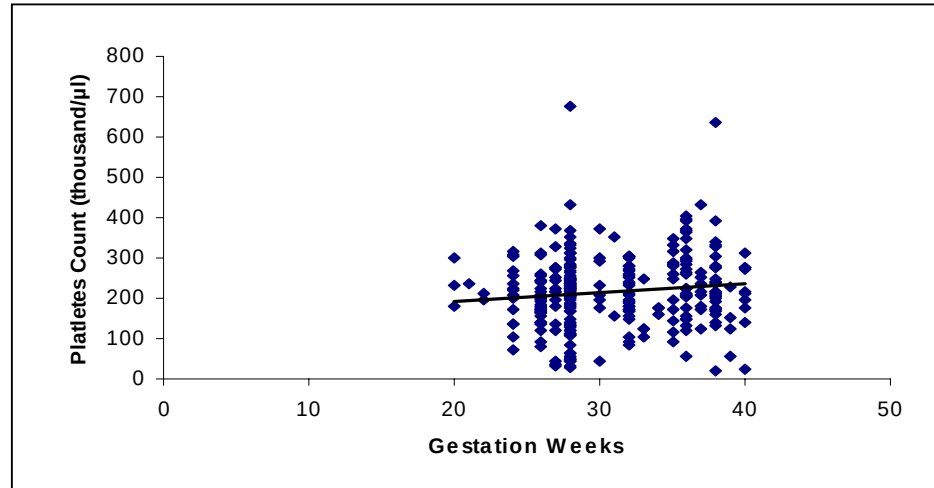


Figure-3.71: Correlation between Gestation weeks and platelet count in the patients of Pregnancy Induced Hypertension.

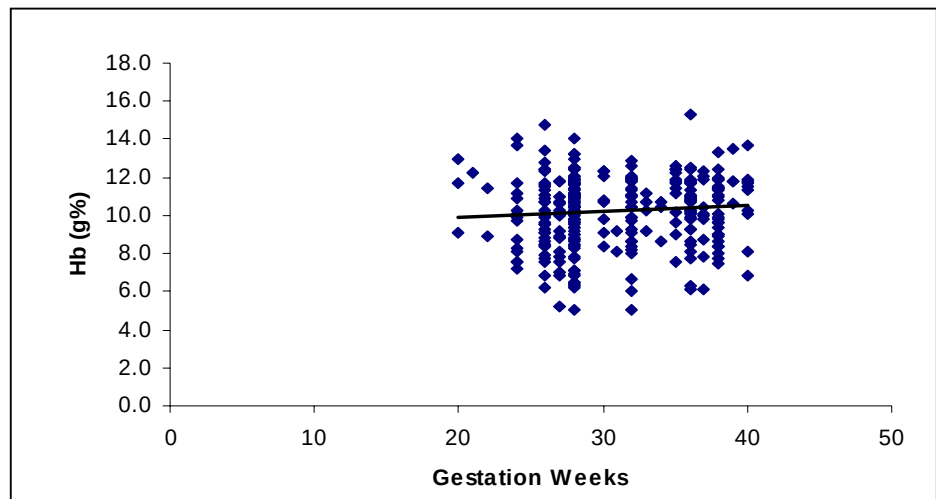


Figure-3.72: Correlation between Gestation weeks and hemoglobin concentration in the patients of Pregnancy Induced Hypertension.

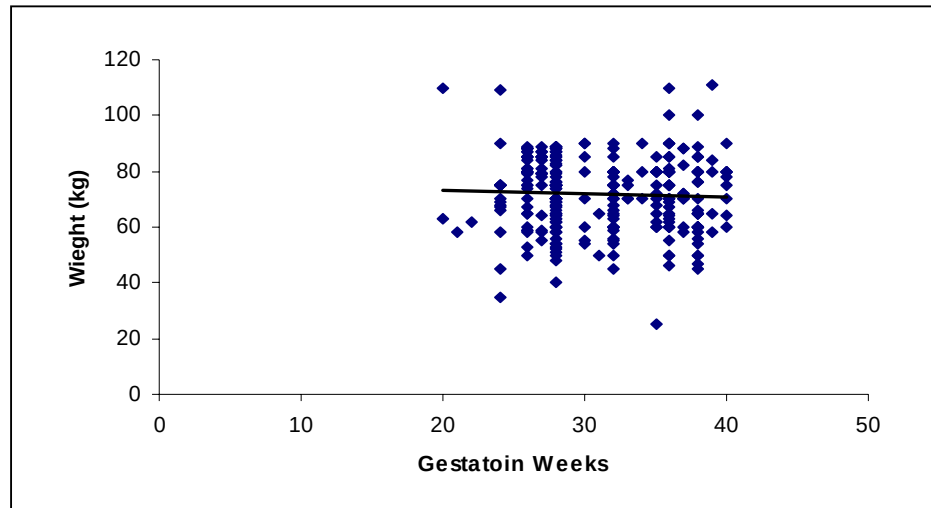


Figure-3.73: Correlation between Gestation weeks and weight in the patients of Pregnancy Induced Hypertension.

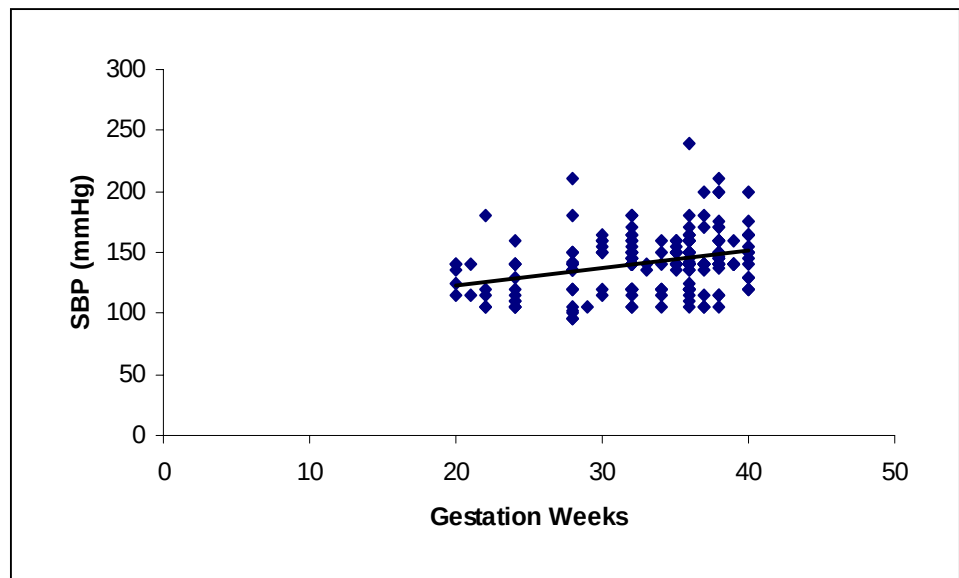


Figure-3.74: Correlation between Gestation weeks and systolic blood pressure in the patients of Pregnancy Induced Hypertension.

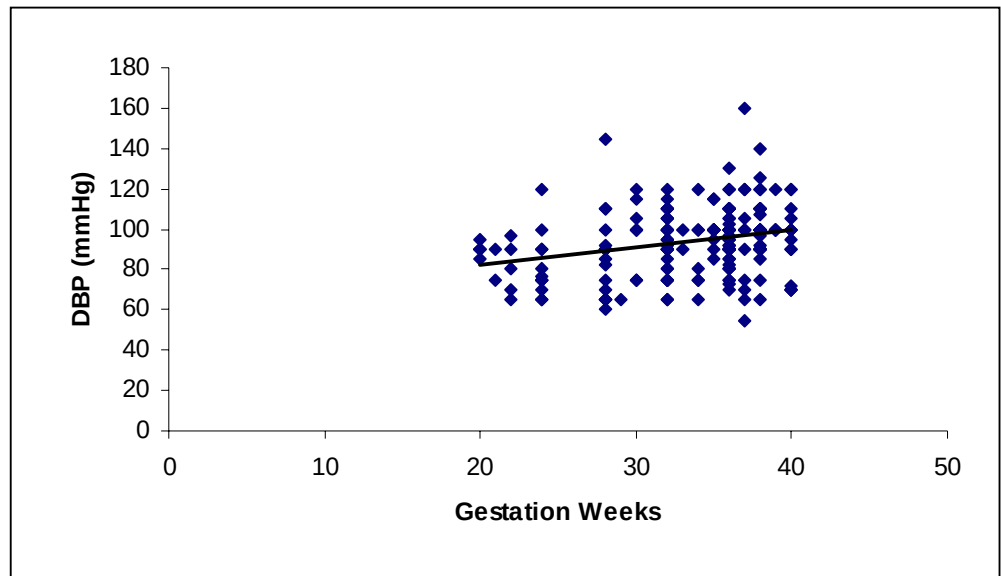


Figure-3.75: Correlation between Gestation weeks and diastolic blood pressure in the patients of Pregnancy Induced Hypertension.

DISCUSSION

Pregnancy-Induced Hypertension (PIH) continues to be a main obstetric problem in present-day healthcare practice. It affects not only maternal health but also puts fetal development at risk. The high blood pressure problems of pregnancy are very frequent. During pregnancy and the puerperium it is accountable for 12% of maternal mortality worldwide¹²⁴.

Pregnancy induced hypertension (PIH) is a syndrome of hypertension in pregnancy, with or without edema and proteinuria. In a number of patients, the clinical appearance is mild, presenting only with small increase in blood pressure or protein in the urine. Though, in other patients severe maternal and fetal complications¹²⁵, such as the HELLP syndrome, eclampsia, preterm delivery, abruptio placenta, intra-uterine fetal death or fetal growth restriction may take place.

High blood pressure in pregnant women is related with incidence of large placental infarcts and decreased placental growth. It result¹²⁶ in fetal malnutrition, decreased placental perfusion and reduced fetal growth.

Elevated plasma lipids are believed to be probable cause of endothelial cell activation. In women with PIH free fatty acids and TG concentrations are elevated in blood and are increased prior to 20 weeks' of conception in women who afterward became patient of PIH. Linoleic acid is one of the fatty acids which is found higher in women with PIH. In the endothelial cells oxidative stress is stimulated by the linoleic acid. A concentration-dependent decrease¹²⁷ in the

discharge of prostacyclin is illustrated by endothelial cells incubation with linoleic acid. During pregnancy serum lipoprotein increase considerably¹²⁸⁻¹³⁰ and are two times higher in pregnancy induced hypertension. In normal pregnancy the major striking changes in the lipid profile is serum hypertriglyceridemia, which according to earlier studies¹³¹ may be elevated two to three times in the third trimester when compared to the non pregnant women.

Studies have revealed¹³²⁻¹³⁴ that patients having pregnancy induced hypertension are more exposed to cardiovascular diseases, signifying that PIH and cardiovascular disorders may share similar mechanisms¹³⁵⁻¹³⁶. In normal pregnancy adaptive alteration occur in women's physiology to setup needs for the rapidly developing fetus¹³⁷. Alteration that takes place in pregnancy includes insulin resistance, hyperlipidemia and up-regulation of inflammatory markers¹³⁵⁻¹³⁸.

Maternal age is one of essential risk factor in changing lipid metabolism in women with pregnancy induced hypertension. Women age greater than 40 years had nearly two fold high threat of having pregnancy induced hypertension, whether they were having first pregnancy (RR 1.68, 95% CI 1.23- 2.29) or multiple pregnancy (1.96, 1.34 - 2.87).The US nationwide data¹³⁹ proposed that the danger of pregnancy induced hypertension increases by 30% for each additional year of age past 34. Young age of pregnant women did not appear to influence the danger of developing PIH, whichever cut off age was used. In the other studies¹⁴⁰, the threat of PIH is greater when the age of pregnant women is less than 25 years. In our study the mean age of patients in the eclampsia group (C) was considerably lower (25.24 ± 0.54 years) among the groups. The

difference in the age of PIH patients was significantly lower ($P < 0.05$), in comparison to normotensive pregnant women. Maximum number (32%) of patients were recorded in age < 20 years in eclamptic patients of group C, that means eclampsia is more prevalent in younger age group. More than 19% of patients each, in group of A and B were those having age greater than 35 years in contrast to 8.9 % in the normotensive pregnant women. Overall in PIH group of patients, 18.6% had age less than 20 years and 14.4% had age greater than 35 years. This means that younger/older age of pregnant women contribute to a greater frequency of pregnancy induced hypertension in this region.

The danger of pregnancy induced hypertension is higher¹⁴⁰ when the age of pregnant women is less than 25 years. In our study, 42.6% of the patients were less than 25 years of age. A study from Andhra Pradesh, India reported¹²⁶ that primiparous patients with PIH below 20 years of age were 26% while only 15% of the controls were less than 20 years, signifying that younger age of pregnant women was a causative feature to pregnancy induced hypertension. Therefore, it can be assumed from the results of this study that younger maternal age is a significant characteristic causing higher occurrence of pregnancy induced hypertension in the region.

In our study of eclamptic patients (group C), almost 12% women were those, who had got married in a teenage ≤ 15 years, i.e. at the age when the reproductive organs of maternal are not yet fully developed. Maximum number (11.8%) of patient with marriage age > 30 years were recorded in group 'A' of pregnant women. The odds ratio for women with marriage age less than 15 years was 3.07 (95% confidence interval (1.45 to 6.53), χ^2 10.36 & $P < 0.001$) when compared

with women with marriage age 21-25 years as referent. This means that a woman, if married in younger age of < 15 years will be three times more prone to develop pregnancy induced hypertension. Although, in this study marriage age has been evaluated to be a significant threat for PIH, no data exists for comparison in literature to address this important risk factor.

In our study, mean weight of pregnant women in group A and B was higher as compared to patients in the eclampsia group-C and healthy pregnant women. Women in group A were found to be more obese ($30.96 \pm 1.08 \text{ kg/m}^2$) in contrast to women in group D of control ($28.94 \pm 0.82 \text{ kg/m}^2$) pregnant women. Although six different studies¹⁴¹⁻¹⁴⁶ that determined body mass index (BMI) before pregnancy used different ranges, they all illustrated similar effects, signifying two fold increase in the threat of PIH with an elevated BMI (2.47, 1.66 - 3.67). One cohort study¹⁴⁴ showed that women with a BMI > 35 kg/m² prior to pregnancy had over four folds risk of PIH in contrast to women with a pre-pregnancy BMI of 19-27 kg/m² (4.39, 3.52-5.49). If all these studies¹⁴⁷⁻¹⁴⁹ emphasizing on elevated BMI are combined and matched with normal BMI at initial registration then it is evaluated that the threat of pregnancy induced hypertension is amplified by 50%. According to a cohort study¹⁴⁷, a BMI > 35 kg/m² at booking doubles the risk of pregnancy induced hypertension (OR 2.12, CI 1.56 - 2.88). Confounding factor can influence the relation between BMI and PIH as women with elevated BMI may be older and at higher threat of chronic hypertension. However, available odds ratios that have been adjusted to control some of these factors into consideration yet recommend an increased risk with an elevated BMI. A study¹⁵⁰ comparing normal and low body mass index at

registration evaluated that the exposure of pregnancy induced hypertension was considerably reduced with a body mass index $< 20 \text{ kg/m}^2$ (odds ratio 0.76, CI 0.62 - 0.92, adjusted for smoking and diabetes). In our study also, the risk of PIH was gradually increasing with the increase of BMI and pregnant women with BMI $\geq 27 \text{ kg/m}^2$ were 2.3 times more at risk to develop pregnancy induced hypertension, in contrast to women with normal BMI $< 23.0 \text{ kg/m}^2$.

Documentation on association between pregnancy induced hypertension and dyslipidemia has clinical importance. The occurrence of metabolic syndrome amongst women < 20 years is 23.4%, as illustrated from the results of Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994). These results, both with the high incidence of overweight and obesity, recommend the susceptibility of women of reproductive age to hypertensive disorders of pregnancy.

According to three cohort studies¹⁵¹⁻¹⁵³, primiparity almost triples the risk for pregnancy induced hypertension (OR 2.91, CI 1.28 - 6.61); this is supported by adjusted odds ratios for primiparity from two other cohort studies¹⁵⁴⁻¹⁵⁵. Different case-control studies^{151, 155-159} propose that women with pregnancy induced hypertension are two times expected to be primiparous as women without PIH (OR 2.35, CI 1.80 - 3.06). A study from Canada reported¹⁶⁰, that women with hypertensive disorders were more expected to be nulliparous (range 42.2% - 78.2%) when matched with normotensive (41.9%) pregnant women. In our three study groups of PIH patients, 20-59% of pregnant women were primiparous. Highest number 65(59%) of primiparous pregnant women were recorded in the group of eclamptic patients, that is consider to be most severe form of disease. Overall 38.5% patients were primiparous in three patient groups of pregnancy

induced hypertension in contrast to 23% in the control group. In our study, primiparous women were two times more liable to be eclamptic (OR 2.08, CI (1.08 - 4.03), χ^2 5.55, $P < 0.01$) when compared to women having parity of 2-4, while women with parity greater than seven were 1.6 times (CI 0.71-3.76) more at risk to develop pregnancy induced hypertension.

Worldwide¹⁶¹⁻⁶³, hypertensive disorders in pregnancy cause difficulties in about 10–16% of pregnancies and are important source of maternal, fetal and neonatal morbidity and mortality. In our study, there was a greater threat of C-section (8.4%) to women with pregnancy induced hypertension (OR 1.29, 95% CI 0.49-3.63, χ^2 0.30, $P < 0.58$) in contrast to the healthy pregnant women (6.6%). Also according to our findings, hypertensive disorders in pregnancy had a significant effect on rate of still birth and low birth babies. There was a significant ($P < 0.09$) increased risk of still birth (17%) among infants born to women with pregnancy induced hypertension (OR 1.87, 95% CI 0.85-4.26, χ^2 2.76,) compared to women with normotensive pregnancies (9.9%). Similar greater risk of stillbirth among women with chronic hypertension and superimposed PIH (RR 4.4, 95% CI 2.2-8.8), or hypertensive disorder (RR 1.4, 95% CI 1.1-1.8) and among women with pregnancies complicated by chronic hypertension (RR 2.4, 95% CI 1.2-5.1) compared with normotensive pregnancies is reported by others¹⁶⁴ in literature.

According to three cohort studies^{141, 143, 165}, the probability of pregnancy induced hypertension almost became four fold if diabetes is there prior to pregnancy (3.56, 2.54 - 4.99). According to our findings 5.8% women in the patient group were reported to be diabetic vs. 2.2% in the control group. The risk of pregnancy

induced hypertension almost became triple in PIH patients, if diabetes was present before pregnancy (OR 2.72 CI 0.59-17.28).

In literature¹⁶⁶, family history of hypertension, diabetes or ischemic heart diseases were each associated with a doubling in occurrence of pregnancy induced hypertension. Our results were over-represented for family history of hypertension. Family history of hypertension was given by 62.3% patient and 19.8% control subjects. Women with a family history of hypertension were seven times more at risk to develop pregnancy induced hypertension as compared to those having no family history of hypertension (OR 6.70, CI (3.69-12.28), $P < 0.0001$).

According to the finding of different cohort studies^{141, 167-170}, women will be seven times more at risk of PIH in a second pregnancy who had pregnancy induced hypertension in first pregnancy (OR 7.19, CI 5.85-8.83). In different case-control studies^{155-159, 171-173}, women with pregnancy induced hypertension in their second pregnancy are also seven times more prone to have a history of PIH in their first pregnancy than women in their second pregnancy who do not develop PIH (OR 7.61, CI 4.3-13.47). In our study 8.9% of patients had given the history of prior PIH against none by the normotensive pregnant women.

Pregnancy induced hypertension is a multifactorial disease¹⁷⁴, it has a general affinity towards familial clustering, suggesting that genetic factors might play an essential role. Different cohort studies reported¹⁷⁵⁻¹⁷⁶ that a family history of pregnancy induced hypertension increases the risk of PIH almost three times (OR 2.90, CI 1.70-4.93). Women with severe pre-eclamptic toxemia are more expected¹⁷⁷ to have a mother rather than a mother in law who had pre-eclampsia. In our study, a woman with a family history of PIH was five times more at risk to

develop pregnancy induced hypertension (OR 4.73, CI 1.07-29.24, $P < 0.02$) as compared to those having no such family history.

According to different cohort studies^{141, 143, 151, 158, 178}, when a woman is pregnant with twins, her threat for pregnancy induced hypertension nearly triples (OR 2.93, CI 2.04-4.21). Neither the zygosity nor chorionicity of the pregnancies could change this increased risk¹⁷⁹⁻¹⁸⁰. A study reported that a triplet pregnancy almost triples (OR 2.83, CI 1.25 to 6.40)¹⁸¹ the risk of PIH in contrast to a twin pregnancy. In the present study 9 (2.9%) women were expecting multiple pregnancies in the patient group vs. none in the normotensive women.

Davies et al¹⁷² reported that in women who developed pregnancy induced hypertension the prevalence of renal disease was higher when matched with those that did not (5.3% vs. 1.8%). Only one study¹⁸² compared women having renal disease with urinary tract infections, with a prospective control population matched for age, smoking, parity and date of delivery. In 69 continuing pregnancies, 6.7% (2/30) of the women who had urinary tract infections developed pregnancy induced hypertension (both primi gravida) matched with 2.6% (1/39) of women in the control group. No such findings could be extracted from the present study.

Several investigators¹⁸³⁻⁸⁴ have hypothesized that the relation between a disordered lipid profile, endothelium cell and oxidative stress is of major importance to the patho-physiology of pregnancy induced hypertension. It is reported^{185, 186} that PIH (GH, PE and Eclampsia) is a widespread inflammatory

state where a number of plasma factors that control endothelial functions are changed. According to reported literature^{185, 187}, an endothelial hyperstimulation is originally provoked, finally leading to severe endothelial dysfunction and resulting in distributed microangiopathic disease with hypercoagulation and vasospasm.

The increase of serum lipids through pregnancy in general and during pregnancy induced hypertension in particular is described in a number of studies. Worldwide diverse studies have reported^{136, 188-190} elevated lipid levels in pregnancy induced hypertension patients. Some earlier studies reported that the striking changes in the lipid profile in normal pregnancy is serum hypertriglyceridemia, which may be as high as two to three folds in the third trimester over the levels in non pregnant women¹³¹. In our study also this observation holds true and the rise in serum triglycerides was statistically significant ($P < 0.001$) in pregnancy induced hypertensive patients when compared to women with normal pregnancy. Increased BMI found in the present study could partially clarify the significant increase in triglycerides because increase in weight and body mass index is associated with increase in body fats. The major modulator of this hypertriglyceridemia is oestrogen as pregnancy is linked with hyperoestrogenaemia. Oestrogen induces hepatic biosynthesis of endogenous triglycerides, by rising the hepatic VLDL-TG synthesis, secretion and plasma triglyceride concentration¹⁹¹. This process may be modulated by hyperinsulinism established¹⁹² in pregnancy. During gestation¹⁹³ these interactions along with increased endothelial triglyceride accumulation may result in endothelial cell dysfunction. In PIH increased triglyceride found¹³⁶, is probably deposited in

predisposed vessels, such as the uterine spiral arteries and contributes to the endothelial dysfunction, both directly and indirectly through generation of small, dense low density lipoprotein cholesterol. Moreover, this hypertriglyceridemia may be linked¹⁹⁴ with hypercoagulability.

In the present study, cholesterol concentration increased in the patients of pregnancy induced hypertension, but no significant changes in total cholesterol could be observed. These results are consistent with the findings reported in studies conducted in other populations^{136, 187}. However some of researchers^{126, 195-96} have found considerable rise in serum cholesterol in toxemia of pregnancy. It was reported in the Finnish and Peruvian population¹⁹⁷⁻⁹⁸ that patients with pregnancy induced hypertension had higher mean triglyceride and lower mean serum HDL-C concentrations than the control group. In our study, the mean value of HDL-C was about 16.8% lower in the pregnancy induced hypertensive patients over the pregnant women with normal pregnancy. Statistically the variation was highly significant ($P<0.001$).

A tendency of lesser quantities of serum alpha lipoprotein fraction in women with toxemia, particularly in the third trimester is reported by many workers^{136, 187, 199}. Oestrogen is accountable for induction of triglycerides and HDL-C and inhibition of serum LDL-C and oestrogen level falls in pregnancy induced hypertension²⁰⁰. The low level of HDL-C in pregnancy induced hypertension is however not only because of hypo-oestrogenemia but also due to insulin resistance¹⁹⁷. The change in LDL-C cholesterol was non significant in the two groups of patient and control. In present study, serum VLDL-C level rose significantly ($P<0.001$) in the patient

group, which may be due to hyper-triglyceridemia leading to increased entry of VLDL-C that carries endogenous triglyceride into circulation. According to the reports of some researchers²⁰¹ the VLDL-C level might raise up to 2.5 folds at term over the pre-pregnancy level. VLDL-C level further elevates in pregnancy induced hypertension as found in the present study in validation with those of other researchers^{136, 194} perhaps due to increased VLDL-C which accumulate over the maternal vascular endothelium, mainly those of uterine and renal vessels²⁰². Further VLDL-C may cause injury to the endothelium, while a particular toxicity-preventing-activity-protein protects against the VLDL-induced damage in the pathogenic process of toxemia²⁰³.

A study conducted on Ghanaian women with pregnancy induced hypertension reported²⁰⁴ that there was a significant increase in triglycerides and LDL-C in the patient groups compared to the control. The lipid peroxidation marker Malondialdehyde (MDA), among the pregnancy induced hypertension subjects was significantly increased as compared to the normotensive pregnant women. A significant positive correlation between MDA and systolic and diastolic blood pressure was also observed. The study obviously indicated that Ghanaian women presenting with pregnancy induced hypertension are very prone to dyslipidemia as well as lipid peroxidation.

It is well known that APO-B100 is a protein component of a variety of lipoproteins which are LDL-C, VLDL-C, IDL-C and lipoprotein (a). In the present study, levels of APO-B100 concentrations in the patients of pregnancy induced hypertension were low, however the difference in the mean values was non significant, when compared to control group. A significant difference in APO-A1

levels was seen in pregnancy induced hypertensive group in contrast to that of control group. In our view, this can be originated from polymorphism of APO-A1 of HDL-C and/or functional disorder of HDL-C. Apoprotein polymorphism of lipoproteins in diabetics has been studied²⁰⁵⁻²⁰⁶ earlier. A low HDL-C level in diabetic patients without associated decrease in APO-A1 levels has been reported by Erbagci, et al²⁰⁶. We have not found any literature on this point in pregnancy induced hypertensive patients. Although it is probable a concomitant HDL-C and APO-A1 levels, our finding recommend that lipoprotein concentrations come out to be better biochemical markers of dyslipidemia in the pregnancy induced hypertension than the corresponding apolipoproteins.

Similar results are reported by Bayhan. G. et al from Turkey²⁰⁷. The study was aimed to estimate changes in lipid profile, serum levels of Malondialdehyde and lipoprotein(a) and placental MDA in pregnancy induced hypertensive women, and to assess the atherogenic role of these changes in the pathophysiology of PIH. For the purpose a cross-sectional study was conducted on 20 normal pregnant women, 25 women with mild pre-eclampsia and 28 women with severe pre-eclampsia in the third trimester. Serum levels of total cholesterol, triglycerides, low-density lipoprotein cholesterol, MDA, Lp(a), and placental MDA were significantly higher, and Apo A-I and HDL-C levels were significantly lower, in severely pre-eclamptic and mildly pre-eclamptic women than in the normal pregnant women, but no difference was noted in Apo-B among groups. Serum level of Lp(a) was positively correlated with BMI in severely pre-eclamptic women ($r=0.489$, $P=0.008$). A significant positive correlation was also noted between systolic blood pressure and serum level of MDA in women with severe eclampsia ($r=0.375$,

P=0.049). The study suggested that high TG, LDL-C, Lp(a), and lipid peroxidation and low Apo-A1 and HDL-C levels are main danger for atherosclerosis among women with pregnancy induced hypertension.

Another study from China²⁰⁸ investigated the serum lipoprotein and apolipoprotein concentration in PIH patients, normotensive pregnant women and non-pregnant women. Twenty eight women with PIH, 31 normotensive and 24 non-pregnant were included in the study. According to the study serum TG, apoC-II and apoC-III were more elevated in normotensive pregnant women by 3.5, 2.4 and 2.8 times respectively, in contrast to those in non-pregnant women ($P < 0.001$). Serum TC, HDL-C, Apo-AI, Apo-B100 and Apo-E were also elevated in normotensive pregnant women by 21%, 33%, 55%, 79% and 77% respectively, in contrast to those in non-pregnant women ($P < 0.001$). In normotensive pregnant women TG: HDL-C ratio was also significantly elevated as compared to non-pregnant women ($P < 0.01$). In either group, no change was noted in serum HDL cholesterol. Serum apoC-II, apoC-III and TG levels were highly increased in PIH patients by 2.8, 4.0 and 2.3, times respectively, in contrast to those in non-pregnant ones ($P < 0.001$). Serum TC, HDL-C, apo-AI, apo-B100 and apo-E were also increased in PIH patients by 27%, 26%, 52%, 90% and 67% respectively, when compared with those in non-pregnant women ($P < 0.001$). TG: HDL-C in PIH patients was also significantly higher ($P < 0.01$) than that in non-pregnant women. Serum HDL cholesterol were increased in pregnancy induced hypertensive patients by 29%, in contrast to non-pregnant women. Only serum HDL-C concentration in PIH women was elevated over that in normotensive pregnant women. No remarkable changes were noted in other lipoprotein and apolipoprotein levels among the groups of pregnancy induced hypertensive

patients and normotensive pregnant women. The results from this study are contrary to our findings, showing that there was no remarkable difference in the levels of serum apolipoprotein according to the severity of the disease among the subgroups of PIH patients.

We found a tendency towards higher LPA concentrations in all of the three groups of PIH patients, although the differences from healthy pregnant controls did not arrive at statistical significance in gestational hypertensive women (group-A) and group of pre-eclampsia (group-B). In women with eclampsia we noted considerably lower LPA concentrations in contrast to other two patient groups. Our results are in accordance to other studies²⁰⁹⁻¹⁰ which shows elevated LPA level in women with pregnancy induced hypertension but dissimilar to a study²¹¹ presenting lower LPA level in women with pregnancy induced hypertension in contrast to healthy pregnant controls. Lipoprotein (a) can work as acute phase reactant in the presence of endothelial dysfunction or inflammation. In these circumstances²¹¹ there is a transient raise in LPA concentration²¹³⁻¹⁵. The LPA level depends²¹² on the rate of its synthesis in the liver and it is thought that during an acute phase reaction there is an enhanced biosynthesis action of the liver resulting in elevated synthesis of lipoprotein (a) and other acute phase reactants like α_1 -antitrypsin and C-reactive protein²¹⁴⁻¹⁵. An other important clarification for the enhanced LPA concentration is that LPA plays a vital role in facilitating lipid delivery to endothelial lesion sites^{212, 213, 216}.

The findings of our study are in agreement to that reported by Zhao.Y. et al²¹⁷. They looked at lipoprotein(a) level in 32 woman with pregnancy induced hypertension to find the effect of it on the pathogenesis of the disease and

compared the findings with 20 normal pregnant woman (control group). The PIH group was further divided into the mild, moderate, and severe PIH. The serum lipoprotein (a) levels were higher in PIH group as compared to normotensive women (228 ± 187 mg/L vs. 106 ± 93 mg/L). The serum lipoprotein (a) levels were higher in all PIH subgroups than that in the control group. The serum levels of TC, LDL-C and triglycerides in the PIH group were higher than those in control, while the level of HDL-C in the PIH group was lower (0.98 ± 0.16 mmol/L vs. 1.09 ± 0.17 mmol/L) than that in control. This study has revealed that lipoprotein(a) levels are higher in pregnant woman with PIH and linked with severity of the disease. It may involve in the pathogenesis of pregnancy induced hypertension.

Jacob B. et al²¹⁸ determined, whether maternal plasma lipoprotein(a) concentrations are higher in the second trimester, before the progress of pregnancy induced hypertension and other obstetrical disorders, in women at risk. In the initial part of cross-sectional study, serum levels of Lp(a) were compared among 16 women with PIH, 35 normotensive pregnant women and 18 healthy non-pregnant women. In the second part of study blood samples were prospectively collected from 82 women at threat of pregnancy induced hypertension, at 14–24 weeks of conception, and Lp(a) concentration were matched to those in whom pregnancy induced hypertension or other obstetrical complications developed and those in whom they did not. In the said study, plasma concentrations of Lp(a) were considerably elevated in women with pregnancy induced hypertension than in normotensive pregnant and healthy non pregnant women (41 ± 31 vs. 24 ± 16 and 15 ± 10 mg/dl, respectively; $P=.001$). In the second part of the study, 9(11%) women developed pregnancy induced hypertension and 19(23%) had obstetrical

problems such as preterm delivery, fetal or neonatal loss and intrauterine growth restriction. There were no difference in plasma Lp(a) levels between the women with pregnancy induced hypertension and those without such disorders, though Lp(a) levels were considerably raised in women with other complications than in those with either PIH or uncomplicated pregnancies (40 ± 29 vs. 17 ± 13 or 28 ± 18 mg/dl, respectively; $P=.05$). This means, high plasma levels of Lp(a), linked with clinically recognized PIH, are not identified prior to the manifestation of complications in pregnant women at risk.

The literature on lipoprotein(a) during normal pregnancy and pregnancy complicated by PIH or intrauterine growth restriction was reviewed by Gwendolyn T.R.²¹⁹, for a period January 1966 to May 2003. It comes out from the review that Lipoprotein (a) increase with progress in gestation or remained unchanged during normal pregnancy. Women with PIH had higher, unchanged or lower lipoprotein (a) levels in contrast to normotensive control women. Available studies on lipoprotein(a) in pregnancy vary largely in the methods used to determine lipoprotein (a), study design, sample size and community of the study population. Therefore, these studies give up conflicting results and no explicit observation on the function of lipoprotein (a) in ordinary and complicated pregnancy was found.

We have also calculated the ratios between different lipids like LDL-C: HDL-C, TC: HDL-C, TG: HDL-C and HDL-C: VLDL-C for the patients and control groups. There was a great increase in LDL-C: HDL-C, TC: HDL-C, TG: HDL-C and HDL-C: VLDL-C ratio in pregnancy induced hypertensive women in contrast pregnant women with normal blood pressure. According to different studies^{194, 199},

, LDL-C: HDL-C ratio elevates considerably in eclamptic patients in contrast to normotensive pregnant women. On the contrary, HDL-C: VLDL-C ratio persistently reduce in both pre-eclampsia and eclampsia. On the other hand TG: HDL-C increased notably in PIH. Trend was a little dissimilar in TC: HDL-C which reduces during pregnancy but elevated significantly in both pre-eclampsia and eclampsia¹⁹⁴. Though the association of these ratios in pregnancy and PIH is yet to be recognized, the significance of altered TC: HDL-C, TG: HDL-C and HDL-C: VLDL-C ratios can not be ignored as they point toward more threats in PIH. Dyslipidemia mediate activation of the endothelial cells to the placental derived endothelial disturbing factors like lipid peroxides and trophoblastic components or combination of placental derived factor with the lipoproteins could be considered as probable contributor for pathogenesis of pregnancy induced hypertension²²⁰.

Our results are comparable with findings from the few existing prospective studies^{127, 185}, case-control studies^{136, 195} and many prospective cohort studies²²¹⁻²²² of maternal fasting or non fasting serum lipid and lipoprotein concentrations in pregnancy induced hypertension and normotensive pregnancies. In these PIH patients, decrease of HDL cholesterol regardless of elevation in other lipid components is a probable threat for atherosclerosis²²³.

In our study, we observed that there was a 1.48 fold increase in danger of pregnancy induced hypertension among women with TC >240 mg/dL (95% 0.80 - 2.75) vs. < 200 mg/dL and a 3.51 times elevation in the threat of pregnancy induced hypertension among women with triglyceride levels 200-499 mg/dL (95% CI 1.5-8.22) vs. < 150 mg/dL. The OR for extreme lower quartile of HDL-C (<40 vs. >60 mg/dL) was 8.57 (95% CI 3.28-22.71, P 0.00001) A linear increase

in the risk of pregnancy induced hypertension was observed with increasing tertiles of LDL cholesterol, triglyceride concentrations, HDL cholesterol, TC to HDL-cholesterol ratio and LDL-C: HDL-C ratio (all $P < 0.001$ except for LDL cholesterol where trend for change among the groups remained non significant). Our findings are in accordance without come from the few existing prospective cohort studies^{221, 222,224-226}, and many case-control studies^{136, 195-197}, of maternal fasting or nonfasting plasma lipid and lipoprotein concentrations in pregnancy induced hypertension and normotensive pregnancies. In a prospective cohort study on 393 pregnant women, Wladimiroff et al²²⁶ described that women with serum TC concentrations > 233 mg/dL, compared with those whose concentrations were < 194 mg/dL, experienced a fivefold increased danger of PIH (95% CI 1.2 - 22.5) after accounting for confounding factors like gestational age and maternal body mass index. Remarkably, results from two prospective studies^{225, 227} also point out that maternal hypertriglyceridemia is evident as early as 10 to 20 weeks of gestation in women at risk to develop pregnancy induced hypertension. In a study by Lorentzen et al²²⁵, mean triglyceride concentrations of 19 women who afterward developed PIH were 50.4 ± 19.4 mg/dL at 16–18 weeks of gestation in contrast to 34.91 ± 11.64 mg/dL for control women who had normotensive pregnancies ($P < .01$). Ware- Jauregui et al in a case-control study reported²²⁸ that women with triglyceride concentrations > 284 mg/dL had a fivefold increased threat of PIH as matched with women whose concentrations were < 189.0 mg/dL. The investigators also noted statistically significant lower concentrations of HDL-C in patients versus control subjects ($P < .027$). After adjusting for confounders the odds for extreme quartile of HDL-C (< 33.01 verses > 50.00 mg/dL) was 0.38 (95% CI 0.18 - 0.81)²²⁸. Similar observations were recorded in a study²²⁹ on sub-

Saharan African women, showing an inverse association between PIH risk and HDL-C concentrations (OR = 1.00, 0.87, 0.66, and 0.68 with first quartile as the referent; P = 0.169 for trend). Our result, when taken together with those of earlier prospective studies²²⁴⁻²²⁷ indicate that dyslipidemia, mainly hypertriglyceridemia, is the clinical appearance of PIH and thus may be of pathophysiologic and etiologic importance in this fairly common complication of pregnancy. The strength of our study merit consideration over earlier studies. The reason being we had sufficient numbers of gestational hypertension, pre-eclampsia and eclampsia patients and control subjects to exhibit statistically significant associations. The relationship between dyslipidemia and the threat of PIH is biologically logical and is well-matched with what is known about the pathophysiology of pregnancy induced hypertension. In the literature three hypothesized mechanism for the association between PIH and dyslipidemia have been described. First, investigators¹²⁷ have found that high plasma lipid and lipoproteins may stimulate endothelial dysfunction secondary to oxidative stress. They also illustrated that dyslipidemia may damage trophoblast invasion thus contributing to a cascade of pathophysiologic events that proceed to the progress of pregnancy induced hypertension¹²⁷. The study²³⁰ is support by the fact that triglyceride collection in endothelial cells is related with reduced release of prostacyclin. A considerable shift in LDL-C particle sizes to subtypes of smaller diameter¹³⁶ has also been related with a rise in triglyceride levels. In pregnancy induced hypertension formation of the smaller variant of LDL-C has been shown²³¹⁻²³² to add to endothelial dysfunction during rise in intracellular calcium in vascular smooth muscle and stimulation of thromboxane synthesis by endothelial cells. The second method is the pathologic process of PIH via deregulation of lipoprotein lipase

follow-on in a dyslipidemic lipid profile. In the third trimester pre-heparin hepatic lipase levels were significantly raised ($P < .04$) in pre-eclamptic patients compared with eight normotensive control women¹³⁶. Enderssen et al²³³ and Lorentzen et al²²⁴ showed that sera from pregnancy induced hypertension women had both an elevated lipolytic levels and increased ratio of free fatty acids to albumin, resulting in increased endothelial uptake of free fatty acids, which are further esterified to triglycerides. A third probable mechanism may be via the metabolic syndrome. Kaaja et al¹⁹⁷ noted that in pregnancy induced hypertension metabolic characteristics of hyperuricemia and hyperinsulinemia are also there. Furthermore, women with a past record of PIH, as compared with their BMI matched corresponding women with no such a background, have higher fasting insulin, lipid levels, coagulation and inflammatory factors after several years of delivery²³⁴. The incidence of pregnancy induced hypertension²³⁴ is also related to environmental and genetic factors that adds to the pathogenesis of metabolic syndrome and associated vascular problems. Documentation of a relationship between dyslipidemia and pregnancy induced hypertension has clinical implication. Conclusion from the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994), pointed out²³⁵ that in pregnant women age >20 years the occurrence of metabolic syndrome is 23.4%. These results, jointly with the elevated incidence of overweight and obesity, propose the susceptibility of women of reproductive years to hypertensive problems of pregnancy. Findings from our study, when taken jointly with these notes, emphasize the significance of designing epidemiologic and clinical studies planned to recognize the determinants of pregnancy induced dyslipidemia i.e. maternal lifestyle characteristics both before and during pregnancy. Information

from these studies may add to the progress and assessment of medical and behavioral interference meant at decreasing pregnancy complications and improving the maternal health.

Lipoproteins concentrations are changing continuously with the advancement of pregnancy. In our study, a linear drift has been seen in all the fractions of lipoprotein concentration with advancement in pregnancy, except in the HDL-C concentration which had decreased with increase in the gestation weeks. Mean lipoprotein concentrations in second and third trimester of pregnancy induced hypertensive and normotensive women were compared. A significant change was seen in the concentration of HDL-C ($P < 0.01$), VLDL-C ($P < 0.05$), TG ($P < 0.05$), APO-B100 ($P < 0.05$) and LPA ($P < 0.05$), when pregnancy induced hypertensive women in the second trimester were compared with those in their third trimester. In the control group of normotensive pregnant women, significant changes could only be noted for TC ($P < 0.01$) and LDL-C ($P < 0.001$) when women in two groups of second and third trimester were compared. Gratacós E. et al²²⁷ has estimated serum TC and TG concentration in women at the first, second and third trimesters of pregnancy with hypertension during pregnancy and matched for age and BMI normotensive pregnant women. Hypertensive women were further divided as having mild gestational hypertension, severe gestational hypertension, mild pre-eclampsia, severe pre-eclampsia, chronic hypertension and superimposed pre-eclampsia. Cholesterol levels were not statistically different among patients and normotensive women in any form of hypertension. Triglyceride concentrations were considerably elevated at 20 and 34 weeks' pregnancy, than controls in women with severe gestational hypertension, mild and severe pre-eclampsia, and superimposed pre-eclampsia, but not in mild gestational

hypertension or chronic hypertension. A considerable increase in TG was already present at 10 weeks in mild and severe pre-eclampsia. The study suggested that variations in lipid metabolism seen in pre-eclampsia are already present in the first trimester of pregnancy. Pre-eclamptic and severe gestational hypertension women offered a similar pattern of triglycerides, while in this respect chronic hypertension resembled mild gestational hypertension. This supported the perception that, even though in several patients gestational hypertension correspond to essential hypertension, a few of these women, probably the most severe patients, present with non proteinuric pre-eclampsia or true pregnancy-induced hypertension.

In women with pregnancy induced hypertension one of the risk factor is giving birth to first child by the affected women. In the present study 120 (30%) women were primiparous against 21 (23%) women in the control group of pregnant women. On comparison of blood lipid levels in normal pregnancy and in primiparous women with pregnancy induced hypertension, highly significant difference were recorded in HDL-C ($P < 0.001$), TC: HDL-C ratio ($P < 0.001$), TG: HDL-C ratio ($P < 0.0001$), HDL-C: VLDL-C ratio ($P < 0.0001$) and APO-A1 level ($P < 0.001$). However no significant difference could be found in total cholesterol of primiparous women with pregnancy induced hypertension and normotensive primiparous pregnant women. Similarly a non significant difference ($P > 0.05$) was noted in LDL-C, APO-B100, HDL-C: APOA1 ratio and LDL-C: APO-B100 ratio. In the eclampsia group the difference in TC, HDL-C, VLDL-C, TC: HDL ratio and TG: HDL-C ratio were more prominent as compared to control pregnant women. Our results are partly in agreement to those reported¹²⁶

in Indian population, wherein it's stated that serum TC, TG, LDL-C and VLDL-C was substantially higher in primiparous PIH patients when compared to control subjects.

Another prospective study²³⁶ conducted on 470 primi gravida women between 28 to 32 weeks of pregnancy estimated serum concentration of total cholesterol, low-density lipoprotein, high-density lipoprotein cholesterol, and triglyceride. After that, they were observed for any warning signs of gestational hypertension and pre-eclampsia until 40 weeks of gestational age. Serum lipid concentration among women with gestational hypertension and pre-eclampsia were compared with those of matched normotensive pregnant women. The number of patients with gestational hypertension and pre-eclampsia were 32 (6.8%) and 25 (5.3%) respectively. At the beginning of the study, the mean concentration of serum triglyceride between women who afterward developed pre-eclampsia or gestational hypertension and those who did not varied significantly ($p < 0.0001$, $p < 0.03$) respectively.

Thrombocytopenia is the most common hematological abnormality found in eclampsia and pre-eclampsia. The platelet count in our study was: control 261.44 ± 8.27 thousands/uL, gestational hypertension 223.24 ± 7.64 thousands/uL, pre-eclampsia 227.50 ± 9.35 thousands/uL and in the patients of eclampsia was 198.60 ± 9.28 thousands/uL. When platelet count was compared among the control and study groups, a significant decrease in platelet count was found as the mean blood pressure increased in all patient groups. In our study platelet count in four groups were compared as very low (< 100), low (100-150) and normal platelet count > 150 thousand/ μ L. Our finding indicates that the number of women with very low count is more in women with eclampsia (13.1%) versus 1.1% in the

control women. Normal platelet count > 150 thousand/ μL was recorded in 85 (95.5%) of control pregnant women against 70(65.4%) in the group of eclamptic patients. When the value of platelet estimation was compared between control and patient groups (group A, B and C) altogether as PIH, a significant decrease in platelet count was observed. In the patient group 8.7% of pregnant women had severe thrombocytopenia as compared to 1.1% in the control group. These patients were nine times more likely to have severe eclampsia as compared to those having platelet count greater than 151 thousand/ μL (OR 9.44, CI (1.34-189.9) P 0.008, χ^2 7.01). Severity of PIH and thrombocytopenia observed are closely associated which indicates that thrombocytopenia is directly proportional to the severity of pregnancy induced hypertension.

Thrombocytopenia, defined as a platelet count less than 100,000 thousand/ μL was found in 11.6% of all patients with pregnancy induced hypertension as reported by Romero R²³⁷. In the said study the relative risk of proteinuria, thrombocytopenia and the extent of hypertension to maternal and perinatal outcome were estimated. Thrombocytopenia was the major contributor to the occurrence of abdominal pain, the existence of schistocytes in the peripheral smear, liver dysfunction fetal distress, proteinuria and the need for blood transfusions. Thrombocytopenia was also linked with a higher occurrence of intrauterine growth retardation and preterm delivery. Thrombocytopenia was described as an independent and significant risk factor for the incidence of maternal and perinatal complications in pregnancy induced hypertension.

A similar study from India reported²³⁸ platelet number in 30 normal pregnant women and 90 pregnant women with varying degree of pregnancy induced

hypertension. In the mentioned study mean platelet count was 223 ± 0.19 thousand/ μL in mild pre-eclampsia, 182 ± 0.45 thousand/ μL in pre-eclampsia, 121 ± 0.49 thousand/ μL in eclampsia patients and 238 thousand/ $\mu\text{L} \pm 0.33$ in control group. When the platelet count was compared among control and study groups, a considerable reduction in platelet count was noted in the patient group. In an effort to see the relationship between mean blood pressure of different groups and platelet estimation, an inverse relationship between mean blood pressure and number of platelets was recorded. In comparison of women among various groups with normal, low and very low platelet number, it was found that the number of women with very low count was more in women with eclampsia. The platelet number in our study was compared with other studies. The values in our study correlated well with the values of other studies.

CONCLUSION

Women who developed hypertension after 20 weeks of gestation had 5.45%, 3.5%, 39%, 38.6% and 26.98% higher concentrations of TC, LDL-C, VLDL-C, TG and LPA levels respectively, than control subjects. A significant decrease of (16.76%) and (18.5%) was respectively noted in HDL-C and APO-A1 of patient group when compared with normotensive control pregnant women, while no significant change in APO-B100 levels was seen among the groups. Total cholesterol: HDL-C ratios, LDL-C: HDL-C ratio and TG: HDL-C ratios were higher (32.3%, 29.8% & 66.4% respectively) among women with pregnancy induced hypertension and were found highly significant ($P < 0.001$) as compared to normotensive women. In the PIH group LDL: APO-B100 was raised to a significant level of $P < 0.01$, while the difference between the two groups was found non significant for LDL: APO-B100 ratio ($P > 0.05$). HDL-C: VLDL-C ratio were decreased by 38.23% in the patients and were highly significant as compared with control subjects ($P < 0.001$).

In conclusion, the results of our study propose that an abnormal lipid metabolism and predominantly low HDL-C and high TG concentrations, may add to the promotion of vascular dysfunction and oxidative stress seen in pregnancy induced hypertension. It is, therefore, essential that, blood lipid concentrations be estimated in pregnant women during antenatal care since it could be useful in the early revealing and prevention of obstetric complications such as pregnancy induced hypertension.

We currently rely on secondary prevention of pregnancy induced hypertension: Women who have formerly had the disease, needs to be closely monitored throughout pregnancy. Most of women who develop pregnancy induced hypertension, however, are only diagnosed once they have developed the full-blown appearance of the condition, by which time treatment choices are limited. Rather than being a separate condition, PIH has been formerly expressed as the extreme end of a maternal systemic response stimulated by pregnancy itself. Nevertheless, if signs of endothelial dysfunction and abnormal placenta could be noticed preceeding to the onset of clinical disease, they would describe a tremendously attractive aim for emerging therapeutic strategies. In addition, any such management would be most likely to be useful if they could be started in early gestation. In regular clinical practice, we presently screen for a number of conditions in early pregnancy, most of which have a far lower incidence than pregnancy induced hypertension, and it is expected that in time we will be capable to do the same for pregnancy induced hypertension. It is not likely that a single marker will prove to be a perfect predictive device for pregnancy induced hypertension; a combination of clinical information concerning history and risk factors along with blood biomarkers or urine in those at risk is more rational. There is clearly a great need for development of predictive means for pregnancy induced hypertension. These developments could well be the solution to improving care for women with this disturbing condition.

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Publications from the thesis:

Rubina Nazli, Muhammad Rasul Jan, Jasmin Shah, Tasleem Akhtar, Jamilur Rehman, Mudassar Ahmad Khan. Changes in lipoprotein concentration of primiparous women with pregnancy induced hypertension. PJMR 2009; 48(4): 83-87.

Mohammad Rasul Jan, **Rubina Nazli**, Jasmin Shah, Tasleem Akhtar. A study of lipoproteins in normal and pregnancy induced hypertensive women in tertiary care hospitals of the North West Frontier Province-Pakistan. Accepted for publication in “Hypertension in Pregnancy” (American Journal, Impact factor 1.48)

Rubina Nazli, Mohammad Rasul Jan et al. Prevalence of thrombocytopenia in Pregnancy Induced Hypertension. Under reviewing process in “Hypertension in Pregnancy” journal.

Rubina Nazli, Mohammad Rasul Jan et al. Changes in the hematological parameters in the patients of pre eclampsia. J. of Public Health (American)

Rubina Nazli, Mohammad Rasul Jan et al. Lipid metabolism in the patients of pregnancy induced hypertension. Submitted to “Hypertension in Pregnancy”

A STUDY OF LIPID METABOLISM IN WOMEN OF
PREGNANCY INDUCED HYPERTENSION CASES

Case NO: _____ Date:_____/_____/_____

A. Registered Un-registered OPD

B. Name: _____ C. Age: _____ yrs: D. Cast: _____

E. Education:

Illiterate

Under primary

Primary

Middle Secondary

Matric

Higher

Secondary

Graduate

Masters

Other: _____

F. Occupation:

House Wife

Govt.Job

Private Job

Earning at home

G. Husband Name: _____

H. Husband Education:

Illiterate

Under primary

Primary

Middle Secondary

Matric

Higher secondary

Graduate

Masters

Other: _____

I. Husband Occupation: _____

J. Monthly Income Rs.:

< 2,500

2500-5000

>5000-10000

>10000-20000

>20000

K. Address: _____

Maternal HX:

L. Age at marriage: _____ yrs

M. Gestation week: _____

N. EDD: _____

O. No of pregnancies: _____

P. No of live births: _____

Q. No of still birth: _____

R. No of Abortions: _____

S. No of C- sections: _____

T. No of low birth weight babies: _____

U. No of alive children: _____

V. Prior PIH

Yes

No

DK

W. Any complications in the last pregnancy:

Yes

No

DK

 if yes X. specify_____

Present Hx:

Y.	Diabetic:	☐	☐	☐	Z.	Hypertensive:	☐	☐	☐
AA.	Any heart disease:	☐	☐	☐	AB.	Kidney disease:	☐	☐	☐
AC.	Expecting Twins/triplet:	☐	☐	☐	AD.	No of prenatal visits: _____			

Sign & symptoms of PIH:

AE.	Swelling on face:	☐	☐	☐	AF.	Feet:	☐	☐	☐
AG.	Abdominal pain:	☐	☐	☐					
AH.	Severe headache:	☐	☐	☐	AI.	Change in reflexes:	☐	☐	☐
AJ.	Reduced output of urine:	Yes	No	DK	AK.	No urine:	☐	☐	☐
AL	Blood in the urine:	☐	☐	☐	AM	Convulsion/seizures:	☐	☐	☐
AN	Dizziness:	☐	☐	☐	AO	Coma:	☐	☐	☐
AP	Vomiting:	☐	☐	☐	AQ	Rapid weight gain:	☐	☐	☐
AR.	Nausea:	☐	☐	☐					

Complications of Eclampsia:

AS.	Visual:	☐	☐	☐	AT.	Cerebrovascular:	☐	☐	☐
AU.	Cardiovascular:	☐	☐	☐	AV.	Pulmonary:	☐	☐	☐
AW.	LRT infections:	☐	☐	☐	AX.	Pulmonary edema:	☐	☐	☐
AY	Bronchospasm:	☐	☐	☐	AZ	Pulmonary embolism:	☐	☐	☐
BA.	Aspiration pneumonia:	☐	☐	☐	BB.	Hepatic:	☐	☐	☐
BC.	Renal:	☐	☐	☐	BD	Haemostatic:	☐	☐	☐
BE.	Obstetrical:	☐	☐	☐					

Family history:

BF.	Family Hx of Hypertension	☐	☐	☐	If Yes	BG.	☐	☐	☐
BH.	Family Hx of PIH:	☐	☐	☐	If Yes	BI.	☐	☐	☐

Measurements

Blood Pressure-1:	BJ.	Systolic:_____	BK. Diastolic:_____
Blood Pressure-2:	BL.	Systolic:_____	BM. Diastolic:_____
Mean Blood Pressure:	BN.	Systolic:_____	BO. Diastolic:_____
	BP.	Weight: _____Kg	BQ. Height: _____Cms

LAB INVESTIGATIONS

BR.	Serum Cholesterol _____	BS	HDL_____	BT.	LDL. _____		
BU.	VLDL. _____	BV.	Triglycerides. _____	BW.	Lipoprotein a _____		
BX.	Lipoprotein b _____	BY.	Hb%. _____				
	Platelets count. _____						
Urinary Protein:	Nil	Traces	+	++	+++	++++	Pus cells_____