Dissertation on

CORRLEATION OF ELEVATED SERUM LDH LEVELS WITH ADVERSE MATERNAL AND PERINATAL OUTCOME IN PREECLAMPSIA.

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ETHICS COMMITTEE

CERTIFICATE

Name of the Candidate: Dr. N. Menisri

Course : MS (OG) Post Graduate

Period of Study : 1 year

College : Coimbatore Medical College & Hospital.

Dissertation Topic : Correlation of elevated serum lactate dehydrogense with adverse maternal and perinatal outcome in pre eclampsia

The Ethics Committee, Coimbatore Medical College has decided to inform that your Dissertation Proposal is accepted and you are permitted to proceed with the above Study.

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Certified that, this is the bonafide dissertation done by ***Dr.N.MENISRI*** and submitted in partial fulfilment of the requirement for the degree of ***M.S., Obstetrics and Gynecology*** , Branch –II of ***THE TAMILNADU DR.M.G.R. Medical university Chennai.***

Guide and Associate professor

Dr. Murugalakshmi., MD.,DGO.

HOD and PROFESSOR

Dr. Manonmani., MD., DGO.

Department of obstetrics and Gynecology

DEAN

Dr. ASOKAN., MS.,Mch.

Coimbatore medical College

Coimbatore

CERTIFICATE –II

This is to certify that this dissertation work titled " **CORRLEATION OF ELEVATED SERUM LDH LEVELS WITH ADVERSE MATERNAL AND PERINATAL OUTCOME IN PREECLAMPSIA"** of the candidate **Dr.Menisri N** with registration number 221616304 for the award of M.S. in the Branch of OBSTETRICS AND GYNECOLOGY. I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded file contains from introduction to conclusion pages and result shows 6% (6 PERCENTAGE) of plagiarism in the dissertation.

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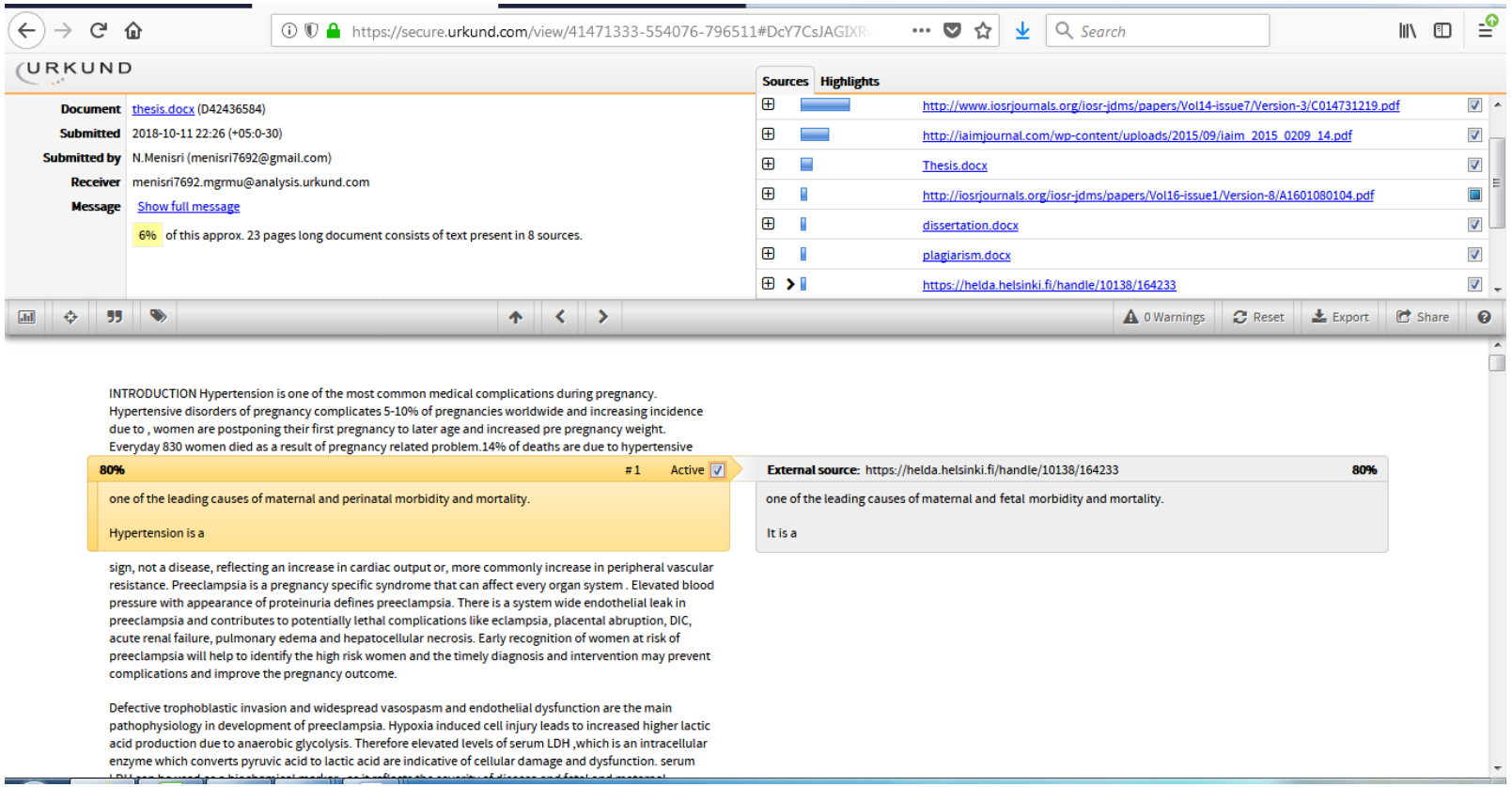
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INTRODUCTION Hypertension is one of the most common medical complications during pregnancy. Hypertensive disorders of pregnancy complicates 5-10% of pregnancies worldwide and increasing incidence due to , women are postponing their first pregnancy to later age and increased pre pregnancy weight. Everyday 830 women died as a result of pregnancy related problem.14% of deaths are due to hypertensive
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Active
one of the leading causes of maternal and perinatal morbidity and mortality.
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sign, not a disease, reflecting an increase in cardiac output or, more commonly increase in peripheral vascular resistance. Preeclampsia is a pregnancy specific syndrome that can affect every organ system . Elevated blood pressure with appearance of proteinuria defines preeclampsia. There is a system wide endothelial leak in preeclampsia and contributes to potentially lethal complications like eclampsia, placental abruption, DIC, acute renal failure, pulmonary edema and hepatocellular necrosis. Early recognition of women at risk of preeclampsia will help to identify the high risk women and the timely diagnosis and intervention may prevent complications and improve the pregnancy outcome.
Defective trophoblastic invasion and widespread vasospasm and endothelial dysfunction are the main pathophysiology in development of preeclampsia. Hypoxia induced cell injury leads to increased higher lactic acid production due to anaerobic glycolysis. Therefore elevated levels of serum LDH ,which is an intracellular enzyme which converts pyruvic acid to lactic acid are indicative of cellular damage and dysfunction. serum

DECLERATION

I solemnly declare that the dissertation titled " **CORRLEATION OF ELEVATED SERUM LDH LEVELS WITH ADVERSE MATERNAL AND PERINATAL OUTCOME IN PREECLAMPSIA"** was done by me from MAY 2017 TO JULY 2018. Under the guidance and supervision of prof. **DR. M.G.R Medical University** towards the partial fulfilment of the requirement for the award of MS degree in Obstetrics and Gynecology (Branch –II).

DR.MENISRI N

Date:

Place:

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I deeply express my sincere appreciation and acknowledgment to all assistant professors in the Department of Obstetrics and Gynaecology who had helped me for the past three years in the compilation and preparation of thesis, which alone had made this possible.

I take this opportunity to thank many patients who have allowed me to intrude upon their suffering and their case details. I cannot name them, for reasons of confidentiality, but I do thank them most sincerely.

Last but not the least i would thank almighty god for blessing in every part of my thesis.

CONTENTS

INTRODUCTION

Hypertension is one of the most common medical complications during pregnancy. Hypertensive disorders of pregnancy complicates 5-10% of pregnancies worldwide and increasing incidence due to , women are postponing their first pregnancy to later age and increased pre pregnancy weight. Everyday 830 women died as a result of pregnancy related problem.14% of deaths are due to hypertensive disorders complicating pregnancy. Hypertensive disorders remain one of the leading causes of maternal and perinatal morbidity and mortality.

Hypertension is a sign, not a disease, reflecting an increase in cardiac output or, more commonly increase in peripheral vascular resistance. Preeclampsia is a pregnancy specific syndrome that can affect every organ system. Elevated blood pressure with appearance of proteinuria defines preeclampsia. There is a system wide endothelial leak in preeclampsia and contributes to potentially lethal complications like eclampsia, placental abruption, DIC, acute renal failure, pulmonary edema and hepatocellular necrosis. Early recognition of women at risk of preeclampsia will help to identify the high risk women and the timely diagnosis and intervention may prevent complications and improve the pregnancy outcome.

Defective trophoblastic invasion and widespread vasospasm and endothelial dysfunction are the main pathophysiology in development of preeclampsia.

Hypoxia induced cell injury leads to increased higher lactic acid production due to anaerobic glycolysis. Therefore elevated levels of serum LDH ,which is an intracellular enzyme which converts pyruvic acid to lactic acid are indicative of cellular damage and dysfunction.

serum LDH can be used as a biochemical marker , as it reflects the severity of disease and fetal and maternal outcome. Identifying high risk patients with elevated LDH and their close monitoring and prompt management may prevent complications with subsequent decrease in maternal and perinatal morbidity and mortality.

AIM AND OBJECTIVES

AIM

To Study the correlation between the elevated serum lactate dehydrogenase level with the severity of disease and maternal and perinatal outcome in preeclampsia.

OBJECTIVE

1. Correlation of the levels of serum lactate dehydrogenase with severity and maternal and fetal complications of preeclampsia.
2. Role of serum LDH as a biochemical marker in preeclampsia so as to modify the treatment and to decrease the maternal morbidity and mortality.

REVIEW OF LITERATURE

Hypertension in pregnancy is one of the deadly triad –haemorrhage, hypertension and infection, contributing to maternal mortality and

morbidity. It complicates 5-10% of pregnancies. According to World health organisation (WHO) ,16% of maternal death were attributed to hypertensive disorder in developed countries. In united states, 7.4% of 2009 maternal deaths were related to preeclampsia and eclampsia.

The national high blood pressure Education programme (NHBPEP) classified hypertensive disorders in pregnancy into four types. ACOG (2013) has retained the basic classification and it describes four types as:

1. Preeclampsia and Eclampsia syndrome

2.Chronic hypertension of any etiology

3.Preeclampsia superimposed on chronic hypertension

4.Gestational hypertension-definitive evidence for the preeclampsia does not develop and hypertension resolves by 12 weeks postpartum.

DIAGNOSTIC CRITERIA

GESTATIONAL HYPERTENSION –

Blood pressure more than systolic Bp more than 140mmHg and diastolic Bp more than 90mmHg after 20 weeks of gestation in a women with previously normal pressure. Bp should be more than 140/90mmHg on at least two occasions, measured at 6 hours apart.

PREECLAMPSIA

Hypertension with proteinuria (≥300mg/24 hr.) / urine protein:creatinine ratio ≥0.3/persistent 1+ in dipstick. Proteinuria is an important diagnostic criterion .some women with preeclampsia may not have overt proteinuria. The Task Force (2013) suggested other diagnostic criteria including:-

- Thrombocytopenia – less than 1,00,000/µl
- Renal insufficiency – serum.creatinine >1.1mg/dl or doubling of baseline
- Liver involvement – elevated serum transaminase –twice normal
- Cerebral symptoms –Headache, visual disturbances, convulsions.
- pulmonary edema.

Preeclampsia is a multisystem disorder causing widespread vascular endothelial dysfunction and vasospasm. It leads to transudation of plasma, ischemia and thrombotic sequale.

INCIDENCE

Incidence of preeclampsia depends on

- Race, ethnicity, parity, genetic predisposition.
- Environmental, socioeconomic and seasonal influences (*Lawlor, 2005; palmer1999).*

Nulliparas and young age women are more prone to develop preeclampsia. *"The Maternal-fetal medicine unit* "study in 2300 nulligravida, gave the incidence of 5%in whites, 9% in Hispanic and 11 % in African-American women. *Staff and co-workers (2014)* reviewed worldwide studies and estimated the incidence of preeclampsia as 3-10% in nulliparous women.

RISK FACTORS

Along with above mentioned, other risk factors associated with preeclampsia are

- Obesity ,Maternal age, multifetal gestation
- Hyperhomocystenemia ,metabolic syndrome
- Previous history of PIH ,Pre-existing medical disorders like chronic hypertension, diabetes, immunological disease-SLE and antiphospholipid antibody syndrome.

Women with BMI >35mg/m² have the risk of 13.3% to develop preeclampsia when compared to BMI<20/m² (4.3%).Incidence of preeclampsia in twin pregnancy is 13% when compared with singleton pregnancy (5%). In the United States, the incidence of preeclampsia is 1.8% among white women and 3% in black women. Extremes of age grouped women have increased risk of preeclampsia. There is increased the risk of preeclampsia in a second pregnancy from 14.1% to 25.3% in

women with preeclampsia in a first pregnancy, with delivery between 32 and 36 weeks' gestation.

An analysis of 456,668 singleton births found that early-onset (<34 weeks) and late-onset (≥34 weeks) preeclampsia shared some etiologic features, but their risk factors and outcomes differed.

Shared risk factors for early- and late-onset preeclampsia are :-

Older maternal age , Hispanic race, Native American race, and male fetus.

Risk factors associated with early-onset preeclampsia are:-

Black race, chronic hypertension, and congenital anomalies.

Risk factors associated with late-onset preeclampsia are:-

younger maternal age, nulliparity, and diabetes mellitus.

The incidence of preeclampsia increased as gestation progressed and the rate for early-onset preeclampsia was 0.38% compared with 2.72% for late-onset preeclampsia. Early-onset preeclampsia was significantly associated with a high risk of fetal death (adjusted odds ratio [AOR], 5.8), but not late-onset preeclampsia (AOR, 1.3). whereas, the AOR for perinatal death or severe neonatal morbidity was significant for both early-onset (16.4) and late-onset (2.0).Smoking reduces the risk for hypertension in pregnancy (*Bainbridge,2005;Zhang,1999).*It is due to up regulation of placental

adrenomedullin expression ,that regulates the volume haemostasis.(*Kraus &associaties,2013).*

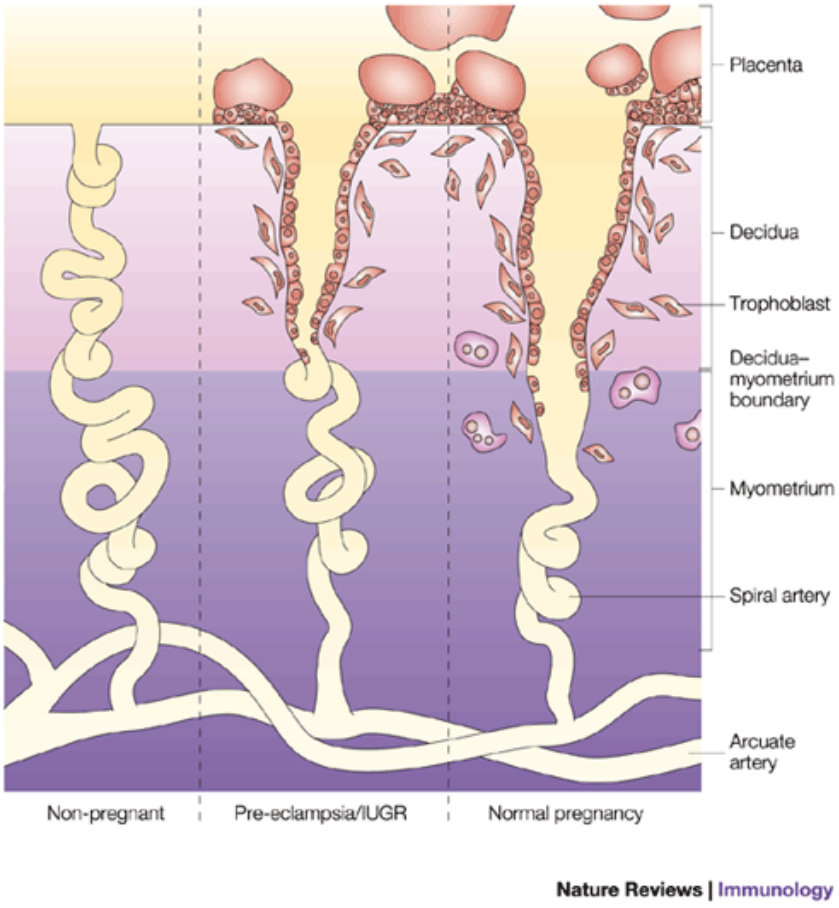
ETIOLOGY

Number of mechanism were proposed . currently important are-

- Abnormal trophoblastic invasion
- Immunological factors
- Maternal maladaptation to cardiovascular or inflammatory changes of normal pregnancy
- Genetic factors.

ABNORMAL TROPHOBLASTIC INVASION

In normal placentation there is extensive remodelling of spiral arterioles in decidua basalis. Trophoblastic cells replace the vascular endothelial and muscular lining and transform the small, muscular arterioles to large capacitance and low-resistance vessels. This allows increased blood flow to the maternal-fetal interface. This remodelling of arterioles begins in the first trimester and ends by 18-20 weeks gestation. Whereas in preeclampsia there is incomplete trophoblastic invasion of spiral arterioles. studies showed that degree of incomplete trophoblastic invasion of the spiral arteries is directly correlated with the severity of maternal hypertension. (*Madazali,2000)*



IMMUNOLOGICAL MALADAPTATION

The survival of the fetus which is an semiallogenic graft to mother is due to immunological neutrality at maternal –fetal interface. In preeclampsia there is dysregulation of maternal tolerance to paternally derived placental and fetal antigens(*Erlebacher,2013).* The histological changes at maternal –placental interface are similar to those seen in acute graft rejection. Factors attributed to this dysregulation are

-immunisation from previous pregnancy

-some inherited human leucocyte antigen (HLA) and natural killer (NK) cells receptor halotypes

-shared susceptible genes with hypertension and diabetes.

Redman and colleagues (2014) studied that in preeclampsia, extravillous trophoblasts express reduced amounts of immunosuppressive nonclassic HLA-C. Also in normal pregnancy there is increased activity of Th2-helper cells (humoral mediated immunity) in relation to Th1 cells. Whereas in preeclampsia Th1 activity is increased and the Th1:Th2 ratio changes.

GENETIC FACTORS

Preeclampsia is a multifactorial polygenic disorder. In a study conducted by *Ward and Taylor (2014)*, 20-40% risk of developing preeclampsia for the daughters of preeclamptic mothers.11-14% risk for sisters and 22-47% risk for twins. Interactions of hundreds of inherited genes predisposes to preeclampsia. Candidate genes commonly associated with preeclampsia syndrome are

MTHFR(C677T)-*methyl tetrahydofolate reductase,*
F5(leiden)-*factor 5 leiden*,
AGT(M235T) *Angiotensinogen,*

NOS3(Glu 298 Asp) –*Endothelial nitric oxide*,
F2 (G20210A)-*Prothrombin (facto II),*
ACE-*Angiotensin converting enzyme*,
CTAL4 – *Cytotoxic T*-lymphocyte *associated protein*,
LPL-*Lipoprotein lipase ,*

SERPINE 1-*Serine peptidase inhibitor.*

PATHOGENSIS

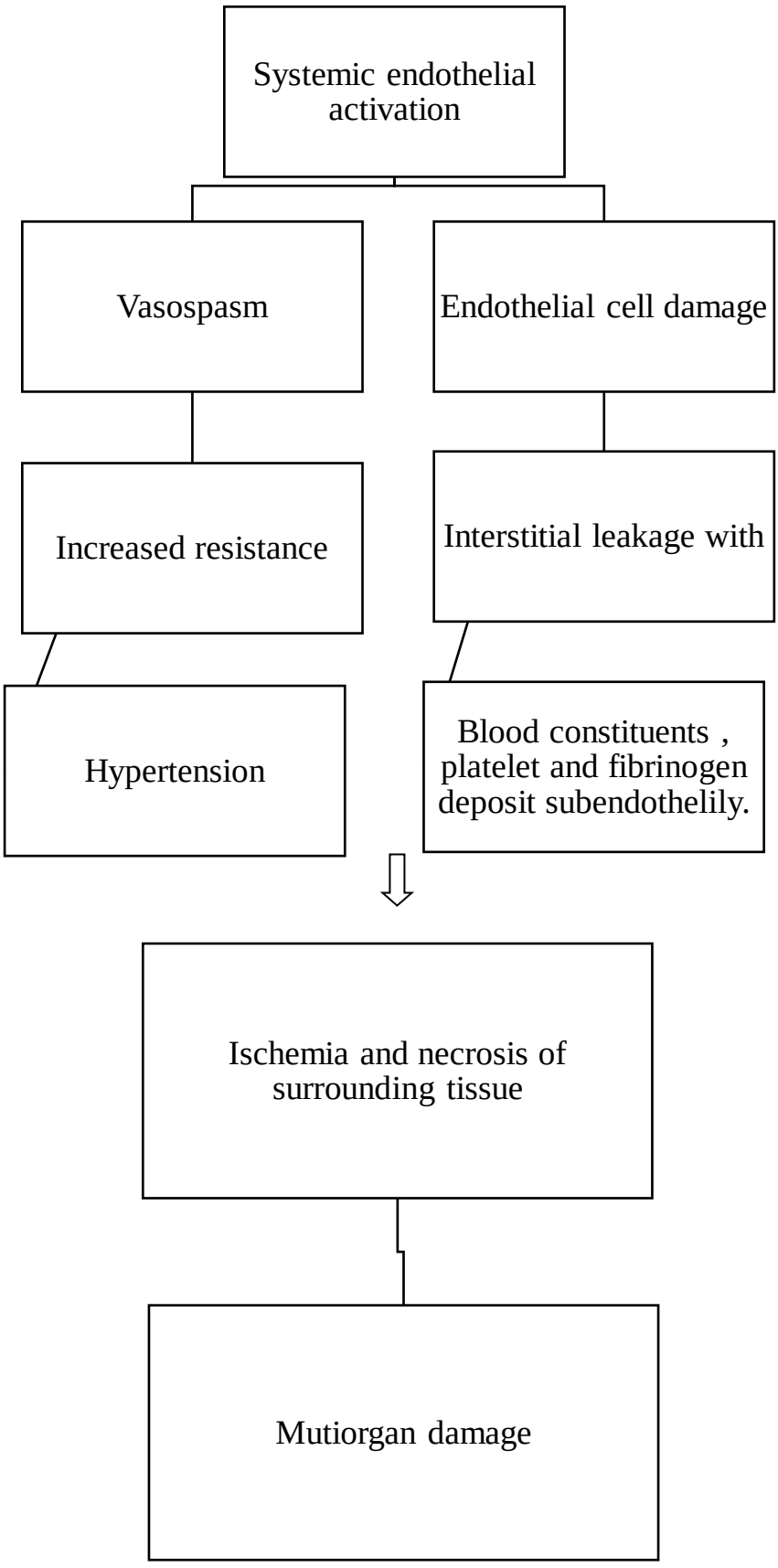
According to Redman and co-workers, the two stage disorder theory of preeclampsia is

Stage 1-faulty endovascular remodelling that downstream and cause stage 2

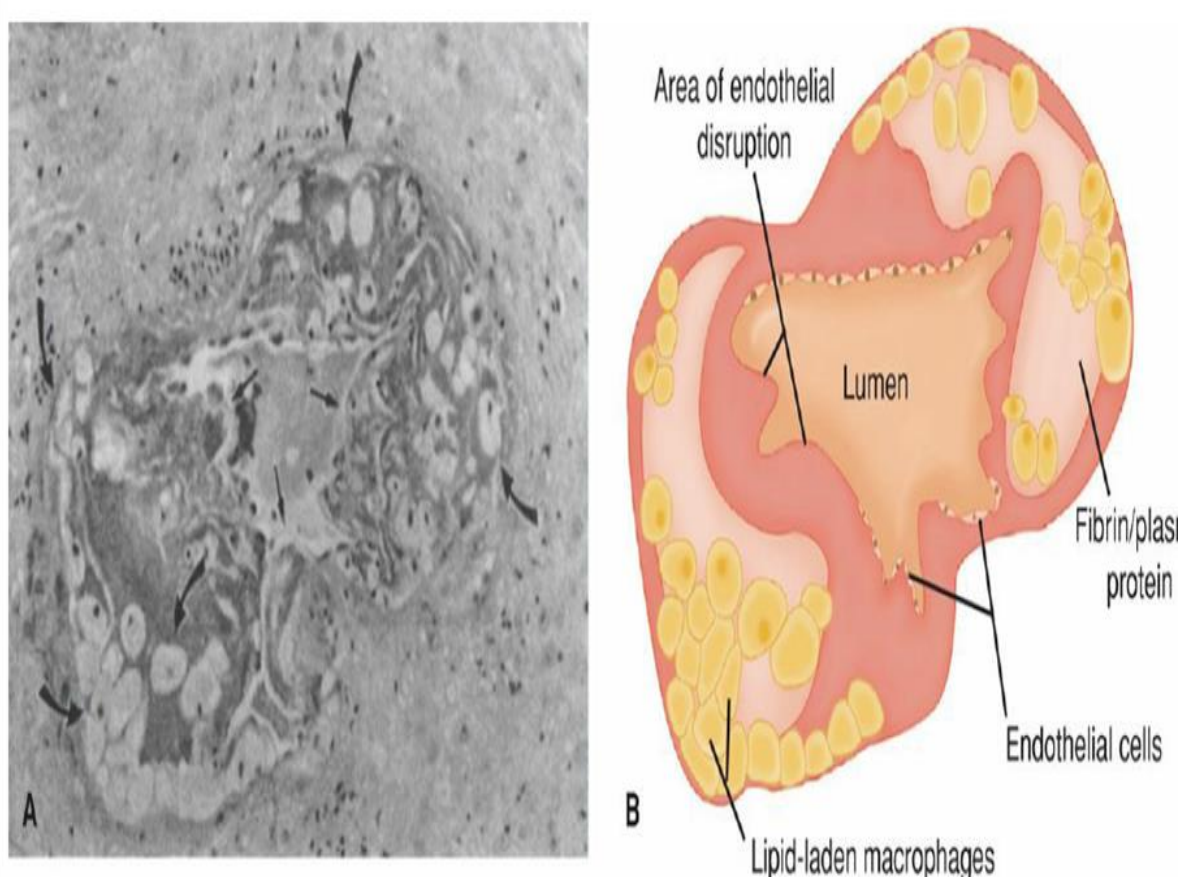
Stage 2-endothelial cell activation which is susceptible by pre-existing maternal conditions like cardiovascular , renal disease, diabetes ,immunological / hereditary influences.

Abnormal trophoblastic invasion resulting in narrow spiral arteries leads to placental hypoperfusion from the release of placental debris and micro particles that cause an exaggerated systemic inflammatory response. These result in widespread vasospasm, endothelial damage, capillary leak and sub endothelial deposition of blood constituents (platelet and fibrinogen) hypercoagulability, and platelet dysfunction, all of which contribute to organ dysfunction and the various clinical features like thrombocytopenia,

edema and proteinuria. .



Dewolf and co-workers(1980) studied the arteries from implantation site and reported the following early preeclamptic changes under electron microscopy –endothelial damage ,leakage of plasma constituents into vessel wall , proliferation of myointimal cells , atherosis (lipid laden macrophages) and medial necrosis.



Electron microscopic view of endothelial damage showing areas of endothelial disruption and lipid laden macrophages.

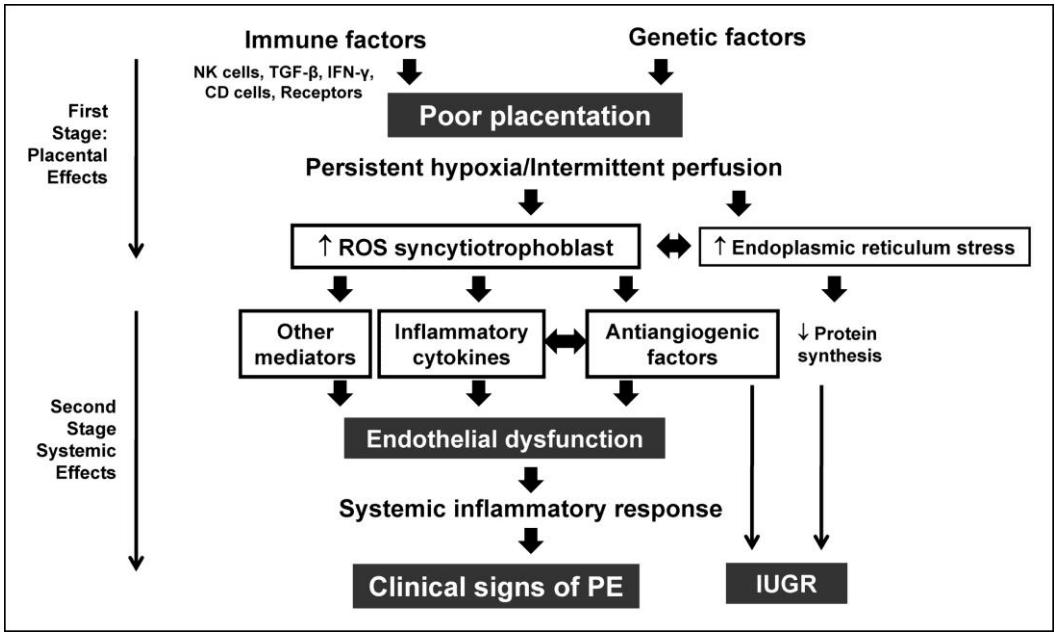
Endothelial cell activation

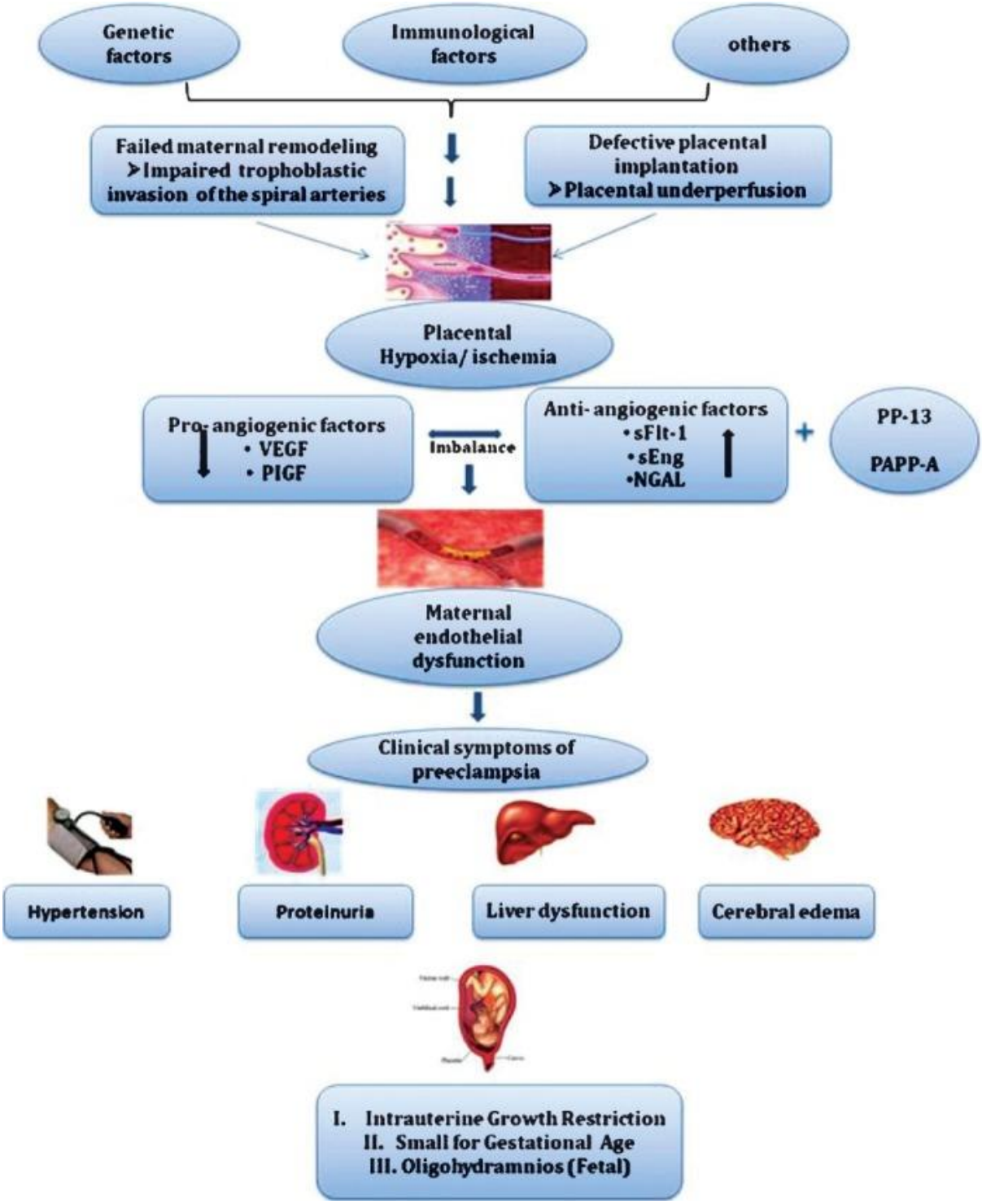
Intact endothelium has anticoagulant properties. Nitric oxide is synthesised by endothelium . It blunt the response of vascular smooth muscle by agonist and helps to maintain the low vascular resistance for fetoplacental circulation. Whereas injured endothelium ,promotes coagulation and increased sensitivity to vasopressor due to reduced nitric oxide synthesis. In addition, endothelial prostaglandin (PGI2) synthesis reduced and increased synthesis of thromboxane A2 results in TXA2:PGI2 ratio declines leads to increased sensitivity to infused vasopressors.

Angiogenic and antiangiogenic factors

Number of pro and antiangiogenic factors are involved in Placental vasculogenesis. Hypoxia at the uteroplacental interface leads to the release of antiangiogenic factors like Soluble Fms like tyrosine kinase(sFlt-1) and soluble endoglin(sEng) which inactivate and decrease free PIGF and VEGF concentrations.

These antiangiogenic factors ,metabolic factors and inflammatory mediators like cytokines – TNF-α (tumour necrosis factor –α), interleukins (IL) provoke endothelial cell injury and oxidative stress .this leads to production of reactive oxygen species , free radicals, lipid macrophages and activation of micro vascular coagulation and multiple organ damage.

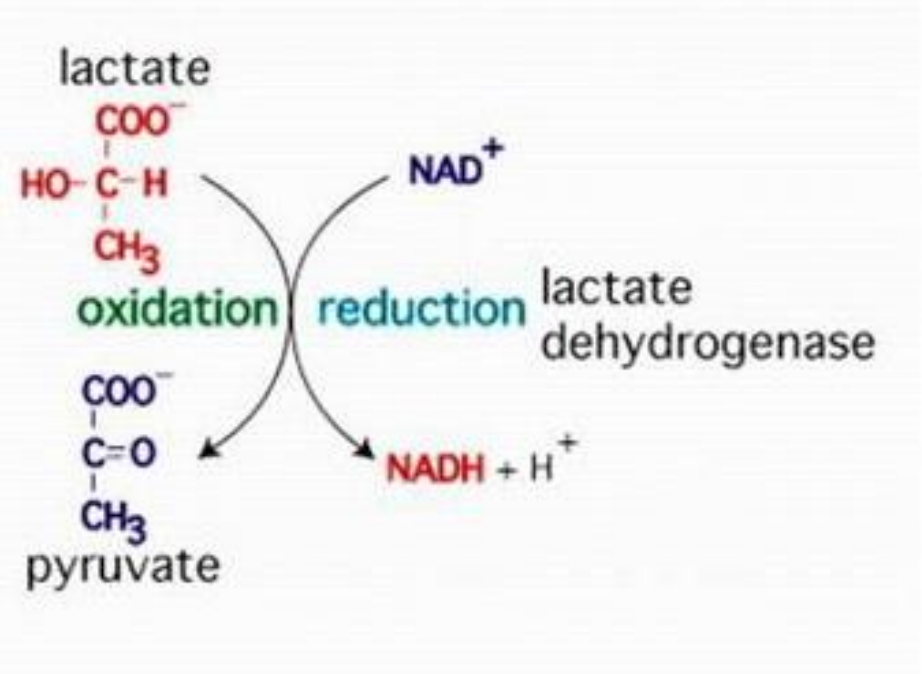

Immune factors
NK cells, TGF-β, IFN-γ, CD cells, Receptors
Genetic factors
Poor placentation
First Stage: Placental Effects
Persistent hypoxia/Intermittent perfusion
↑ ROS syncytiotrophoblast
↑ Endoplasmic reticulum stress
Other mediators
Inflammatory cytokines
Antiangiogenic factors
↓ Protein synthesis
Second Stage Systemic Effects
Endothelial dysfunction
Systemic inflammatory response
Clinical signs of PE
IUGR



ETIOPATHOGENESIS OF PREECLAMPSIA

ROLE OF LACATAE DEHYDROGENASE

Lactate dehydrogenase is an intracellular enzyme found in body tissues such as lungs , kidney, liver ,heart ,muscles and blood cells. It catalyses the interconversion of NADH and NAD+. It converts pyruvate ,the final product of glycolysis to lactate .



Under anaerobic conditions the NADH cannot be reoxidised through the respiratory chain and the pyruvate is reduced to lactate, which is catalysed by lactate dehydrogenase enzyme. This permits the oxidation of NADH, permitting another molecule of glucose to undergo glycolysis. Glycolysis in erythrocytes always terminate in lactate production due to absence of mitochondria, whereas in other tissues like brain, renal medulla, retina and skin derives much of their energy from glycolysis and oxidise lactate.

Serum lactate levels also increased in septic shock, cachexia. Liver, kidney and heart normally takes up lactate and oxidise it, under hypoxic conditions. LDH levels are increased in conditions causing tissue hypoxia and cellular damage.

Normal adult range 0-250 U/L.

In preeclampsia , since there was widespread cellular hypoxia and tissue damage due to vasospasm and endothelial cell injury will result in increased serum levels of lactate dehydrogenase. Therefore measurement of serum LDH levels will predict the of severity cellular damage and multiorgan damage and following complications which was taken in our study. Elevated levels of serum LDH were found in association with Preeclampsia with following studies.

STUDY 1-

A Case control study was done in the Department of Obstetrics and Gynaecology., SMGS Hospital,Govt. Medical College, Jammu, with 200 women in antenatal period after 28weeks of gestation. They divided them into two groups ,those with normal blood pressure and in second group ,those with preeclampsia and eclampsia. They were further subdivided as mild and severe preeclampsia depending on the clinical features after excluding the criteria of patients with gestation of less than 20 weeks ,

diabetes ,renal disease , epilepsy , liver disorder, haemolytic anemia, muscle injury , trauma, bone fracture, and on drugs (aspirin, fluoride, narcotics). The patients were followed until delivery in OPD and in wards. Many number of patients in group -1 had spontaneous onset of labour while in patients in group 2 had induction of labour. The study showed that elevated blood pressure was associated with higher levels of serum LDH with P value <0.01. On stastical analysis, with elevated levels of LDH which was subdivided into three cut-off values , (<600 U/l , 600-800 IU/l,>800 IU/l) the occurrence of impending eclampsia, abruption, HELLP Syndrome, primary PPH , vaginal wall hematoma , intracranial haemorrhage and Pulmonary edema was high as compared to control group (esp. with serum LDH >800IU/l.). Simultaneously fetal and neonatal outcome was observed in relation to LDH levels . Fetal complications like IUGR was 24.1% and IUD 17.3%. Neonatal complications (i.e. LDH >800IU/l), 10.4% had RDS, 3.4% had MSAF, and 3.4% had Hypoxic Ischemic encephalopathy and perinatal death with LDH level >800 IU/L. Thus this study concluded that, acute clinical conditions that endanger maternal and fetal life in Preeclampsia correlate well with serum LDH levels.

STUDY –II

This study was conducted in the Department of Physiology, Dhaka Medical College (DMC). In this study,105 pregnant women were selected , aged 18 to 35 years, with 28-40 weeks of gestation .Among the 70 were diagnosed as preeclamptic women . They divided in to two groups women with mild preeclampsia i.e. with systolic BP- >140 to <160mmHg, Diastolic BP - >90 to < 110mm Hg with or without Proteinuria and those with severe preeclampsia (Systolic blood pressure >160mm Hg, Diastolic blood pressure – >110mm Hg with significant proteinuria (> 5gm/24 hrs. or > 2+ on dipstick) .They included 35 healthy pregnant women in third trimester as control. The results were elevated serum LDH level(>200 IU/L) was found in 82.9% of women with mild preeclampsia and 91.4% of women with severe preeclampsia , but in no one of the control women had elevated serum LDH levels. From the results it was concluded that elevated serum LDH levels is associated with severity of preeclampsia. In preeclampsia women with progressively increasing LDH levels indicates the progression of cellular injury . Therefore estimation of serum LDH level estimation in women with preeclampsia is useful for the proper management and to decrease the maternal and fetal mortality and morbidity.

STUDY –III

A prospective study was conducted in King Hussein Medical Centre (KHMC). 111 women with preeclampsia (62 with severe pre-eclampsia and 49 with mild preeclampsia) and 60 healthy women with normal blood pressure as controls were studied. They divided the patients into three groups. Group I includes 60 healthy pregnant women in third trimester, group II includes 49 patients with mild preeclampsia women, and group III includes 62 patients with severe pre-eclampsia.

According to age, gravidity, parity, maternal weight, and hemodynamic and laboratory results , three groups were matched. Group III were further subdivided into 3 categories according to the serum lactic dehydrogenase levels -LDH (<600, 600–800, and >800 IU/l). It was done to identify the group with high risk to develop complications. Exclusion criteria included was Pregestational hypertension , diabetes, , thyroid disease, liver disease and renal disease.

These patients were followed in terms of symptoms and complications of pre-eclampsia like eclampsia ,abruption, intracranial haemorrhage and fetal outcome. Mild preeclampsia patients were admitted to the hospital for 48 hours for blood pressure measurement and investigations and they were discharged if there was no worsening or aggravation of the disease. The results were patients with severe

preeclampsia showed statistically significant increase in terms of systolic and diastolic pressure, urine albumin ,uric acid, serum LDH, and liver enzymes, when compared with group I and II. Serum LDH levels >600 IU/l were seen in 8.3% of the normotensive, 12.2% of the women with mild preeclampsia and 54.8% of women with severe pre-eclampsia.in patients with severe preeclampsia, headache was seen in 69.4% , vomiting in 40.3% , blurred vision in 32.3% , and epigastric pain in 30.6%. Patients with serum lactate dehydrogenase more than 800 IU/l had significant increase in frequency of imminent symptoms like epigastric pain, vomiting (p<0.01) and complications in terms of eclampsia, abruptio placenta, HELLP syndrome, DIC, pulmonary edema and intracranial haemorrhage when compared with the other two groups, (p<0.001.The most frequent complication was eclampsia (30.8%), followed by HELLP syndrome and abruptio placenta. Severe pre-eclampsia women had 5-fold increase in perinatal mortality when compared with controls.

Patients with LDH >600 IU/l showed significant increase in the incidence of perinatal death (p<0.001). 64.4% of deaths was due to respiratory distress , followed by sepsis -16.9%, intraventricular haemorrhage 8.5% , necrotizing enterocolitis 6.8%, and congenital anomalies 3.4%. Intrauterine fetal death was seen in 4.8% of cases, prematurity in 77.9% and intrauterine growth restriction in 33.9%. From

the results, raised levels of serum LDH which is indicative of cellular damage can be used as a biochemical marker as it reflects severity of preeclampsia and the occurrence of complications, and fetal outcome. By detecting those high risk patients with increased LDH levels, close monitoring and optimal management can be done to reduce the maternal and fetal mortality and morbidity.

STUDY –IV

A study was conducted in the Department of Gynaecology and Obstetrics ,Lalla Ded Hospital, Government Medical College, Srinagar for a period of 18months. This observational study was conducted in two groups with Study Group of 100 antenatal patients with blood pressure ≥140/90mmHg and proteinuria ≥300mg/24hours and the Control Group of 100 normal pregnant women.

The patients included are those with Criteria of Primigravida, , age 20-35years, singleton pregnancy in third trimester. Patients with history of chronic hypertension, urinary tract infection ,molar pregnancy, pathological vaginal discharge were excluded from the study. detailed history, general and physical physical examination, routine investigations like Haemoglobin, platelet count, Bleeding time, Clotting time, Blood sugar, Kidney function test, Liver function test, Urine analysis, Ultrasonography, Electrocardiography were done. Then samples were

collected for the estimation of serum Lactate dehydrogenase level, then statistical analysis were done with the results and was described in terms of mean standard deviation and percentages. Mann-Whitney 'U' test and Chi square tests were applied for non-parametric data and the parametric data was analysed by student's t-test . All p-values of less than 0.05 were considered significant. The results showed that difference between the mean age as well as the mean gestational age in the study and the control group were not statistically significant.

The mean body mass index in the in the control group was 25.5± 2.2kg/m2 and the study group was 27.8± 1.6kg/m2.therefore the difference between the mean body mass index of the study group and the control group was statistically significant with p value <0.001. In this study, the mean systolic BP was 153.5±11.3 mmHg and the mean diastolic BP 100.8±10.2mmHg. whereas In controls mean systolic BP was 117.9±10.1 mmHg and mean diastolic BP was 75.2±6.4mmHg.The mean BP of patients in the study group was higher than the control group which was statistically significant. Mean haemoglobin level as well as the mean serum urea and the creatinine concentration in the study group was significantly higher than the control group which were statistically significant. The mean platelet count in the study group was lower than the control group and this difference was statistically significant. The Mean

24 hours urinary proteins in the study group (0.99±1.76g/day) was higher than the control group (0.16±0.10 g/day) which was statistically significant with p value of <0.001. Mean serum bilirubin and serum AST (Aspartate transaminase) , ALT (Alanine transaminase) of the study group was found to be higher in preeclampsia patients than the control group. 28% of pre-eclamptic patients (study group) had elevated serum lactate dehydrogenase levels, whereas only 2% of patients in control group had raised levels of serum LDH. The study group had serum LDH levels of 395.4±146.3 IU/L whereas the serum LDH levels of the control group was 307.2±68.2 IU/L which was statistically significant. The mean serum LDH level in severe preeclampsia patients was 563.7±162.5 IU/Land in patients with mild pre-eclampsia was 347.6±99.1IU/L which was significant statically with a p value of <0.001. severe pre-eclampsia patients with warning symptoms and signs (headache, vomiting ,blurring of vision, oliguria, epigastric pain, thrombocytopenia and elevated liver enzymes) had higher levels of serum lactate dehydrogenase levels (766±175.5 IU/L than those without warning symptoms and signs (375.9±116.4 IU/L) with p value of < 0.001 , which was significant. Thus this study concluded that preeclampsia patients had increased levels of serum lactate dehydrogenase levels when compared with antenatal patients with normal blood pressure and also the levels are increased with the increase in severity of pre-eclampsia and in those with complications.

Thus it can be used as added diagnostic test for early detection of increase in severity of preeclampsia and their maternal and fetal complications .

STUDY –V

A case control study was conducted in the Department of Obstetrics and Gynaecology and the Department of Biochemistry, King George Hospital, Visakhapatnam. A total of 150 pregnant women were included out of which 50 women with normal blood pressure and another 100 women with preeclampsia (50) and eclampsia (50). Preeclampsia women were subdivided into mild and severe preeclampsia.

Patients enrolled in the study were further divided into three groups based on their serum LDH levels as : <600 IU/l, 600– 800 IU/l and >800 IU/l. The subjects included were in the criteria of singleton pregnancy more than 28 weeks of gestation , 18 - 30 years of age. The exclusion criteria included are those with elevated blood pressure before 20 weeks of gestation , those with history of diabetes , renal and liver disease, stroke, coronary artery disease, haemolytic anomies, connective tissue disorders and multiple pregnancy. out of 100 cases ,20% had mild preeclampsia , 13.3% had severe preeclampsia and 33.3% cases had eclampsia. Serum LDH assay was done and the results were , 115 cases had serum LDH levels of <600 IU/l. out of which 29 patients had systolic BP 160 mm Hg and above, 28 patients had systolic BP 140 to 160 mm of Hg and 58

patients had normal systolic BP. 20 women had diastolic BP 110 mm Hg and above, 45 women had diastolic BP of 90-110 mm of Hg and 50 women had normal diastolic BP. those with serum LDH levels between 600 and 800 IU/l are 24 patients out of which , 19 patients had systolic blood pressure of >160 mm Hg and 5 patients had systolic blood pressure in the range of 140 to160 mm of Hg. Out of 24 patients with serum LDH levels 600 - 800 IU/l, 9 patients had diastolic BP 110 mm Hg or more and 15 patients had diastolic BP of 90-110 mm of Hg.The remaining 11 patients had serum LDH levels above 800 IU/l, out of which 9 patients had systolic BP 160 mm Hg and above and 2 patients had systolic BP of 140 to 160 mm Hg. 6 women had diastolic BP 110 mm Hg and above, 5 women had diastolic BP of 90-110 mmHg. After statistical analysis higher levels of serum LDH was associated with high systolic and diastolic BP with p value of <0.001.Mean serum LDH levels were higher in severe preeclampsia (636.20 ± 132.29 IU/L) and eclampsia patients (649.32 ±153.53 IU/L) than the control group (159.06 ± 41.93 IU/L). patients of mild preeclampsia had LDH levels <600IU/l.. Among the patients with LDH levels < 600 IU/L, two had postpartum haemorrhage and one had abruption placenta. whereas in those with who had LDH levels 600–800 IU/l , one women went for pulmonary edema and 5 patients of postpartum haemorrhage was documented. Among those with markedly increased levels of serum LDH

>800 IU/l, one patient had pulmonary edema ,two patients had abruption placenta and three patients had postpartum haemorrhage.

Therefore there was increase in maternal complications with increasing LDH levels which was statistically significant ($P < 0.001$). Perinatal outcome in relation to serum LDH was studied in terms of gestational age, mean birth weight and APGAR scores at 1min and 5 min .On statistical analysis, with higher levels of serum LDH,the average weight of babies were reduced. Likewise, the mean APGAR scores at 1 min and 5 min were lower in subjects with elevated serum LDH levels.

And also in terms of neonatal complications ,increase in serum LDL levels associated with neonatal complications. It was concluded in this study that increasing levels of serum LDH was associated with increase in maternal complications in preeclampsia and eclampsia. So it can be considered as prognostic tool in preeclampsia patients.

STUDY – VI

A comparative study was conducted in the department of Obstetrics and Gynaecology in CSM Medical University, Lucknow with study period of 1 year. Total of 146 pregnant women in third trimester were

studied.Group-1 consists of 39 normal pregnant women. Group 2 consists of preeclampsia patients which were further subdivided into mild preeclampsia (35), severe preeclampsia (36) and eclampsia (36).depending on the levels of serum lactate dehydrogenase into three groups(a) <600 IU/l (b) 600–800 IU/l (c) [800 IU/l. All the subjects were followed until delivery and immediate postpartum period and babies until neonatal period. After statistical analysis it was found that high diastolic pressure was associated with higher levels of serum LDH with p value of <0.001. eclampsia and severe preeclampsia patients had higher levels of serum LDH when compared with patients of mild preeclampsia and control group with statistical significance .Therefore there is increase in severity of the disease with increase in serum LDH levels in serum.

Maternal complications were was followed in terms of abruption placenta, HELLP syndrome, pulmonary embolism, pulmonary edema, renal failure and cerebrovascular accident. After statistical analysis ,there was increase in maternal complications with increasing LDH levels with P value < 0.001. perinatal outcome was studies in terms of mean gestational age at birth, mean birth weight, mean apgar score at 1 and 5 min and stillbirth and neonatal complications .

The mean gestational age and mean Apgar scores at 1 min and 5 min was found to be lower in patients with higher LDH levels. Therefore it

was conclude in this study increased serum lactate dehydrogenase are associated with maternal and fetal complications in preeclampsia and eclampsia patients.

MATERIALS AND METHODS

SOURCE OF STUDY :

The Study group consists of preeclamptic pregnant women who are admitted in the department of obstetrics and gynaecology, at Coimbatore medical college hospital.

DESIGN OF STUDY :

Prospective study

STUDY PERIOD :

May 2017 to April 2018.

SAMPLE SIZE : 200

INCLUSION CRITERIA :

Primi / Multigravida Antenatal women with pre-eclampsia (systolic blood pressure ≥140/90mmHg and proteinuria ≥300mg/24hours or urine dipstick ≥1+) , more than 20 weeks of gestation , 18- 35 years of age with singleton pregnancy.

EXCLUSION CRITERIA :

Antenatal mothers with hypertension at or before 20 weeks of Gestation. Patients with history of liver disease ,haemolytic disease, diabetes mellitus, multiple pregnancy, renal disease, stroke, connective tissue disorders, thyroid disorder, epilepsy , smoking alcohol behaviour and those on hepatotoxic drugs.

METHODOLOGY :

A prospective study in the department of obstetrics and gynaecology in collaboration with department of biochemistry in Coimbatore medical college hospital ,based on serum LDH levels in preeclampsia patients. informed consent was obtained from the patients. Detailed history including age, parity, previous medical disorders was elicited followed by physical examination including the measurement of blood pressure in the right arm, in sitting position with appropriate size cuff. patients with systolic blood pressure >140 mmhg and diastolic blood pressure of >90mmhg and those with proteinuria, measured by urine dipstick ≥1+ /24 hour urinary protein ≥300mg/24hours were enrolled in the study .based on inclusion and exclusion criteria 200 antenatal mothers with preeclampsia were subjected to the study. Then under aseptic precaution 3ml of blood sample were taken from the patients who were enrolled in the study and sent for serum lactate dehydrogenase assay.

Based on their serum LDH levels all the subjects are followed until delivery and early postpartum period ,in terms of complications like eclampsia , cortical vein thrombosis , abruption placenta , acute renal failure ,pulmonary edema and HELLP syndrome and babies are followed till early neonatal period, in terms of intrauterine death , intrauterine growth retardation and iatrogenic prematurity.

OBSERVATIONS AND RESULTS

AGE DISTRIBUTION

Table 1

AGE IN YEARS	NO OF PATIENTS	PERCENTAGE
< 20 yrs.	33	16.50%
21-25 yrs.	116	58%
26-30 yrs.	51	25.50%

The table depicts that 58% of patients falls in the age group of 21-25 years and 25.50% fall in the age group of 26-30 years of age and 16.5% of patients falls in the age group of <20years.

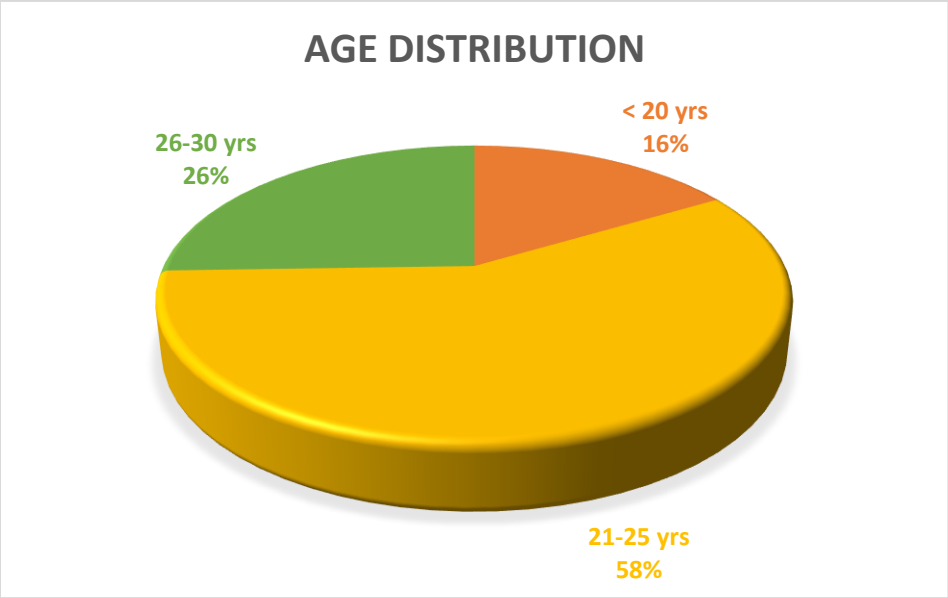


Figure 1

PARITY

Table 2

PARITY	NO OF PATIENTS	PERCENTAGE
PRIMI	102	51.00%
GRAVIDA 2	91	46%
GRAVIDA 3	7	3.50%

This table results shows that out of 200 subjects ,102 (51%) patients belong to primi gravida, 91 patients (46%) ,7 patients (3.5%) belongs to the second and the third gravida, respectively.

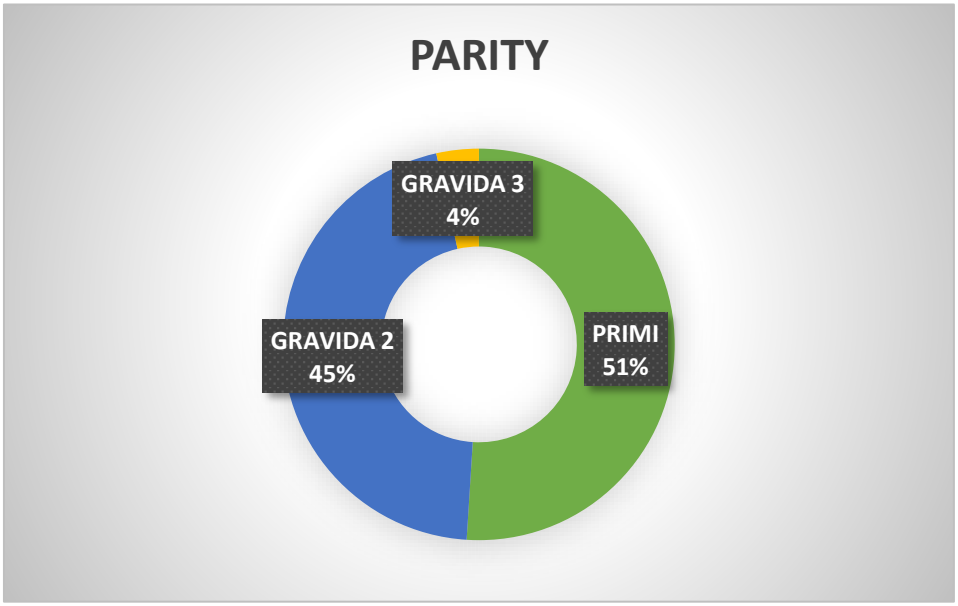


Figure 2

Thereby, majority of the preeclampsia patients in this study belongs to primigravida.

GESTATIONAL AGE

Table 3

GESTATIONAL AGE	NO OF PATIENTS	PERCENTAGE
< 28 WEEKS	9	4.50%
29-36 WEEKS	92	46%
> 36 WEEKS	101	50.50%

In this study , 50.5% of women were delivered in the gestational age of >36 weeks , 46% of women were delivered in the gestational age group of 29-36 weeks and the remaining 4.5% were in < 28 weeks of gestation, which was depicted as pie diagram below(figure .3)

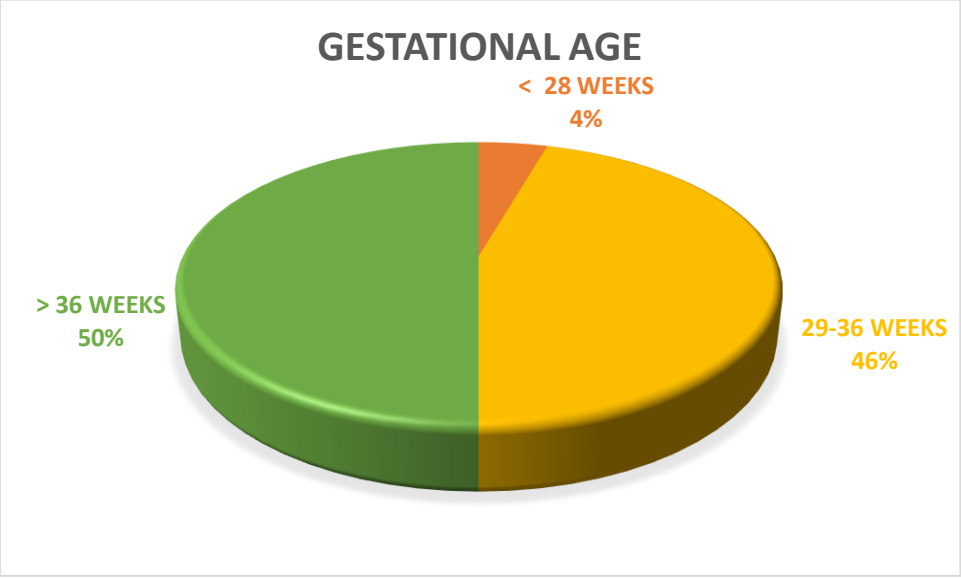


Figure 3

MODE OF DELIVERY

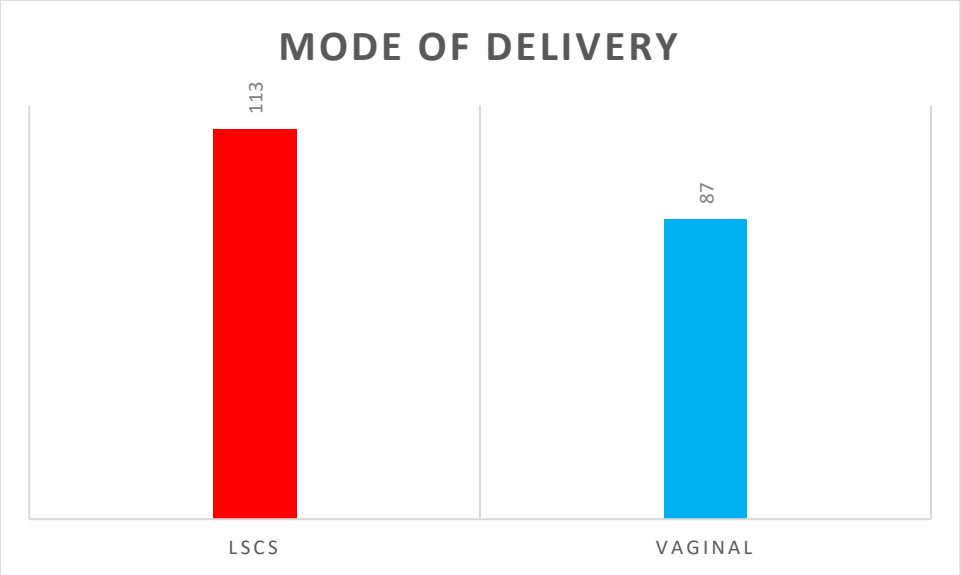


Figure 4

In this study , out of 200 preeclampsia patients ,113 patients are delivered by lower segment caesarean section which is 56.5% and the remaining 87 patients (44%) are delivered by vaginal delivery which is depicted in the following bar diagram.(figure .4)

Table 4

MODE OF DELIVERY	NO OF PATIENTS	PERCENTAGE
LSCS	113	56.50%
VAGINAL	87	44%

SEVERITY OF PRE ECLAMPSIA

Table 5

PRE ECLAMPSIA	NO OF PATIENTS	PERCENTAGE
NON-SEVERE	98	49.00%
SEVERE	102	51%

Out of 200 patients in our study, 98 patients(49%) are in the category of Non severe preeclampsia (systolic BP in the range of 140-160 mmhg and diastolic BP of 90-110 mmhg) and the remaining 102 patients (51%) were in the category of severe preeclampsia (systolic BP of 160mmhg and above and the diastolic BP of 110 mmhg and above)(figure.5)

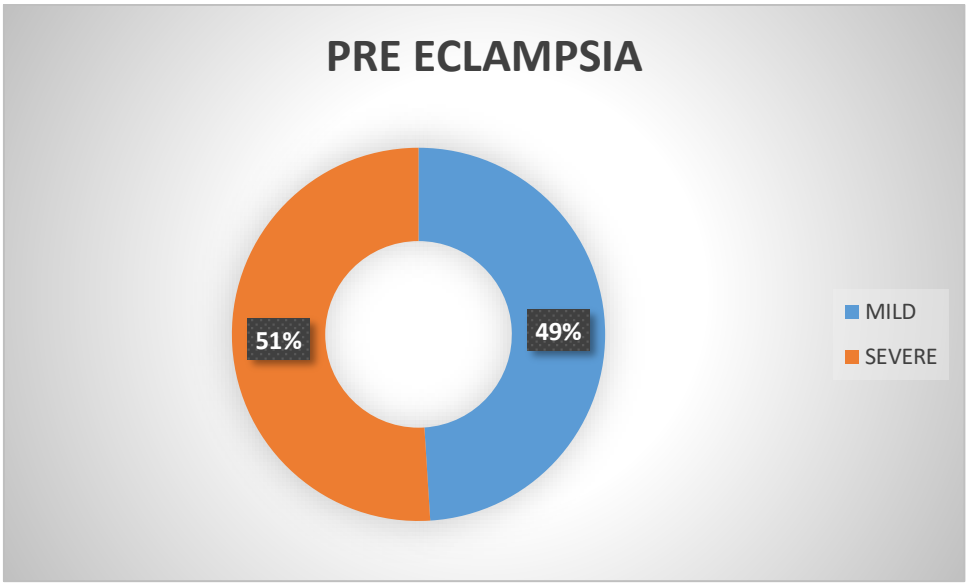


Figure 5

BIRTH WEIGHT

Table 6

BIRTH WEIGHT	NO OF PATIENTS	PERCENTAGE
< 1 KG	8	4.00%
1-2 KG	58	29%
2-3 KG	116	58.00%
> 3 KG	18	9%

Out of 200 patients ,the birth weight of babies born to them are 2-3 kg in 116 women (58%),between 1-2 kg in 58 patients (29%) ,18 (9%) and 8(4%) patients with birth weight of >3kg and <1kg respectively.(figure.6).

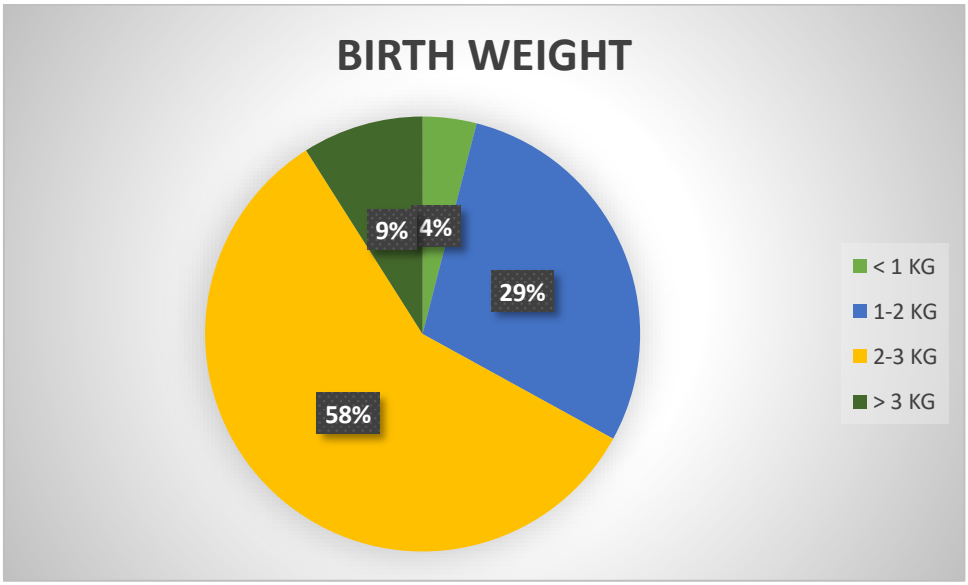


Figure 6

SERUM LDH LEVELS

Table 7

SERUM LDH	NO OF PATIENTS	PERCENTAGE
300- 600	50	25.00%
600-800	78	39%
> 800	72	36.00%

Out of 200 patients in whom Serum Lactate dehydrogenase levels measured,78 patients had serum LDH levels in the range of 600-800 IU/l (39%) ,72 patients had serum LDH of >800 IU/l (36%) and the remaining 50 patients had LDH levels 300-600IU/l (25%), which is depicted in the following figure.7

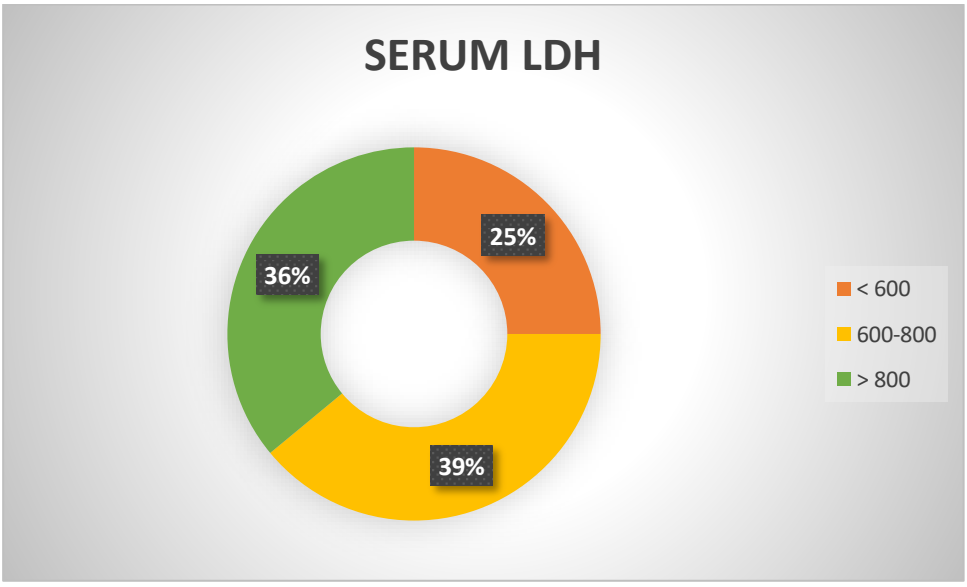


Figure 7

PREECLAMPSIA VS LDH LEVELS

Table 8

PRE ECLAMPSIA	SERUM LDH LEVELS		
	300- 600	600-800	> 800
NON-SEVERE	36	31	31
SEVERE	14	47	41
KRUSKAL WALLIS TEST			
P VALUE - 0.001			
SIGNIFICANT			

To assess the severity of preeclampsia in comparison with serum levels of lactate dehydrogenase, subjects were divided into three subgroups based on the LDH levels as i) those with LDH levels 300-600 IU/l ii) 600 – 800 IU/l iii) >800IU/l. On statistical analysis , it was found that as shown in the table.8,

- In those with LDH levels in the range of 300-600 IU/l, 36 women had Non severe preeclampsia and 14 women had severe preeclampsia .
- Among those who had LDH levels in the range of 600-800 IU/l , 31 women had Non severe preeclampsia and 47 women had severe preeclampsia.
- Those with >800 IU/l , 31 patients had Non severe preeclampsia and 41 patients had severe preeclampsia.

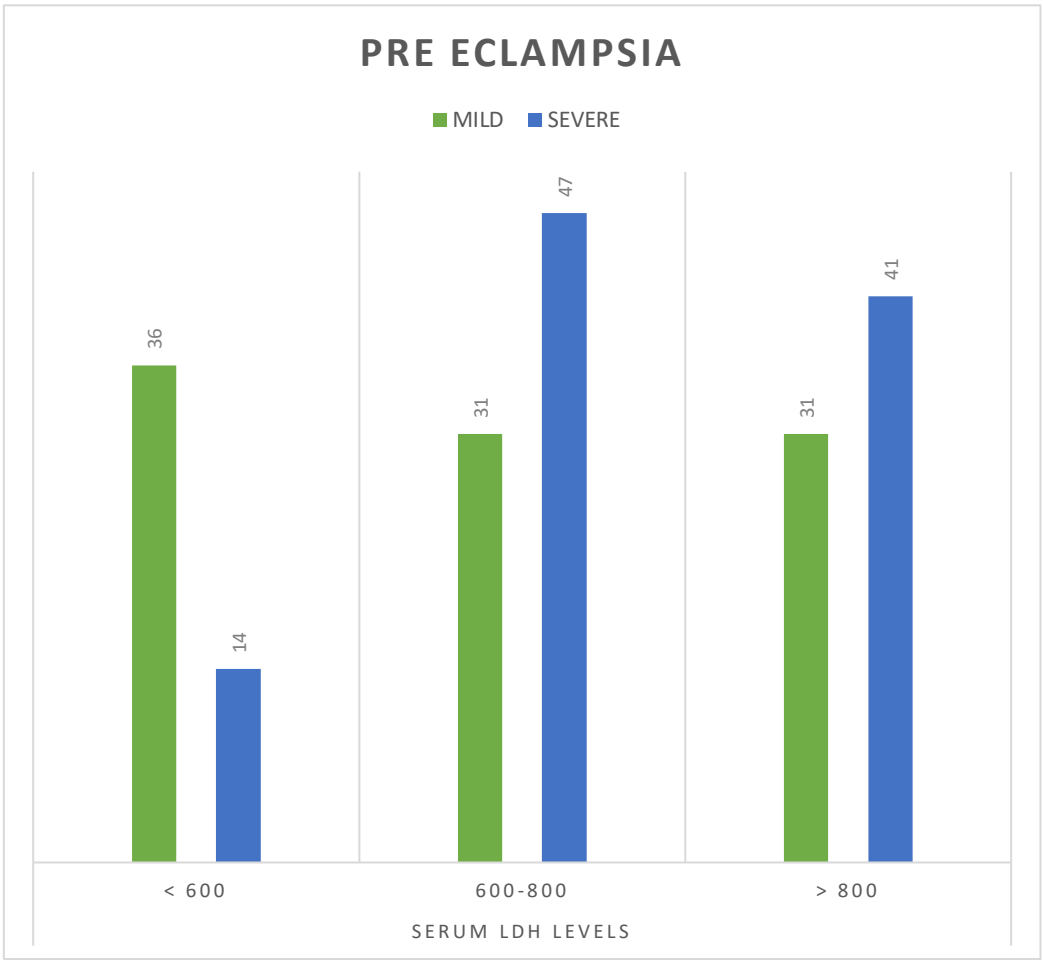

PRE ECLAMPSIA
MILD
SEVERE
36
14
31
47
31
41
< 600
600-800
> 800
SERUM LDH LEVELS

Figure 8

SEVERITY OF PREECLAMPSIA VS MEAN LDH LEVELS

Table 9

PRE ECLAMPSIA	SERUM LDH LEVELS	
	MEAN	SD
NON-SEVERE	793.93	681.37
SEVERE	960.39	528.72
UNPAIRED T TEST		
P VALUE - 0.05		
SIGNIFICANT		

Likewise ,on analysing the mean levels of LDH with severity of preeclampsia in 200 subjects it was found that the mean serum LDH level in severe preeclampsia (960.39) was higher than the women with Non severe preeclampsia (793.93) , which was statistically significant.(table.9)

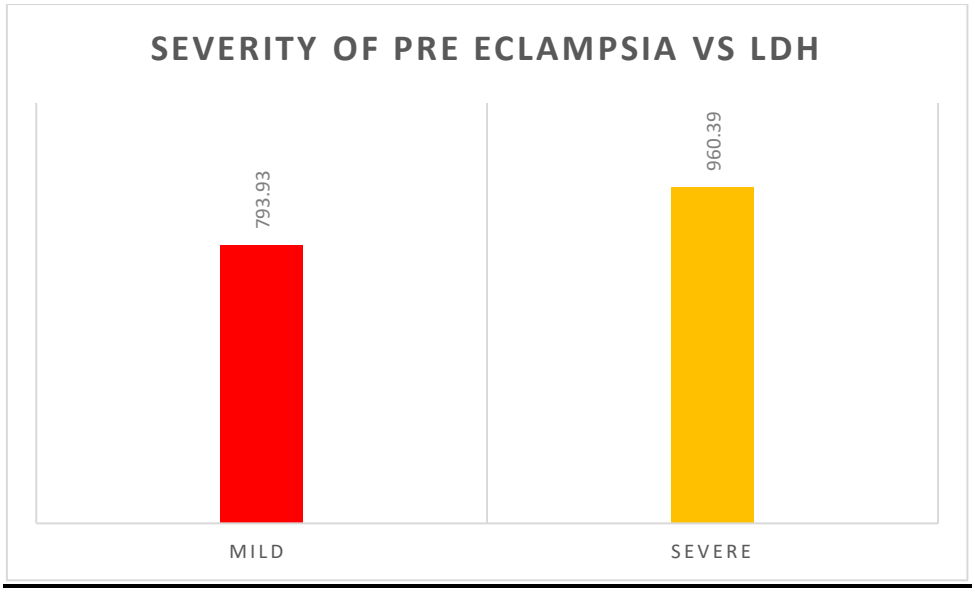


Figure 9

From the results it was observed that increasing levels of serum lactate dehydrogenase is associated with increase in severity of the preeclampsia.(figure 8,9.)

SERUM LDH VS BIRTH WEIGHT

Table 10 Illustrates the mean birth weight of the babies in relation to serum LDH levels.

	BIRTH WEIGHT	
SERUM LDH	MEAN	SD
300- 600	2.62	0.58
600-800	2.32	0.63
> 800	2.04	0.57
ANOVA		
P VALUE - 0.001		
SIGNIFICANT		

In our study ,in patients with serum LDH levels of 300-600 IU/l, the mean birth weight of babies was 2.62 kg ± 0.58, the mean birth weight in those with LDH levels in the range of 600–800 IU/l, was, 2.32kg ± 0.63 whereas in those with LDH levels >800 IU/l ,the mean birth weight was 2.04 kg ±0.57.

Therefore with increase in the levels of serum LDH, there is reduction in the average birth weight of the babies ,which is statistically significant(ANOVA test) with p value of 0.001.(bar diagram .(figure.10)

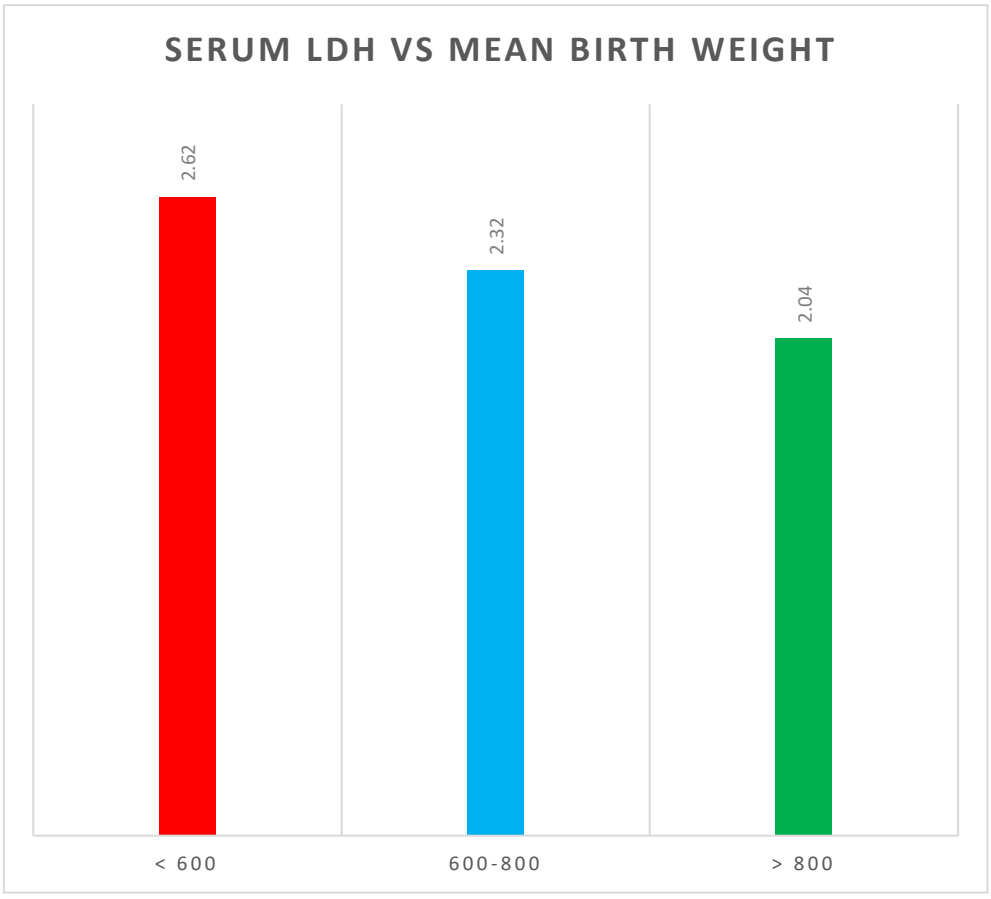


Figure 10

LDH LEVELS VS MATERNAL COMPLICATIONS

1.ECLAMPSIA

Table 11

ECLAMPSIA	NO OF PATIENTS	PERCENTAGE
PRESENT	48	24.00%
ABSENT	152	76%

The above table illustrates that, out of 200 patients in our study, 24% had eclampsia (48 cases).

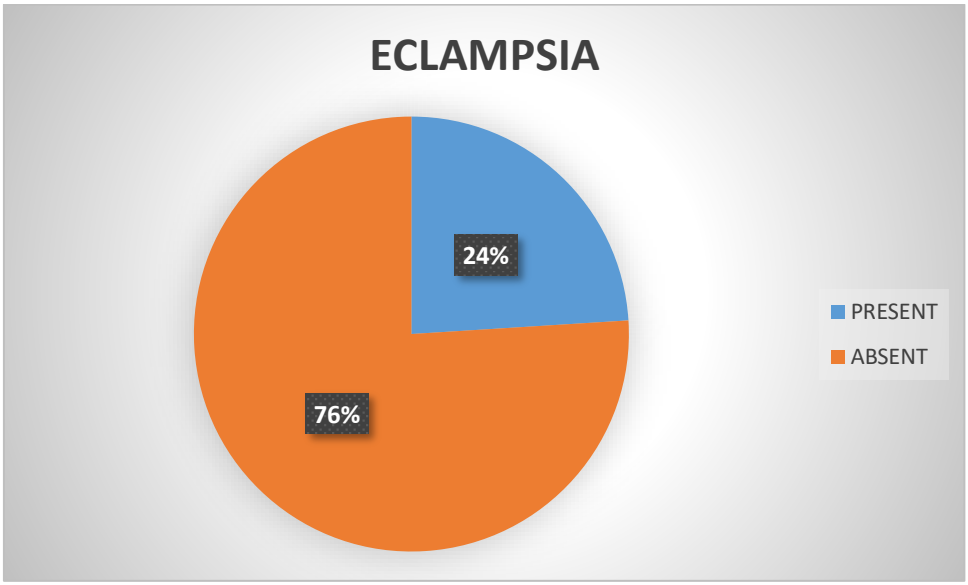


Figure 11

ECLAMPSIA VS LDH

Table 12

ECLAMPSIA	SERUM LDH LEVELS		
	300 - 600	600-800	> 800
PRESENT	12 (24%)	25(32%)	11(15%)
ABSENT	38	53	61
KRUSKAL WALLIS TEST			
P VALUE - 0.05			
SIGNIFICANT			

In relation to LDH levels, among the patients with LDH of 300- 600 IU/l, 12 patients developed eclampsia and in 25 patients with range of 600-800 IU/l and in 11 patients who had LDH levels more than 800 IU/l.

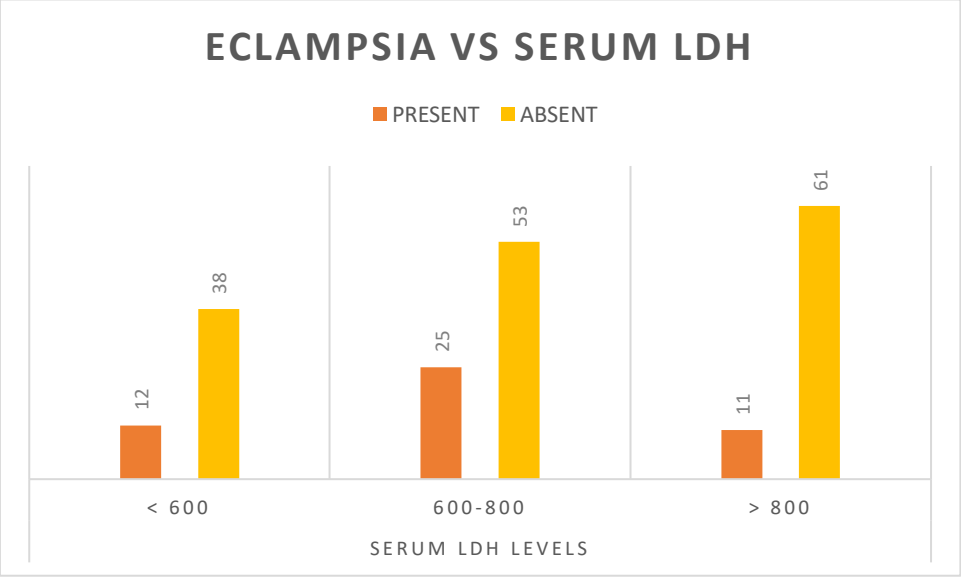


Figure 12

Table 13

ECLAMPSIA	SERUM LDH LEVELS	
	MEAN	SD
PRESENT	789.38	513.82
ABSENT	907.08	639.42
UNPAIRED T TEST		
P VALUE - 0.024		
SIGNIFICANT		

The above table illustrates the relation between the mean LDH level with patients who developed eclampsia .

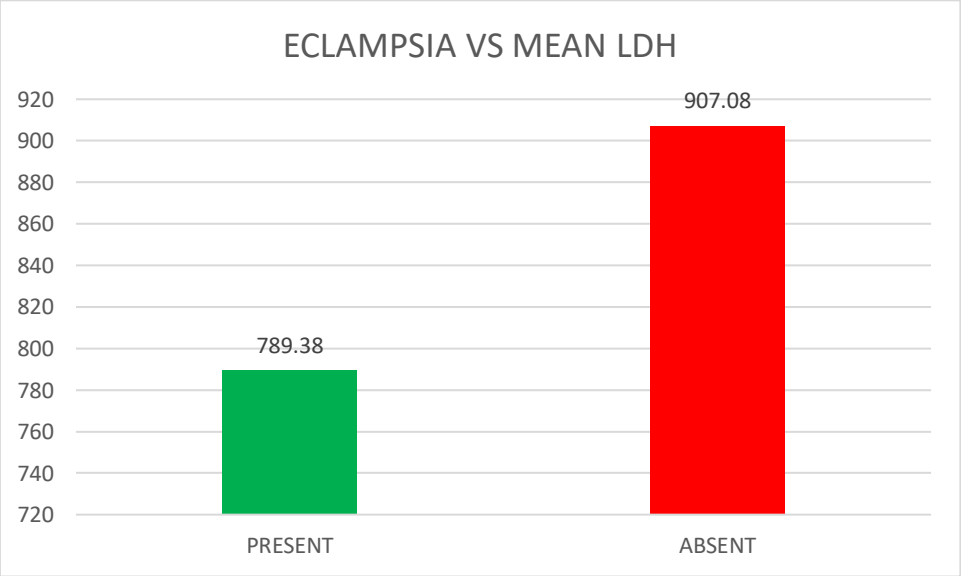


Figure 13

The mean LDH level of 789.38 IU/l is associated with eclampsia in this study.

2.CVT

Table 14

CVT	NO OF PATIENTS	PERCENTAGE
PRESENT	25	12.50%
ABSENT	175	83%

In our study ,out of 200 patients , 25 patients developed cortical venous thrombosis (12.5%), which was shown in the table.14

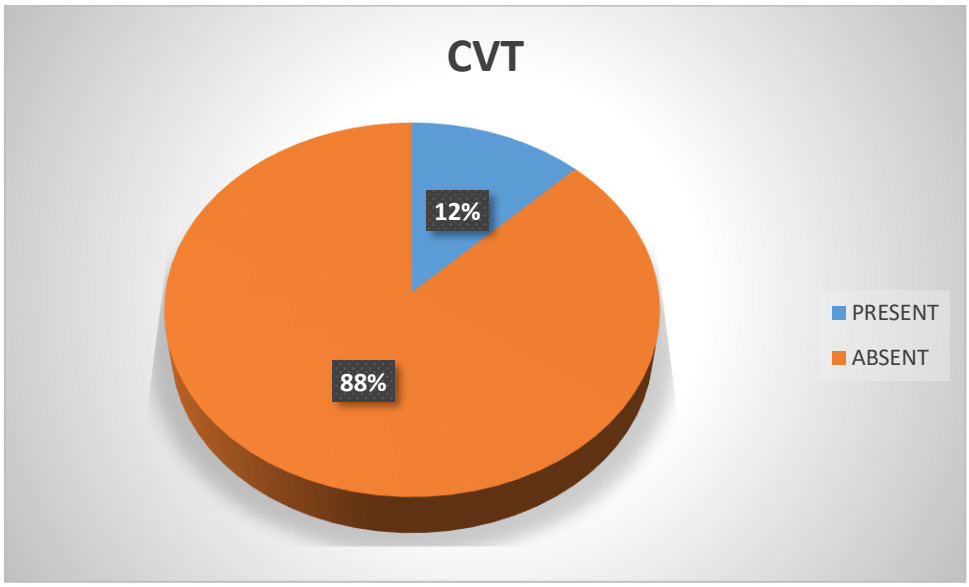


Figure 14

CVT VS LDH

Table 15

CVT	SERUM LDH LEVELS		
	300-600	600-800	> 800
PRESENT	0 (0%)	9(8.9%)	18(25%)
ABSENT	50	71	54
KRUSKAL WALLIS TEST			
P VALUE - 0.001			
SIGNIFICANT			

From the above table, it was showed that none of the patients developed CVT whose LDH level of 300- 600 IU/l and 7 had CVT whose levels are in the range of 600-800 IU/l and in those with LDH level more than 800 IU/l , 18 women developed CVT.

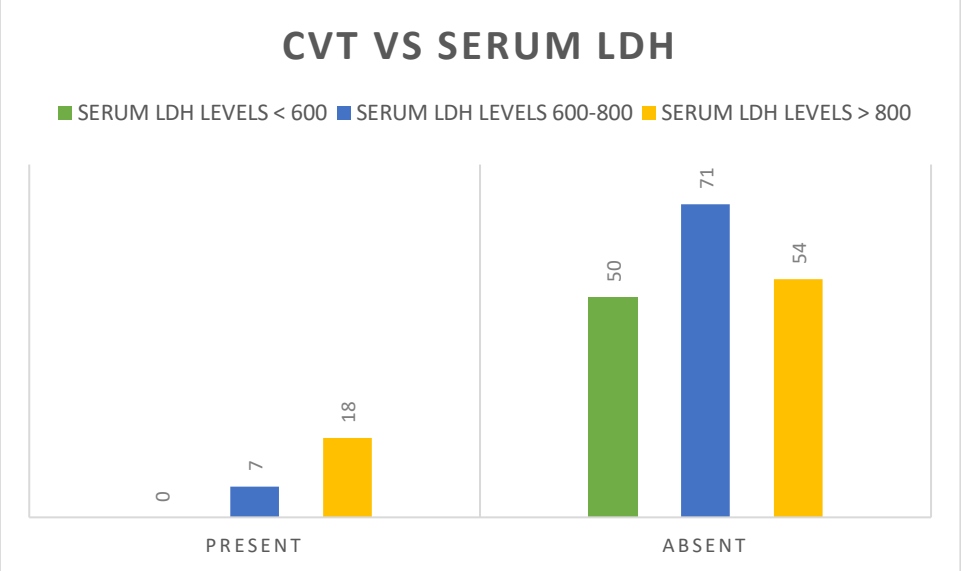


Figure 15

Table 16

CVT	SERUM LDH LEVELS	
	MEAN	SD
PRESENT	1085.7	490.54
ABSENT	849.35	623.58
UNPAIRED T TEST		
P VALUE - 0.042		
SIGNIFICANT		

Table 15 depicts the relation between the serum LDH level and the patients who developed CVT (cortical vein thrombosis).

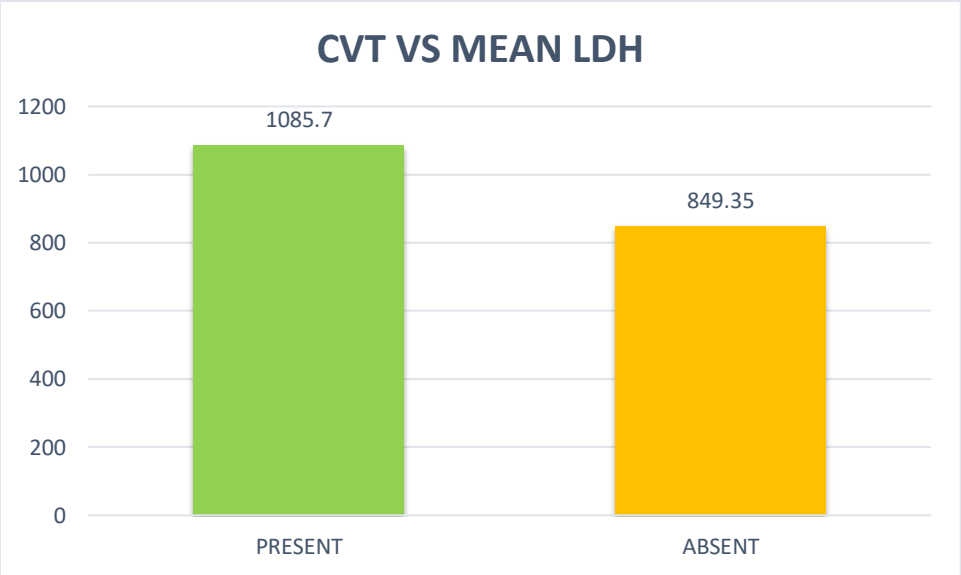


Figure 16

The mean LDH level associated with CVT in our study group 1085.7 with S.D 490.54.on statistical analysis higher level of LDH associated with complication (CVT). This is statistically significant with p value of 0.042.

3.ABRUPTION

Table 17

ABRUPTION	NO OF PATIENTS	PERCENTAGE
PRESENT	29	14.50%
ABSENT	171	86%

During the follow up of 200 subjects with elevated LDH levels during the study period , 29 patients (14.5%) developed abruption placenta.(table.17)

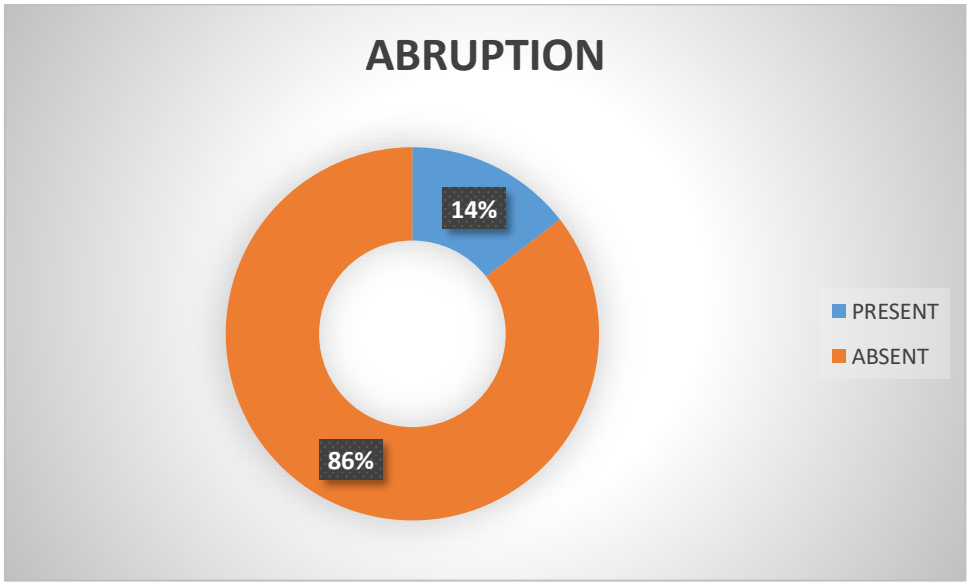


Figure 17

ABRUPTION VS LDH

Table 18

ABRUPTION	SERUM LDH LEVELS		
	300- 600	600-800	> 800
PRESENT	1(2%)	11(14%)	17(23%)
ABSENT	49	67	55
KRUSKAL WALLIS TEST			
P VALUE - 0.004			
SIGNIFICANT			

The above table illustrates that , one women had abruption in those with LDH levels of 300- 600 U/l , whereas in those who had LDH levels in the range of 600-800IU/l ,11 patients had abruption and 17 patients had abruptio placenta in those with levels more than 800 IU/l. this is statistically significant with p value 0f 0.004

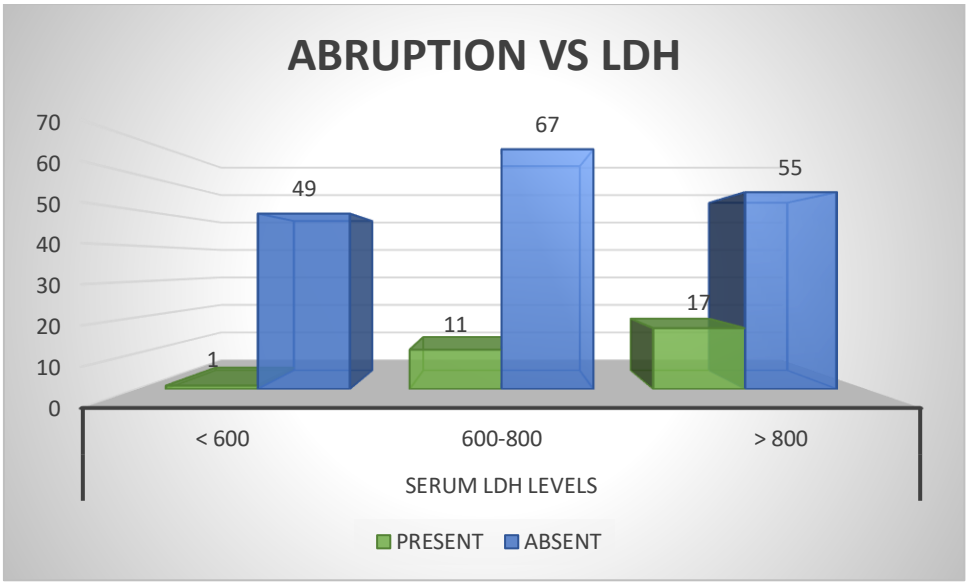


Figure 18

Fig.17 depicts the relation between the serum LDH levels and abruption in this study.

Table 19

ABRUPTION	SERUM LDH LEVELS	
	MEAN	SD
PRESENT	864.07	175.98
ABSENT	881.33	658.78
UNPAIRED T TEST		
P VALUE - 0.889		
SIGNIFICANT		

The mean serum LDH level associated with abruption in our study is 864.07 with standard deviation of 175.98.(table.19)

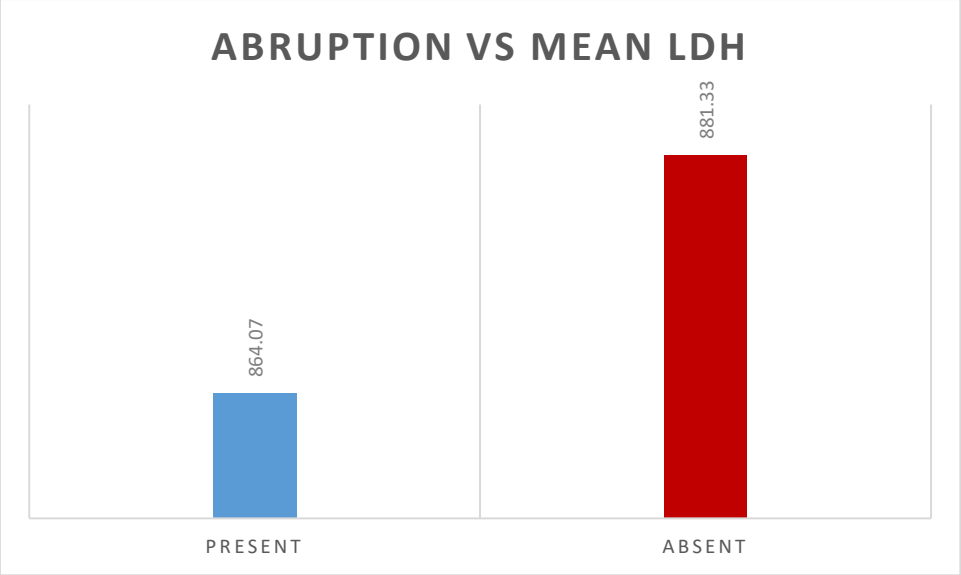


Figure 19

4.ACUTE RENAL FAILURE

Table 20

ARF	NO OF PATIENTS	PERCENTAGE
PRESENT	7	3.50%
ABSENT	193	97%

In our study ,out of 200 subjects 7 patients developed acute renal failure (3.5%)(table.20)

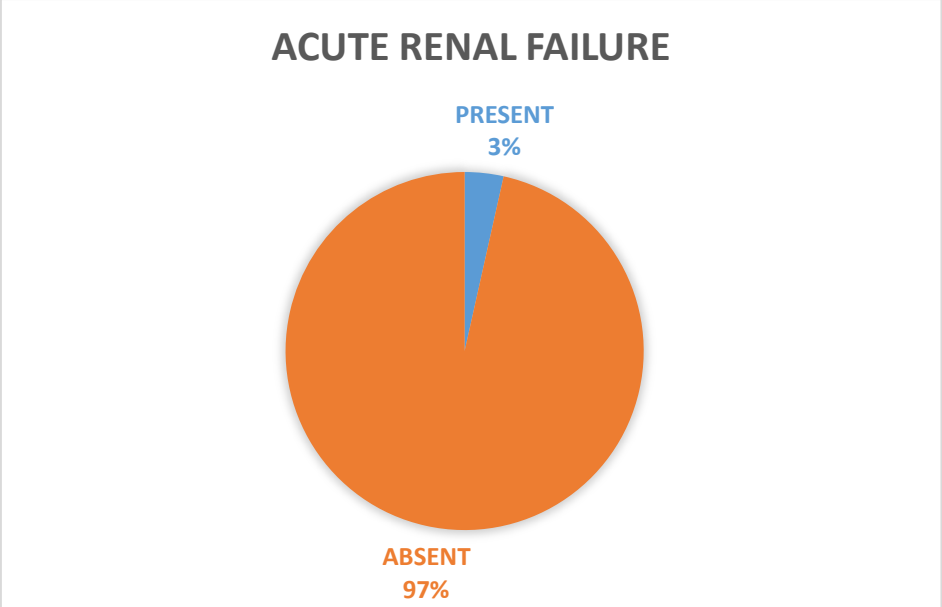


Figure 20

ARF VS LDH

Table 21

ARF	SERUM LDH LEVELS		
	300-600	600-800	> 800
PRESENT	0(0%)	0(0%)	7(9.7%)
ABSENT	50	78	65
KRUSKAL WALLIS TEST			
P VALUE - 0.002			
SIGNIFICANT			

On statistical analysis (kruskal wallis test) it was found that none of the patients developed renal failure with LDH levels of 300-600 IU/l and those in the range of 600-800 IU/l whereas in those with LDH levels >800 IU/l ,7 women developed acute renal failure, which was statistically significant.

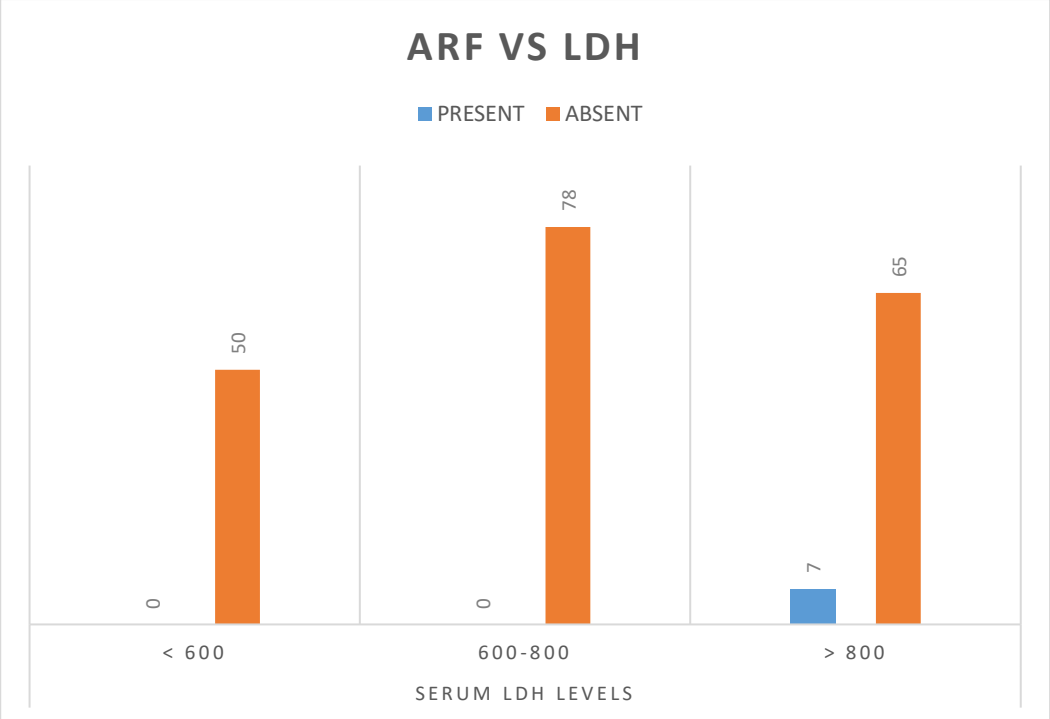


Figure 21

Table 22

ARF	SERUM LDH LEVELS	
	MEAN	SD
PRESENT	1688.43	710.72
ABSENT	849.57	590.14
UNPAIRED T TEST		
P VALUE - 0.001		
SIGNIFICANT		

Table 22 illustrates the relation between the mean LDH level and the patients who had acute renal failure.

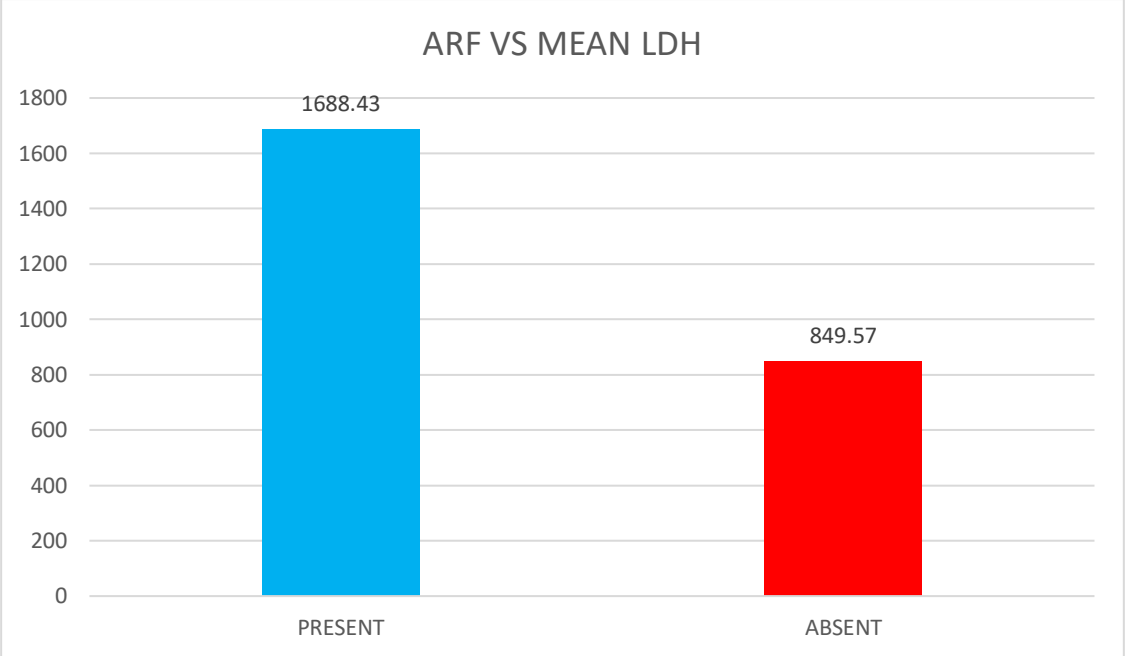


Figure 22

The mean LDH value associated with acute renal failure in our study is 1688.43(fig.22)

5. PULMONARY EDEMA

Table 23

PULMONARY EDEMA	NO OF PATIENTS	PERCENTAGE
PRESENT	11	5.50%
ABSENT	189	95%

Out of 200 patients,11 patients developed pulmonary edema (5.5%) in the study period.(table.23)(fig.23)

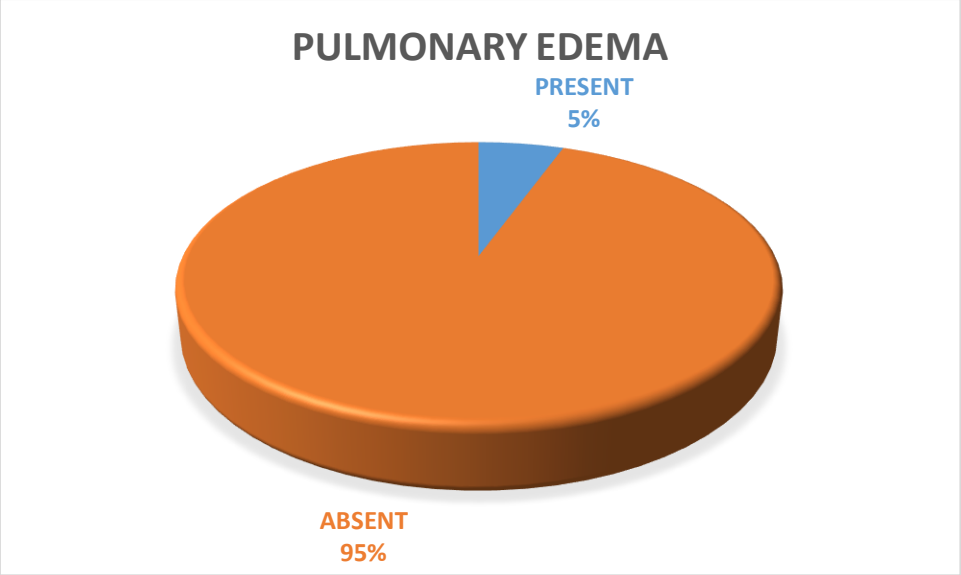


Figure 23

PULMONARY EDEMA VS LDH

Out of 200 patients who were taken in to the study, none of the patients who had serum LDH levels of 300- 800 IU/l, developed pulmonary edema and 11 of those who had LDH levels >800 IU/l developed pulmonary edema, which is statistically significant with p value 0.001.(table. 24)

Table 24

PULMONARY EDEMA	SERUM LDH LEVELS		
	300- 600	600-800	> 800
PRESENT	0(0%)	0(0%)	11(8%)
ABSENT	50	78	61
KRUSKAL WALLIS TEST			
P VALUE - 0.001			
SIGNIFICANT			

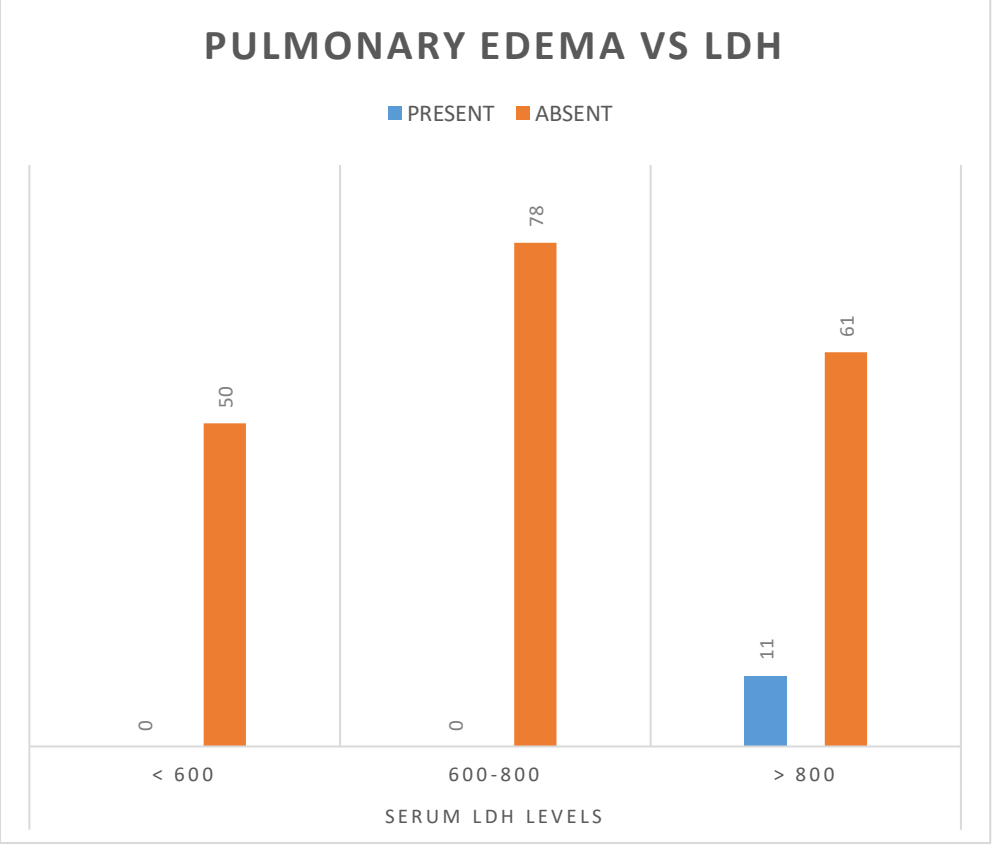


Figure 24

Table 25

PULMONARY EDEMA	SERUM LDH LEVELS	
	MEAN	SD
PRESENT	1776.64	413.4
ABSENT	826.58	581.4
UNPAIRED T TEST		
P VALUE - 0.001		
SIGNIFICANT		

Table .24 illustrates the mean value of LDH associated with pulmonary edema is 1776.64 with standard deviation of 413.4

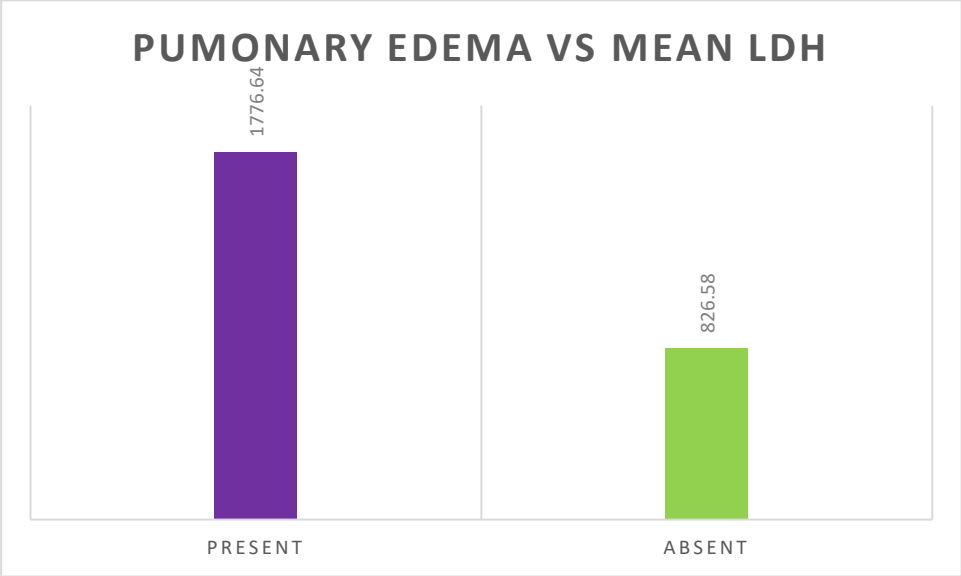


Figure 25

6.HELLP SYNDROME

Table 26

HELLP	NO OF PATIENTS	PERCENTAGE
PRESENT	26	13.00%
ABSENT	174	87%

(Table 25..)26 of 200 subjects developed HELLP syndrome (13%) (HELLP –Haemolysis, Elevated liver enzymes and Low platelet count).

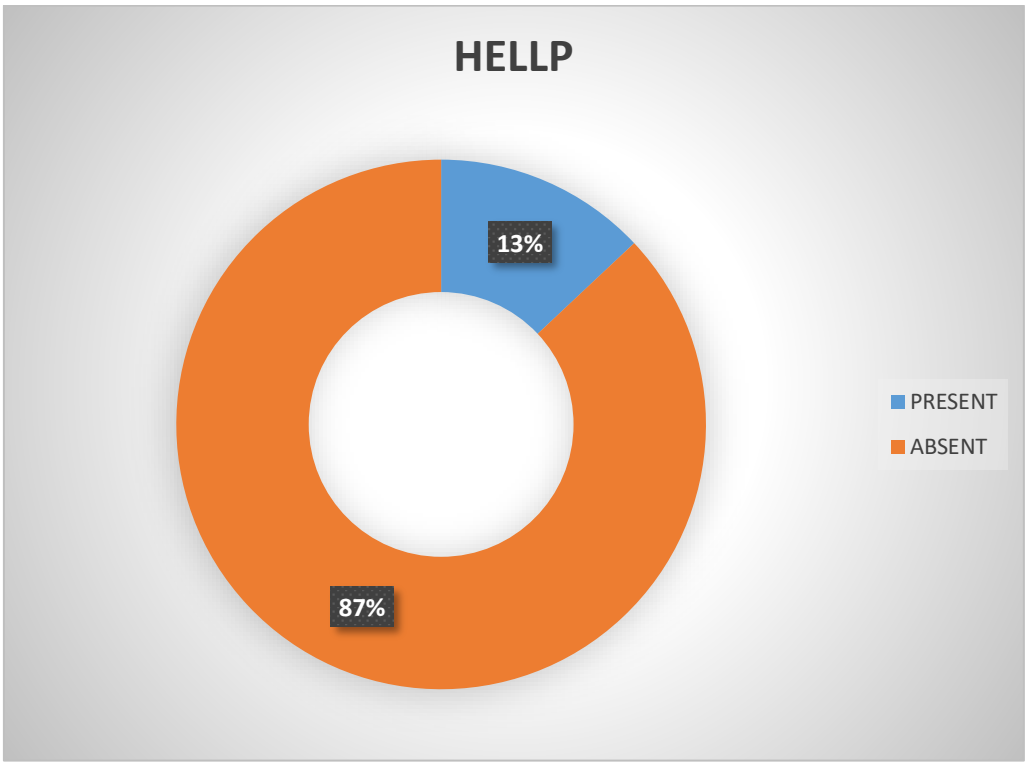


Figure 26

Table 27

HELLP VS LDH

HELLP	SERUM LDH LEVELS		
	300-600	600-800	> 800
PRESENT	0(0%)	18(23%)	8(11%)
ABSENT	50	60	64
KRUSKAL WALLIS TEST			
P VALUE - 0.001			
SIGNIFICANT			

None of the patients who had serum LDH level of 300- 600 IU/l developed HELLP syndrome and 18 of those with LDH in the range of 600-800 developed HELLP syndrome and 8 of the patients with LDH levels > 800 developed HELLP syndrome, which is statistically significant on analysis with p value of 0.001.

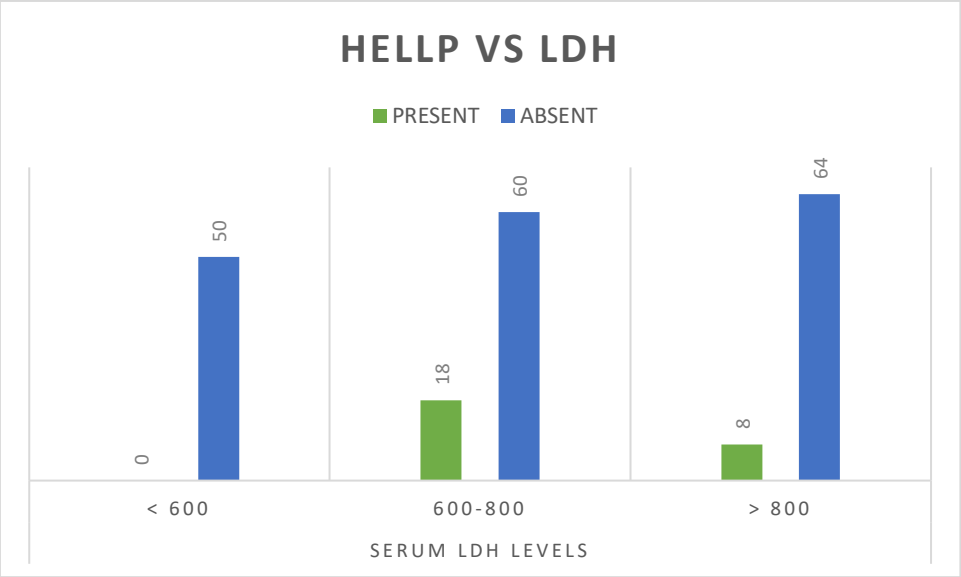


Figure 27

Table 28

HELLP	SERUM LDH LEVELS	
	MEAN	SD
PRESENT	1031.42	437.2
ABSENT	856.03	521.57
UNPAIRED T TEST		
P VALUE - 0.174		
NON SIGNIFICANT		

Mean LDH level associated with HELLP syndrome is 1031.42.(fig.28)

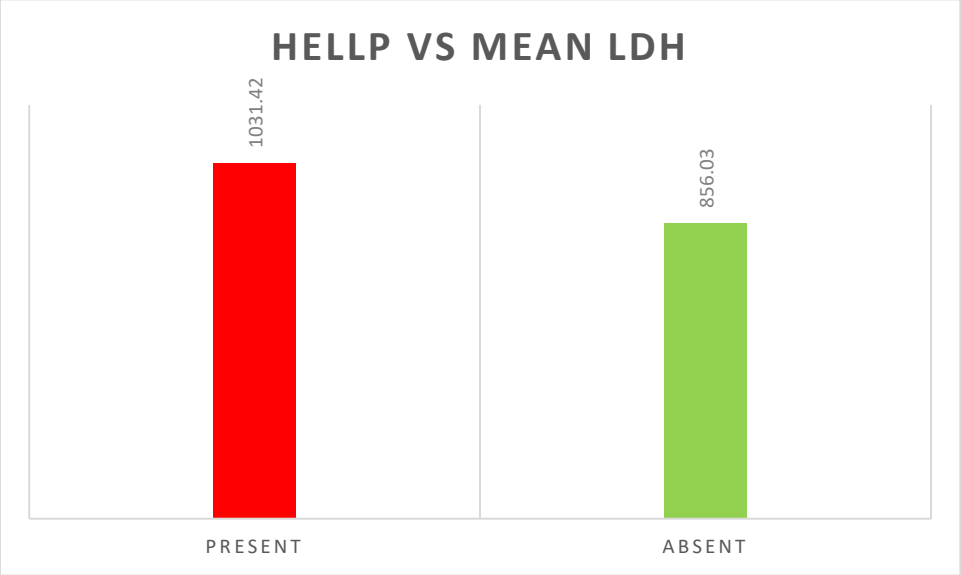


Figure 28

LDH LEVELS AND PERINATAL COMPLICATIONS

1.INTRAUTERINE DEATH

Table 29

IUD	NO OF PATIENTS	PERCENTAGE
PRESENT	22	11.00%
ABSENT	178	89%

22 babies born out of 200 patients had intrauterine death (11%) in our study.(table.29)

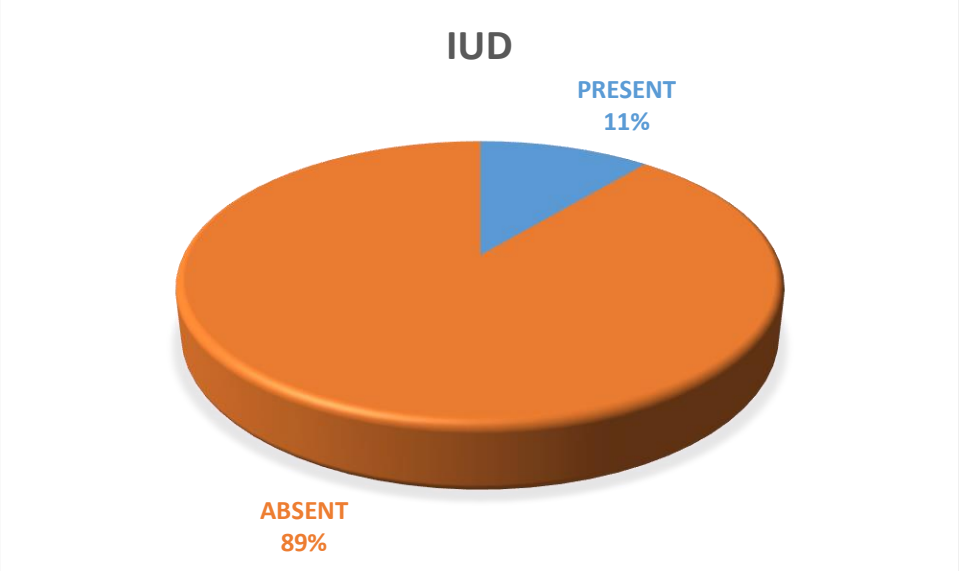


Figure 29

IUD VS LDH

Table 30

IUD	SERUM LDH LEVELS		
	300- 600	600-800	> 800
PRESENT	1(2%)	6(7.6%)	15(21%)
ABSENT	49	72	57
KRUSKAL WALLIS TEST			
P VALUE - 0.005			
SIGNIFICANT			

1 case of intrauterine death was seen in subjects with serum LDH levels of 300-600 IU/l ,6 cases of IUD in those with serum LDH level in the range of 600-800 IU/l and 15 of those with LDH level more than 800 IU/l had intrauterine death

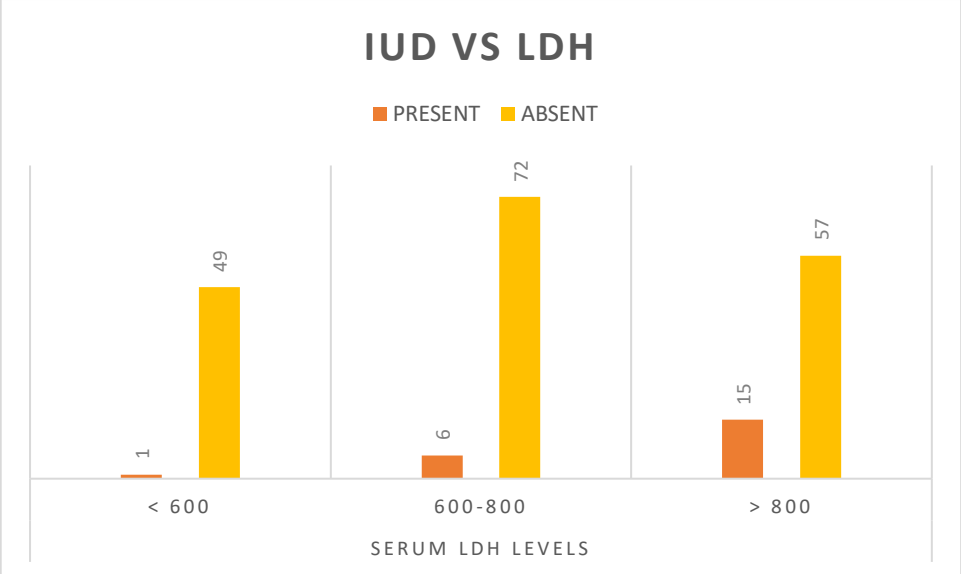


Figure 30

Table 31

IUD	SERUM LDH LEVELS	
	MEAN	SD
PRESENT	990.33	327.57
ABSENT	866.62	638.66
UNPAIRED T TEST		
P VALUE - 0.384		
NON SIGNIFICANT		

Table 29 illustrates the relation between the mean serum LDH and the preeclampsia patients with intrauterine death of the babies.

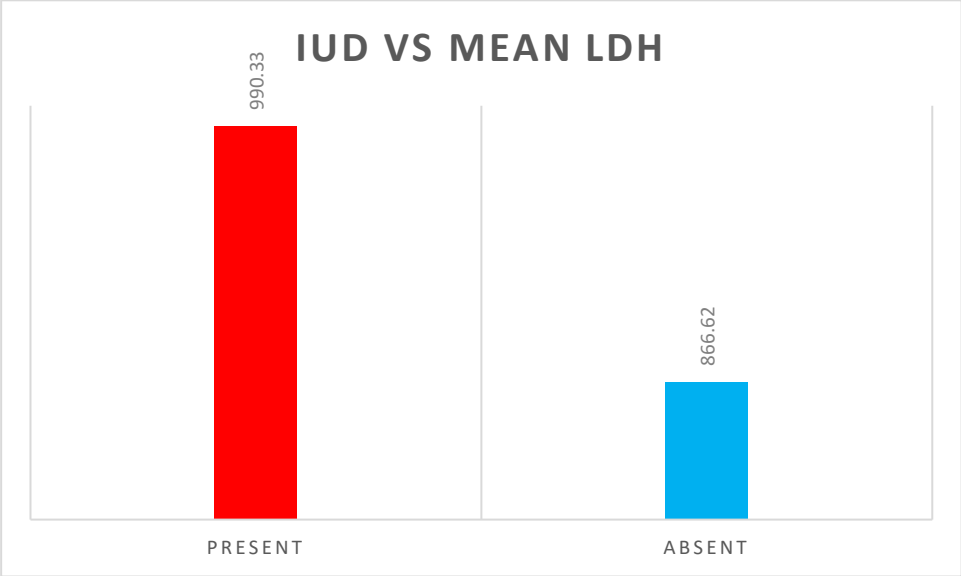


Figure 31

The mean LDH level in those with intrauterine death of the fetus is 990.33(figure.31)

2.FETAL GROWTH RETARDATION

Table 32

IUGR	NO OF PATIENTS	PERCENTAGE
PRESENT	35	17.50%
ABSENT	165	83%

In our study , 17.5% of fetus had Intrauterine growth retardation (table.32)

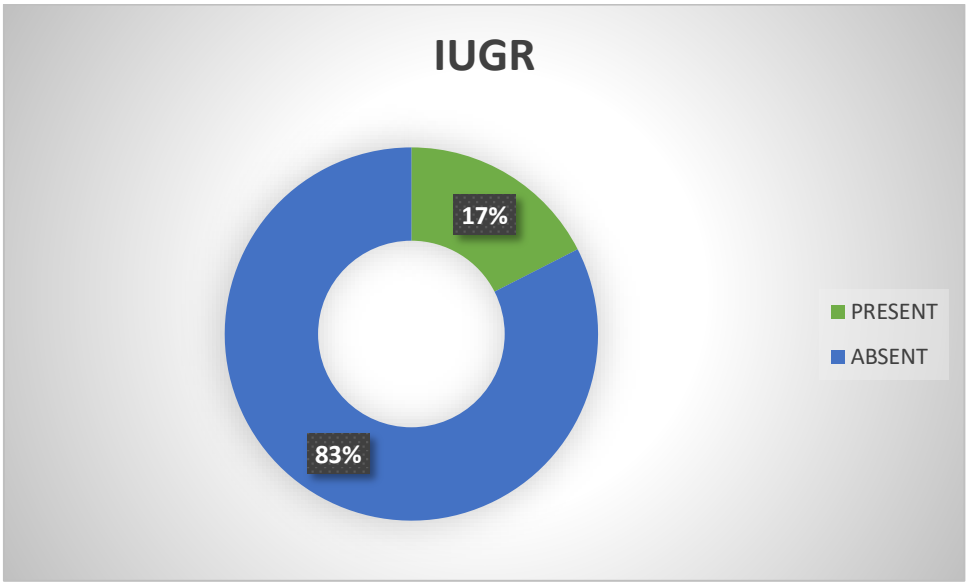


Figure 32

FGR VS LDH

Table 33

FGR	SERUM LDH LEVELS		
	300- 600	600-800	> 800
PRESENT	5(10%)	10(13%)	20(27.7%)
ABSENT	45	68	52
KRUSKAL WALLIS TEST			
P VALUE - 0.029			
SIGNIFICANT			

On statistical analysis ,5 babies with maternal serum LDH level in the range of 300-600 IU/l had fetal growth retardation and 10 of those with LDH in the range of 600-800 IU/l and 20 of those with LDH level > 800 had intrauterine growth retardation ,which was statistically significant (kruskal wallis test) with p value of 0.029. (fig.33)

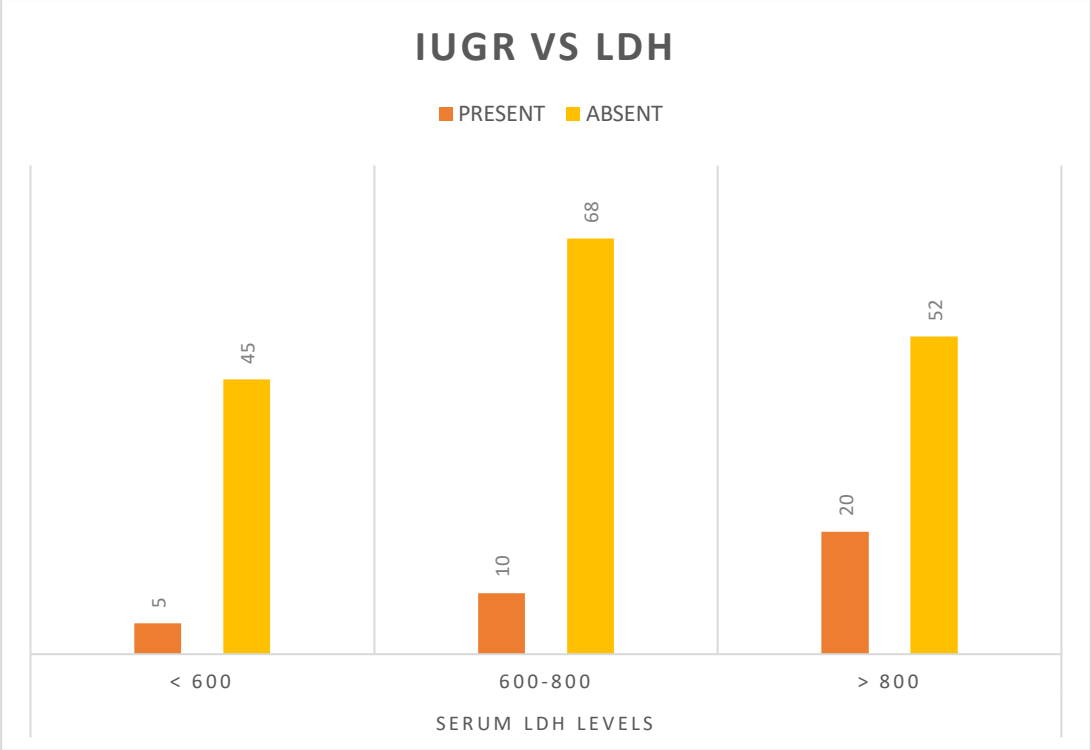


Figure 33

Table 34

FGR	SERUM LDH LEVELS	
	MEAN	SD
PRESENT	923.71	426.82
ABSENT	870.93	646.34
UNPAIRED T TEST		
P VALUE - 0.649		
NON SIGNIFICANT		

The mean serum LDH level associated with fetal growth retardation (923.71) is higher than those without the complication of FGR ,which is statistically significant with p value of 0.649.(table.34)

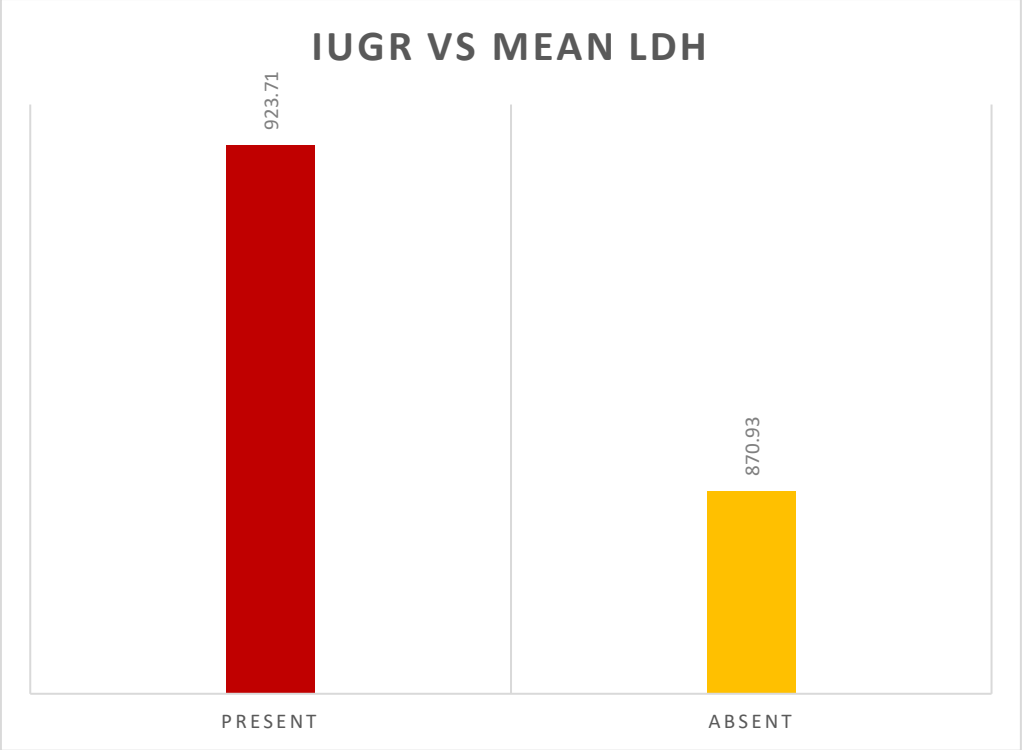


Figure 34

3.IATROGENIC PREMATURITY

Table 35

IATROGENIC PREMATURITY	NO OF PATIENTS	PERCENTAGE
PRESENT	50	49.00%
ABSENT	150	51%

The above table shows that 50 out of 200 patients in our study had premature babies which is iatrogenic due to induction or by caesarean section.

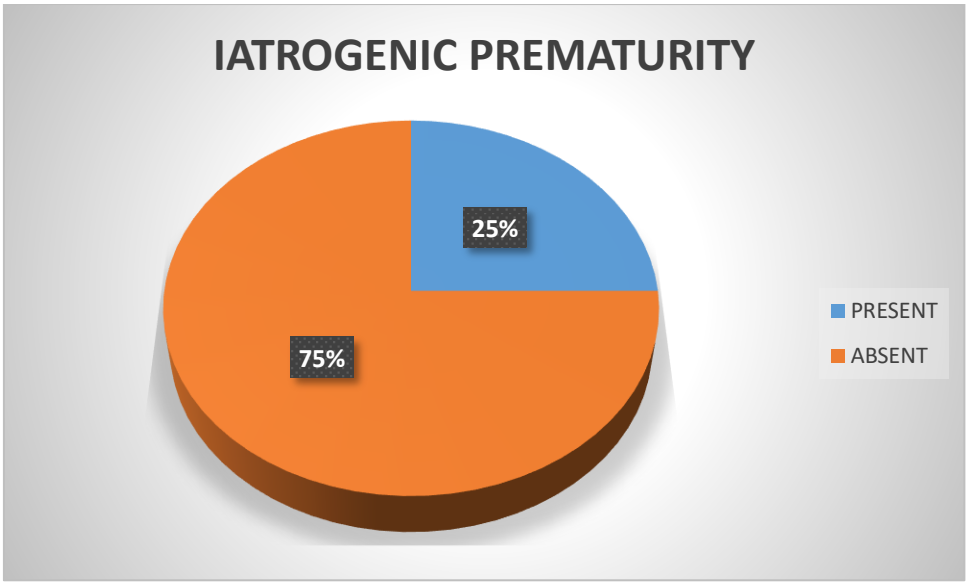


Figure 35

IATROGENIC PREMATURITY VS LDH

Table 36

IATROGENIC PREMATURITY	SERUM LDH LEVELS		
	300-600	600-800	> 800
PRESENT	8(16%)	16 (20.5%)	26(36%)
ABSENT	42	62	46
KRUSKAL WALLIS TEST			
P VALUE - 0.021			
SIGNIFICANT			

The above table illustrates that 26 patients of those with LDH level of 300-800 IU/l had preterm deliveries and 16 and 8 those with LDH values in the range of 600 -800 IU/l and .800 IU/l had iatrogenic preterm deliveries which is statistically significant with p value of 0.021.

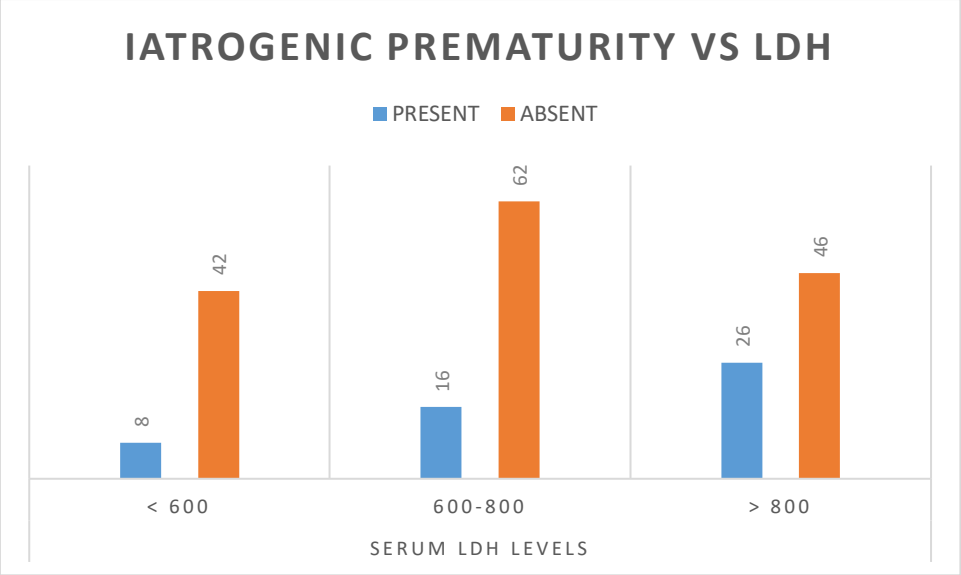


Figure 36

Table 37

IATROGENIC PREMATURITY	SERUM LDH LEVELS	
	MEAN	SD
PRESENT	1133.6	750.83
ABSENT	793.91	535.34
UNPAIRED T TEST		
P VALUE - 0.001		
SIGNIFICANT		

The mean serum LDH level associated with iatrogenic prematurity is 1133.6 with standard deviation of 750.83 is higher than those without, which is statistically significant.(p value 0.001 by unpaired T test) (figure.37)

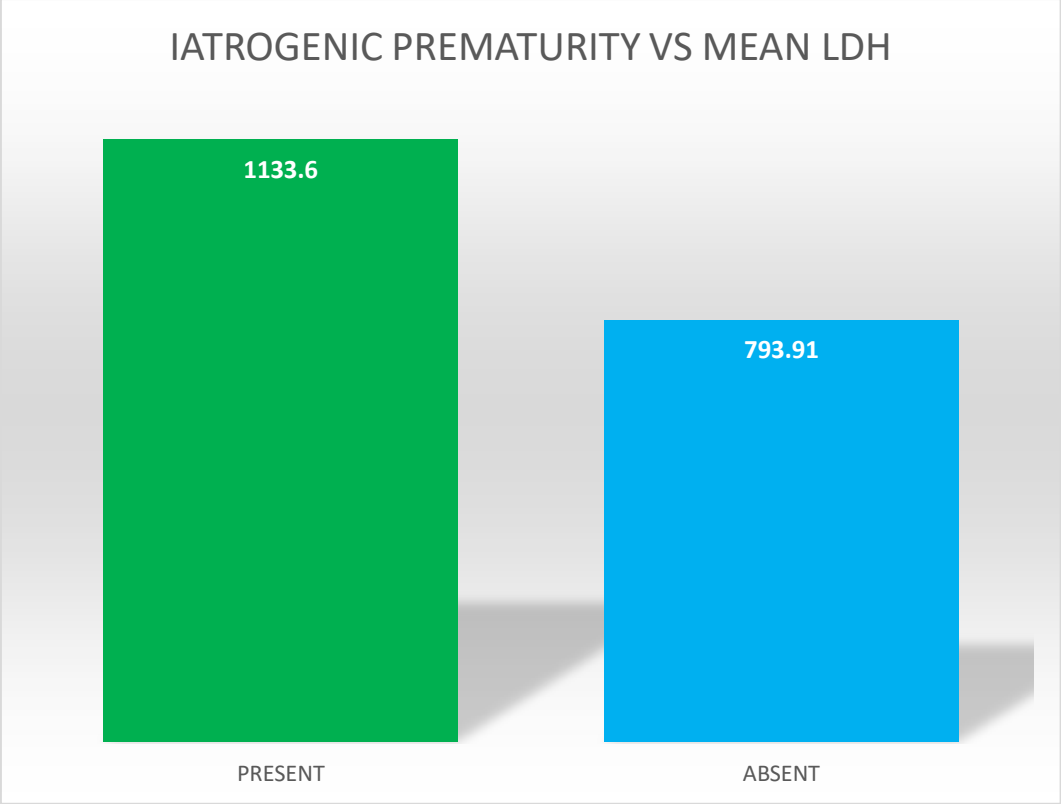

IATROGENIC PREMATURITY VS MEAN LDH
1133.6
793.91
PRESENT
ABSENT

Figure 37

DISCUSSSION

Pre eclampsia, which is a disorder with system wide endothelial dysfunction and vasospasm causing hypoxia and multi organ dysfunction and other complications. several studies have been done with many biochemical markers as predictor as well as for prognosis of preeclampsia. Few of the studies were used lactate dehydrogenase as a predictor of severity of preeclampsia. In this study, complications in antenatal women with preeclampsia and their perinatal outcome , in relation to the serum lactate dehydrogenase levels, is correlated. In anaerobic conditions, Lactate dehydrogenase which is an important cellular enzyme, acts to convert pyruvic acid into lactic acid. Glycolysis is the major energy pathway in placenta. In preeclampsia due to defective placentation and endothelial dysfunction and resulting hypoxia increases glycolysis and lactate dehydrogenase activity. Elevated LDH levels indicates hypoxic environment causing tissue damage. The complications of preeclampsia which are due to widespread endothelial injury and resulting multiorgan damage are eclampsia , abruption placenta, HELLP syndrome, cortical vein thrombosis and renal failure.

On statistical analysis of the data, in our study majority of the preeclampsia patients are belonged to primi gravida which is comparable to study by qublan HS et al..which showed that severe preeclampsia

patients was significantly younger in age with low parity. Jaiswar et all found in their study that Systolic and diastolic BP was significantly higher in patients with higher serum LDH levels which is comparable to our study. Rukhsana Afroz et all found in their study that 91.% severe preeclampsia and 82.9% mild preeclamptic women had raised serum LDH level. likewise in our study, increase in severity of the preeclampsia is associated with increase in serum LDH Levels.(table.7)

Qublan et all found in their study that the mean LDH level in severe preeclampsia (400 and up to 800 IU/l) is higher than in normal control women (299IU/l). In our study the mean LDH level with non severe preeclampsia and severe preeclampsia is 793 IU/l and 960 IU/l respectively.

In our study, among the patients with serum LDH levels in the range of 300- 600 IU/l (50 patients), 24 % (12) had eclampsia and 2% (1) had aruption and none of the patients had complications like HELLP syndrome, acute renal failure, pulmonary edema and cortical vein thrombosis. whereas in those with serum LDH levels in the range of 600- 800 IU/L (78 patients), 32% (25 patients) had eclampsia , 8.9% ((9) had cortical vein thrombosis ,14% (11) had abruption placenta, 23% (18) had HELLP syndrome and none of the patient had other complications like acute renal failure and pulmonary edema . Among those with serum LDH levels more

than 800 IU/l(72) , 15% (11) had eclampsia , 25% (18) had cortical vein tghrombosis,23% had abruption placenta,9.7% (7) had acute renal failure , 8% (11) had pulmonary edema and 11% (8) had HELLP syndrome.

Catazerite et al found in their study that group of women who had elevated LDH developed HELLP syndrome (haemolysis, elevated liver enzymes and low platelet count) which is comparable to our study.(figure.16) .Therefore there is significant increase in incidence of complications and maternal morbidity in those with elevated serum LDH levels which was comparable to the study conducted by martin.et.al .

In the present study, those with serum LDH level in the range of 300-600 IU/l, 1% had intrauterine death if the baby and 16% had growth restricted fetus and 16% of them had preterm babies. whereas in those with serum LDH levels in the range of 600-800 IU/l , 6% of intrauterine death of the fetus ,10% had growth restricted fetus and 16% had iatrogenic preterm delivery by induction of labour and by LSCS. In those with LDH value more than 800IU/l , 15% had intrauterine death of the fetus,27.75% had growth restriction of the fetus and 36% had iatrogenic premature delivery of the fetus which was statistically significant.

In comparable to the study by jaiswer et al, in our study the birth weight of the babies are less with increasing levels of serum LDH levels. (figure.9). The increase in low birth weight babies is due to the preterm delivery by

induction or by lower segment caesarean section. whereas in the study conducted by qublan et al ,there was no significant relation between the serum LDH levels and low birth weight babies. jaiswer et al and qublan et all found in their studies that, there is increase in intrauterine death of the baby in those with increase in serum LDH level which is statistically significant in the present study. Whereas in contrary the mean LDH levels does not significantly associated with perinatal outcome in terms of intrauterine death and FGR (fetal growth restriction) in our study. Whereas, there was statistically significant association between the mean serum LDH level with perinatal outcome in terms of iatrogenic prematurity in our study.(table.34).

CONCLUSION

Preeclampsia and its complications are significantly contributes to maternal and perinatal mortality and morbidity. Timely intervention and management can prevent the complications. From this study, after analysing the data, it is found that there is increase in severity as well as increase in incidence of maternal and perinatal complications with increase serum Lactate dehydrogenase levels in preeclampsia patients. Thus it is concluded that serum lactate dehydrogenase which is an early marker of hypoxia at cellular levels, can be used as a biochemical marker

to assess the severity of the disease and to predict the complications in all preeclampsia patients. Thereby, Close monitoring and early intervention and prompt management of the preeclampsia patients with elevated serum LDH levels can prevent complications and thereby helps to improve the maternal and perinatal outcome in preeclampsia patients.

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ANNEXURE -1

PROFOMA

Name : Age : Ip/Op number :

Unit:

DOA: Address:

DOD: Occupation:

Socioeconomic status:

Obstetric score:

Presenting complaints:

Menstrual history:

Marital history:

Obstetric history:

Past history

Family history:

General examination: BMI: Pallor: Pedal edema:

Vitals: pulse : Blood pressure:

Temperature: Respiratory Rate:

Systemic examination:

Cvs:

\Rs:

CNS:

Abdomen:

P/V:

Investigations:

Complete blood count:

Urine albumin:

Serum LDH:

Renal function test:

Liver function test:

ANNEXURE -11

ABBREVIATION

LDH- Lactate dehydrogenase

PIH- pregnancy induced hypertension

BMI –Body mass index

ACOG- American college of obstetrics and gynaecology

SLE –Systemic lupus erythematosus

HLA- Human leucocyte antigen

NADH- Nicotinamide adenine dinucleotide (reduced)

NAD+ - Nicotinamide adenine dinucleotide (Oxidised)

HELLP- Hemolysis, elevated liver enzymes and low platelet count

FGR- Fetal growth restriction

IUD- Intrauterine death

IUGR- intrauterine growth retardation

LSCS- lower segment caesarean section

SD- standard deviation

CVT- cortical vein thrombosis

ARF- acute renal failure

ANNEXURE -III

CONSENT FORM

yourself Mrs.……. Are being asked to be a participant in the research study titled "**CORRLEATION OF ELEVATED SERUM LDH LEVELS WITH ADVERSE MATERNAL AND PERINATAL OUTCOME IN PREECLAMPSIA"** in Coimbatore medical college Hospital, conducted by Dr.Menisri N , post graduate student in the department of obstetrics and Gynaecology .you are eligible after looking into the inclusion criteria. You can ask any question you may have before agreeing to participate.

Research Being Done

Maternal and fetal complications in preeclampsia patients with elevated serum lactate dehydrogenase

Purpose of the research

To correlate the elevated serum LDH levels and maternal and perinatal outcome in preeclampsia patients

.

Decline from participation

You have the option to decline from participation in the study existing protocol for your condition

Privacy and confidentiality

Privacy of individuals will be respected and any information about you or provided by you during the study will be kept strictly confidential.

Authorization to publish Results

Results of the study may be published for scientific purpose and /or presented to scientific groups, however you will not be identified.

Statement of consent

I volunteer and consent to participate in this study, I have read the consent or It has been read to me . The study has been fully explained to me, and I may ask questions at any time.

…… ……

Signature / Left thumb impression Date

(volunteer)

…….. ……..

Signature of witness Date

ஒப்புதல்படிவம்

பெயர் :

வயது:

பாலினம்:

முகவரி:

கோவை அரசுமருத்துவக்கல்லூரி மருத்துவமனையில் மருத்துவர் நா.மேனிஷ் தலைமையில் நடைபெறும் இந்த ஆய்வில் முழுசம்மதத்துடன் கலந்துகொள்ளசம்மதிக்கிறேன். இந்த ஆய்வில் என்னை பற்றி விவரங்களை பாதுகாப்புடன் இந்த ஆய்வில் வெளியிடஆட்சேபணை இல்லை என்று தெரிவித்துக்கொள்கிறேன்.எந்த நேரத்திலும் ஆய்வில் இருந்து எந்த நேரத்திலும் விலக்கிக்கொள்ளும் உரிமை உண்டு என்று அறிவேன்.

இடம்:

தேதி:

கைகெயாப்பம்/ரேகை