LACTIC ACID DEHYDROGENASE AND URIC ACID - BIOCHEMICAL MARKERS FOR PRE ECLAMPSIA-ECLAMPSIA

Dissertation submitted to

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CERTIFICATE

This is to certify that this dissertation entitled **"LACTIC ACID DEHYDROGENASE AND URIC ACID- BIOCHEMICAL MARKERS FOR PRE ECLAMPSIA - ECLAMPSIA"** is the bonafide original work done by **Dr.DIVYA LAKSHMI.A,** Post graduate, under my overall supervision and guidance in the department of obstetrics & Gynaecology, Stanley Medical College and Hospital, Chennai, in partial fulfilment of the regulations of The Tamil Nadu Dr. M.G.R. Medical University for the award of **M.S. OBSTETRICS & GYNECOLOGY.**

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DECLARATION

I, solemnly declare that this dissertation **"LACTIC ACID DEHYDROGENASE AND URIC ACID- BIOCHEMICAL MARKERS FOR PRE ECLAMPSIA - ECLAMPSIA"** is the bonafide work done by me at the Department of Obstetrics & Gynaecology, Government Stanley Medical College Hospital, Chennai, under the guidance and supervision of **Prof. Dr.N.Thamizhselvi. MD. DGO.,** Professor of Department of Obstetrics & Gynaecology, Government Stanley Medical College, Chennai-600 001.

This dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the University regulations for the award of degree of M.S Obstetrics & Gynaecology examinations to be held in April 2016.

Place: Chennai. Signature of the candidate

Date : **(Dr.DIVYA LAKSHMI.A)**

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CONTENTS

ABSTRACT

BACKGROUND:

Hypertensive Disorders in pregnancy represents the most common medical complication of pregnancy which affects 7-15% of all gestations.WHO reports 16% of maternal deaths due to Hypertensive disease.Preeclampsia accounts for more than half of the cases.It is a disorder with course being progressive and continuous affecting virtually every organsystem.So it should be detected at an earlier stage so that appropriate management can be undertaken to prevent maternal and fetal morbidity and mortality.Preeclampsia is a multisystem disorder with lot of cellular death.LDH being an intracellular enzyme gets elevated in serum due to leakage of enzyme from inside the cells.Uric acid levels are raised in preeclampsia due to its reduced renal clearance.Hence this study was done to correlate serum LDH and uric acid levels with the severity of preeclampsia,Maternal and Fetal outcomes.

MATERIALS AND METHODS:

This study was a comparative observational study conducted among 165 Antenatal women in third trimester attending Antenatal OPD/Labour ward at Stanley Medical College during January to September 2015 after getting ethical clearance from the Institute Ethics Committee.Study group included 50 Normotensives,48 Mild preeeclamptics,53 Preeclamptics and 14 Eclamptics classified based on NHBPEP classification.Clinical History obtained as in structured proforma.After Informed consent from patients,blood samples were

taken for Serum LDH,Uric acid estimation by IFCC and Uricase method respectively.

Study group were divided into 3 subgroups based on LDH levels(<600IU/L, 600-800IU/L, >800IU/L) and based on uric acid levels(<6mg%, >6mg%). LDH and Uric acid values were compared with diagnostic components of preeclampsia such as Systolic BP,DiastolicBP,Proteinuria Gestational age at delivery,mode of delivery,birth weight of babies,maternal complications like Abruption,HELLP,Eclampsia,Pulmonaryedema,Intracranial Haemorrhage, Maternal death,Fetal complications like IUD, IUGR.The results were compared based on One Way Analysis of Variance,chi-square test and differences were considered as significant when $p<0.05$.

OBSERVATION AND RESULTS:

In our study,Extremes of age group(<19yrs,>30yrs) patients had increase severity of preeclampsia. Majority(55%) of patients were Primigravida.There was no association between parity and LDH,Uric acid levels.Among patients with LDH>800IU/L,98% patients had systolic BP>160mmHg.LDH level and systolic BP found to have significant association.Among patients with LDH 600-800IU/L and >800IU/L,60% and 96% respectively had Diastolic BP>110mmHg(P value< 0.001).Increasing LDH levels were associated with increasing severity of proteinuria(P<0.001).There was reduction in mean gestational age at delivery(<36 weeks) and mean birth weight of babies in

groups with higher LDH levels propably due to more number of preterm deliveries in view of severity of preeclampsia.Groups with higher LDH levels(600-800 and >800IU/L) had more maternal and fetal complications($p<0.05$).All those diagnostic variables were compared with uric acid levels.Group with uric acid >6mg% had significant association with Systolic BP,DiastolicBP,Proteinuria,Mean birth weight of babies,maternal and fetal morbidity and mortality.

CONCLUSION:

Serum LDH and uric acid values were significantly high in pre-eclamptic patients depending on the severity of the disease indicating the increased cellular turnover in them. Higher LDH and uric acid levels was associated with diagnostic components of preeclampsia. Hence diagnostic and management strategies may be considered based on S.LDH and uric acid levels and further studies on a larger sample can be done to substantiate our observations on the utility of this parameter as a diagnostic and prognostic component of preeclampsia. Development of new management strategies based on S. LDH and uric acid levels may help in appropriate decision making thereby avoiding unwanted maternal &fetal deaths.

KEYWORDS :

LDH, Uric Acid, Preeclampsia, eclampsia

INTRODUCTION

Hypertensive disorders represents the most common medical complication of pregnancy which affects about 7 – 15 % of all gestations[1].According to World Health Organization(WHO) 16% of maternal deaths were reported due to Hypertensive disease which is higher in proportion than the other leading causes such as Haemorrhage, Sepsis[2].

Of these Hypertensive disorders, Preeclampsia syndrome alone or if superimposed with chronic hypertension is most dangerous. However Gestational Hypertension is followed by signs of Preeclampsia in almost half cases. Preeclampsia syndrome is a pregnancy-specific syndrome that affects virtually every organ system. Disease course is progressive and continuous which gets arrested only by termination of pregnancy. So the disease should be detected at an earlier stage with several Biochemical markers and predictive tests so that appropriate management can be undertaken.

Several biochemical markers have been proposed to identify the women who destined to develop Preeclampsia which were chosen on the basis of pathophysiological abnormalities associated with Preeclampsia which includes markers of Placental Dysfunction, Endothelial cell

dysfunction, angiogenesis, coagulation activation, markers of systemic inflammation[3].

Pre eclampsia- eclampsia is a multi system disorder that leads to lot of cellular death. Lactic Acid Dehydrogenase (LDH) is an Isoenzyme which is intracellular in location which helps in interconversion of pyruvate and lactate inside cells. Any cellular death results in leakage of enzyme from the cell and rise in serum in LDH levels. Hence serum LDH levels is used to assess the extent of cellular damage and severity of pre eclampsia[4].

Uric acid, which is one of the end product of purine metabolism is elevated in patients of pre eclampsia because of decreased renal clearance and increased production[5]. Decreased renal clearance is due to altered renal tubular function and Overproduction of uric acid due to increased breakdowns of purines in placenta. This uric acid impairs nitric oxide production which results in endothelial cell dysfunction which plays a role in pathophysiology of Preeclampsia.

Estimation of serum LDH and Uric Acid level is a simple biochemical test, which quantitates the extent of cellular death and thereby the assessment of severity of preeclampsia.

AIM AND OBJECTIVES

1. To compare serum LDH and Uric Acid levels in normotensive pregnant women and in women with preeclampsia-eclampsia.

2. To correlate serum LDH and Uric acid levels with severity of disease, maternal and perinatal outcome.

REVIEW OF LITERATURE

According to National High Blood Pressure Education Program Working Group(NHBPEP) and ACOG[6,7], Hypertension is defined as

1) Systolic BP of ≥ 140 mmHg and/or

2) Diastolic BP of ≥ 90 mmHg (Korotkoff V) that is measured in 2 occasions 4 – 6 hours apart within 7 days period. Increase in 30mmHg systolic or 15 mmHg Diastolic above the patient's baseline abandoned as the diagnostic criteria in HTN as it is not proved to be good prognostic indicator. However close monitoring is needed in those patients.

Preeclampsia is a multiorgan disease of unknown etiology that leads to development of Hypertension and Proteinuria after 20 weeks of gestation.Classically defined as the triad of **Hypertension, edema and proteinuria**.But recent defnitions does not include edema due to lack of specificity.Appearance of proteinuria remains an important Diagnostic criteria in differentiating Preeclampsia from Gestational Hypertension**.** **Proteinuria** is defined as

- 24 Hour urine protein excretion exceeding 300mg
- Urine Protein:Creatinine ratio ≥0.3(30mg/mmol) or
- Persistent 30mg/dl(Urinary dipstick of 1+ in random urine samples).

CLASSIFICATION OF HYPERTENSIVE DISORDERS IN PREGNANCY:

According to International Society for the Study of Hypertension in Pregnancy (ISSHP), Hypertensive disorders during pregnancy is classified into 4 defined groups as follows:

1. Gestational Hypertension
2. Preeclampsia and Eclampsia
3. Chronic Hypertension
    - ✓ Essential
    - ✓ Secondary
4. Preeclampsia superimposed on Chronic Hypertension.

GESTATIONAL HYPERTENSION:

New onset hypertension developing after 20 weeks of gestation, during labour or in the first 24 hour postpartum without proteinuria or any other systemic features of preeclampsia in a previously normotensive nonproteinuric women and the Blood Pressure resolves within 3 months of postpartum.

PREECLAMPSIA:

Hypertension associated with proteinuria > 0.3 gm/L in a 24 hour urine collection (or) 1+ by qualitative urine examination ,after 20 weeks of gestation.

ECLAMPSIA:

Convulsions occurring in a patient with preeclampsia.

CHRONIC HYPERTENSION:

It is defined as Hypertension present before 20 weeks of pregnancy or that is diagnosed preconceptionally. Blood pressure elevation that persists more than 12 weeks postpartum is also retrospectively considered as Chronic Hypertension.

- ESSENTIAL HYPERTENSION is diagnosed when there is no apparent underlying cause for chronic hypertension.
- SECONDARY HYPERTENSION may be caused by renal parenchymal disease, renovascular disease, endocrine disorders or coarctation of aorta.

PREECLAMPSIA SUPERIMPOSED ON CHRONIC HYPERTENSION:

It is diagnosed when one or more features of preeclampsia develops for first time during pregnancy after 20 weeks of gestation in a women with pre-existing chronic hypertension.

NICE GUIDELINES[8]:

Hypertension is classified according to severity as follows:

1) **MILD HYPERTENSION:** Systolic Blood pressure 140-149 mmHg, Diastolic Blood Pressure 90 – 99 mmHg.
2) **MODERATE HYPERTENSION:** Systolic Blood pressure 150-159 mmHg, Diastolic Blood Pressure 100-109 mmHg.
3) **SEVERE HYPERTENSION:** Systolic Blood PRESSURE 160 mmHg or greater, Diastolic Blood Pressure 110mmHg or greater.

RISK FACTORS FOR PREECLAMPSIA[9]:

COUPLE RELATED RISK FACTORS:

- Primipaternity
- Limited sperm exposure
- Pregnancy after donor insemination, donor egg, donor embryo
- Dangerous male partner

MATERNAL OR PREGNANCY RELATED RISK FACTORS:

- Extremes of Age(Teenage and > than 35 years)
- Parity
- Interval from last pregnancy greater than 10 years
- Obesity
- Insulin resistance/Gestational Diabetes
- Smoking
- Multifetal pregnancy
- Hydrops fetalis
- Hydatiform mole
- Preeclampsia in previous pregnancy
- Family history of Preeclampsia
- Maternal Low birth weight
- Abnormal Uterine artery Doppler at 18 to 24 weeks.

PREEXISTING MEDICAL DISEASE:

- Pre-Gestational Diabetes
- Chronic Hypertension or Renal disease.
- Maternal Immunologic Disease
- Preexisting Thrombophilia, Antiphospholipid antibody Syndrome

ETIOPATHOGENESIS OF PREECLAMPSIA:

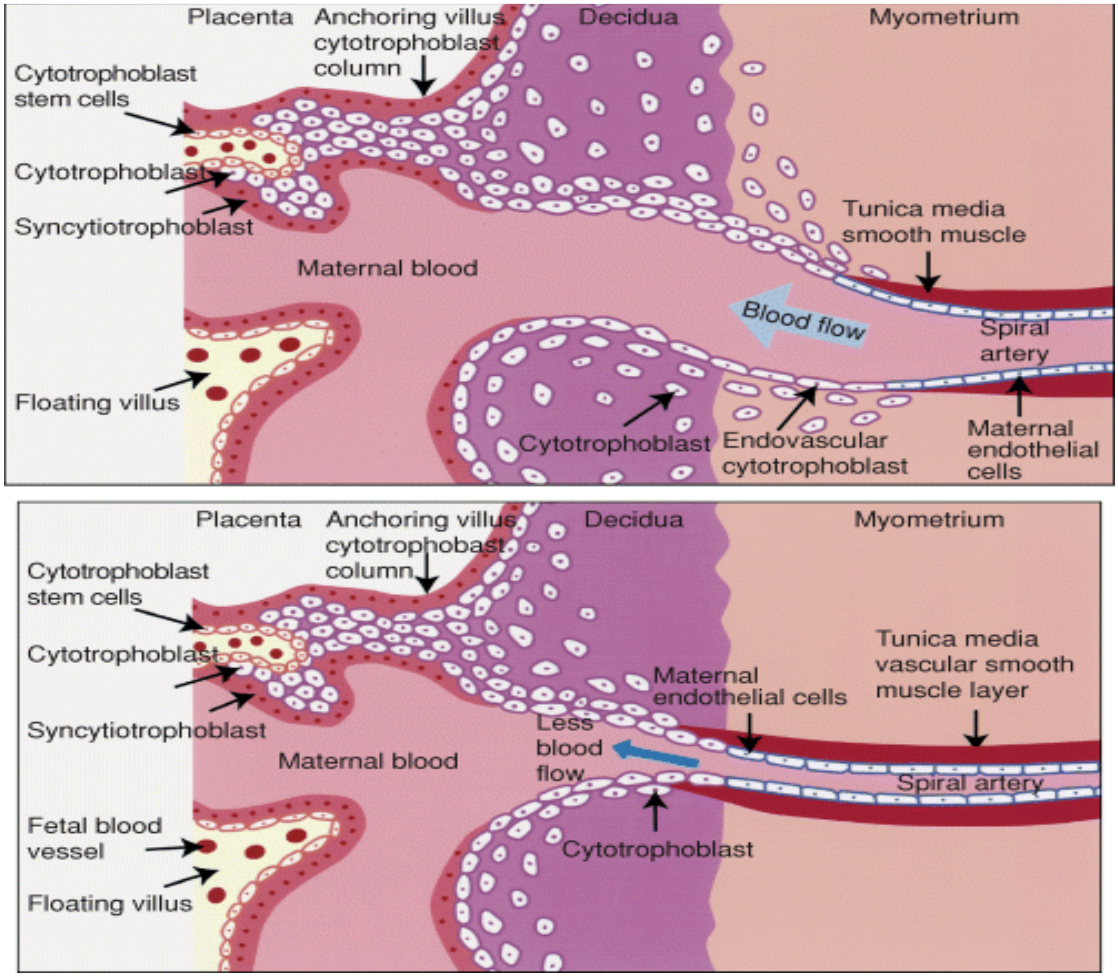
1) ABNORMAL TROPHOBLASTIC INVASION:

It can be explained by **Two-Stage Disorder Hypothesis**[10].

FIRST STAGE occurs before 12 weeks postfertilization ,upto the interface between decidua and Myometrium.First stage involves Endovascular Invasion of spiral arteries by Trophoblastic cells.This migration transforms the small musculoelastic spiral arteries into Large Tortuous channels that carry large amount of blood to the Intervillous space and are resistant to the effects of Vasomotor agents.These Physiologic changes are incomplete in patients of Preeclampsia and Trophoblastic invasion affects only in some of the spiral arteries and does not progress into Myometrial portion of the arteries **(INCOMPLETE TROPHOBLASTIC INVASION)**.This deficiency results in decreased UteroPlacental Perfusion.

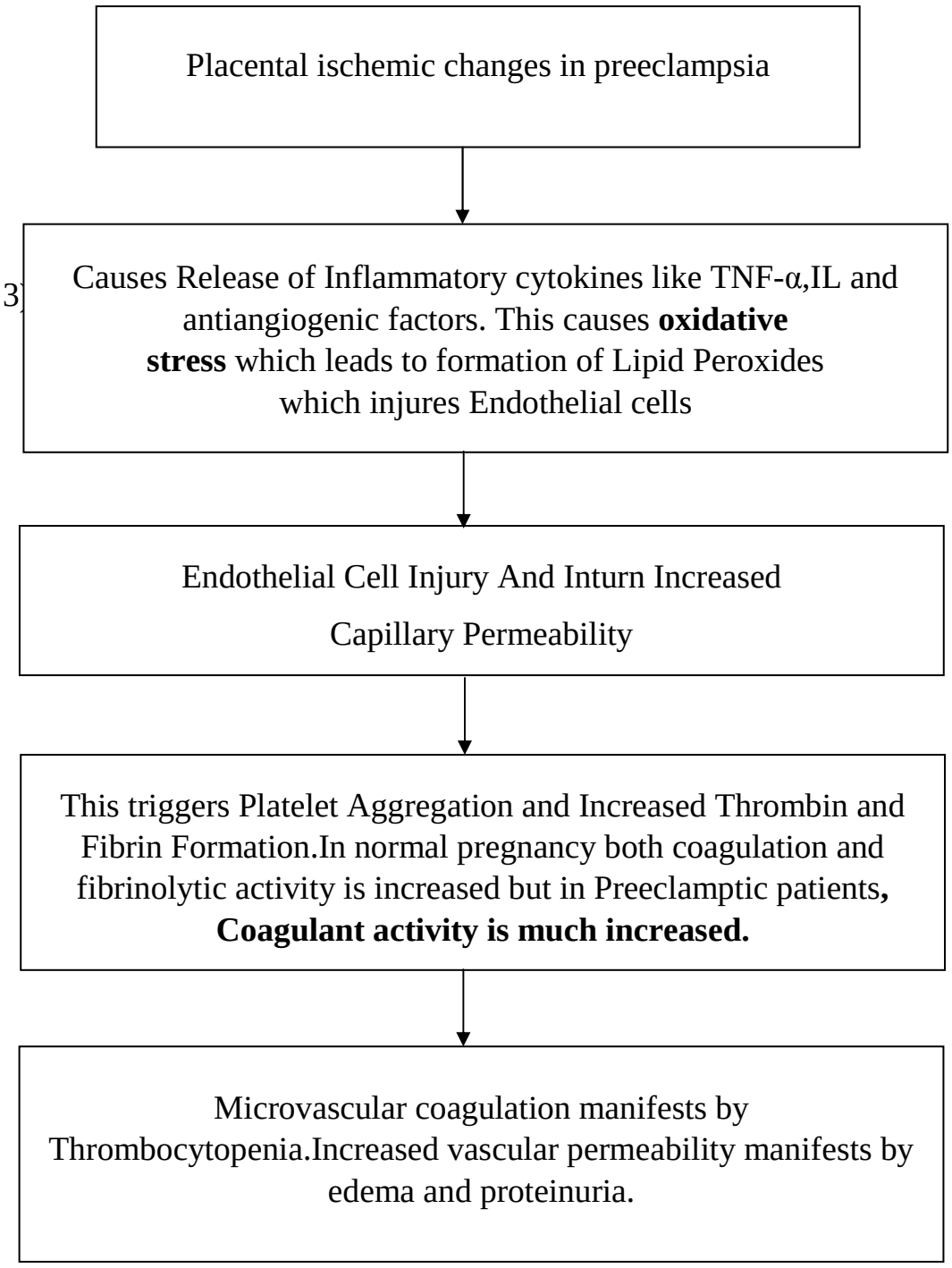
SECOND STAGE occurs normally between 12 and 16 weeks of gestation which involves invasion of intramyometrial segments of spiralarteries.In Preeclampsia, second stage involves the conversion of previous Uteroplacental Maladaptation to **MATERNAL SYSTEMIC SYNDROME** of Preeclampsia which is associated with Endothelial cell activation and generalised Hyperinflammatory state. This anatomic and

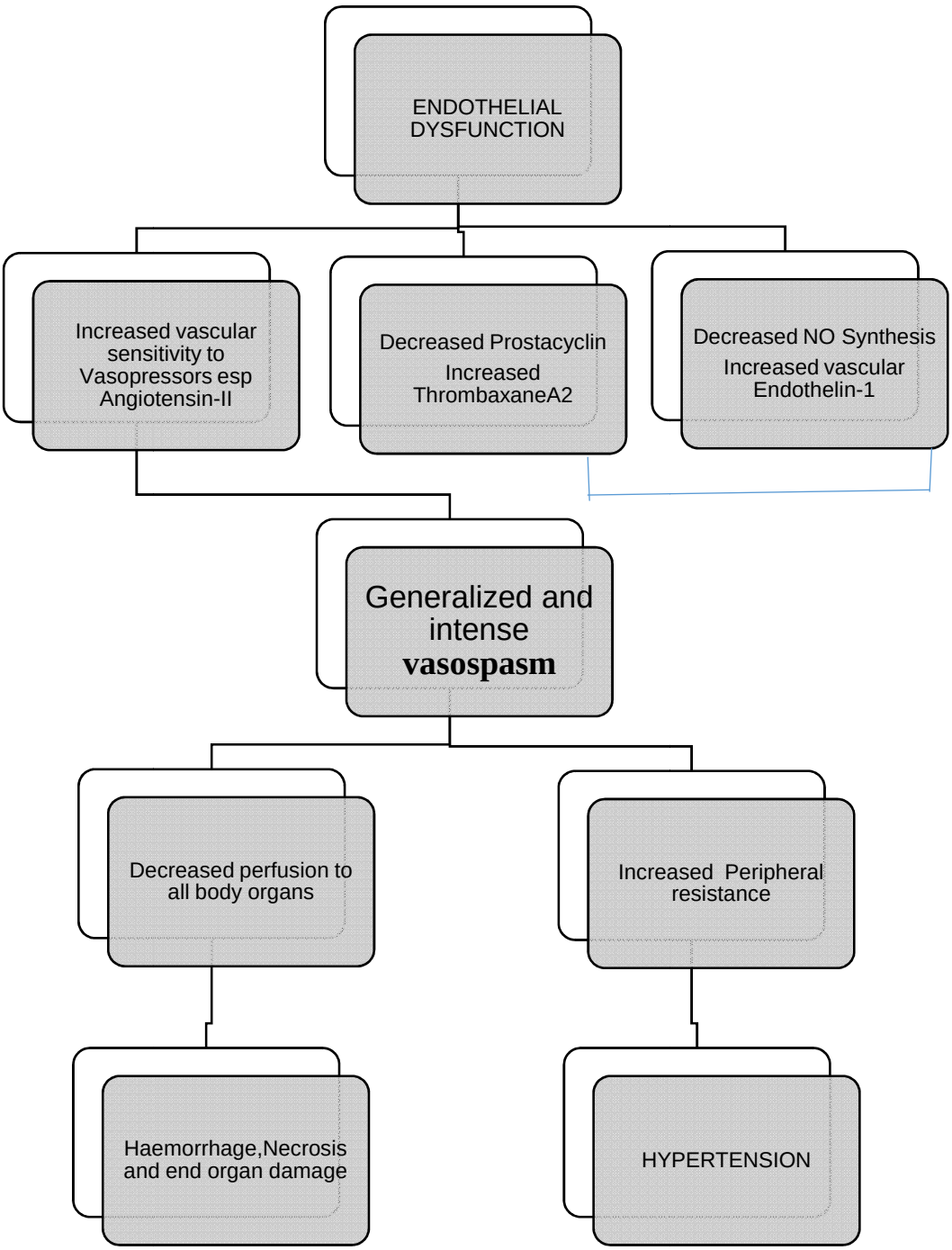
physiologic disruption of normal placentation lead to release of placental debris from the Intervillous space into the Maternal circulation, thereby inciting a Systemic Inflammatory response by stimulating the synthesis of Inflammatory Cytokines, products that affects Angiogenesis and Abnormal Lipid Peroxidation. Severity of Hypertensive disorder is correlated with the magnitude of abnormal Trophoblastic Invasion[11.]



ABNORMAL TROPHOBLASTIC INVASION

2) **ENDOTHELIAL DYSFUNCTION AND VASOSPASM[12]:**




ENDOTHELIAL DYSFUNCTION
Increased vascular sensitivity to Vasopressors esp Angiotensin-II
Decreased Prostacyclin
Increased ThrombaxaneA2
Decreased NO Synthesis
Increased vascular Endothelin-1
Generalized and intense vasospasm
Decreased perfusion to all body organs
Increased Peripheral resistance
Haemorrhage,Necrosis and end organ damage
HYPERTENSION

3) IMMUNOLOGIC FACTORS[13]:

In preeclamptics, there is loss of Maternal tolerance to paternally derived placental and fetal antigens. The placenta being fetal origin has both maternal, paternal haplotypes and Genetic determitants. Of the Histocompatibility Antigens only HLA-G, an immunosuppressive antigen is expressed on the surface of trophoblasts which is a placental cell most intimate to the maternal system.

In Preeclamptics, there is lower level of messenger RNA for HLA-G leading reduced expression of HLA-G on trophoblasts. This causes Immune Maladaptation in Preeclampsia.

4) GENETIC FACTORS[14]:

The hereditary predisposition to develop preeclampsia syndrome is the result of complex interaction of several genes which includes both maternal and paternal. Thus Preeclampsia is multifactorial and polygenic in origin. Genes that are in positive association with Preeclampsia syndrome are as follows:

- ✓ MTHFR Gene which affects Methyl TetraHydroFolateReductase.
- ✓ HLA
- ✓ F5(Factor V Leiden)
- ✓ F2(Prothrombin)

- ✓ AGT(Angiotensinogen)
- ✓ NOS3(Endothelial Nitric Oxide)
- ✓ ACE(Angiotensin Converting Enzyme)
- ✓ CTLA4(Cytotoxic T-Lymphocyte Associated Protein)
- ✓ LPL(Lipoprotein Lipase)
- ✓ SERPINE-1(Serine Peptidase Inhibitor).

5) ANGIOGENIC IMBALANCE:

In preeclampsia, due to worsening Hypoxia at the uteroplacental interface, there is excessive production of AntiAngiogenic peptides especially following 2 peptides.

a) Soluble Fms-like Tyrosine Kinase 1(sFlt-1)
b) Soluble Endoglin(sEng)

a) Soluble Fms-like Tyrosine Kinase 1(sFlt-1)[15]:

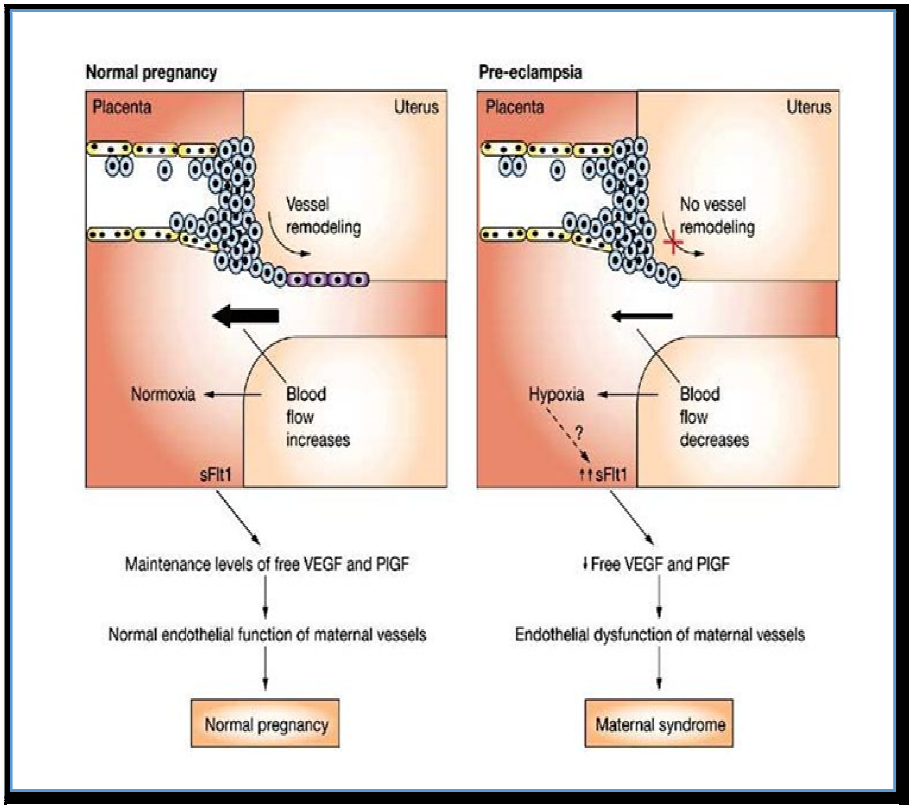
It is a variant of Flt-1 receptor for placental growth factor and VEGF. Increased maternal sFlt-1 levels inactivate and decrease PIGF and VEGF concentrations leading to endothelial dysfunction.

b) Soluble Endoglin(sEng)[16]:

It is a placenta derived 65-kDamolecule that blocks endoglin, which is a surface coreceptor for TGFβ Family.Also

called CD105, soluble form of endoglin inhibits various TGFβ isoforms from binding to endothelial receptors thatresults in decreased nitric oxide dependent vasodilatation.

ANTIANGIOGENIC PROTIENS



6) RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM(RAAS)[17]:

The RAAS axis maintains sodium concentration, Blood volume and Blood Pressure. In normal pregnancy, Renin activity, plasma renin concentration, Angiotensin-II levels, Aldosterone levels are increased. But there is **refractoriness** to the effects of Angiotensin-II. In women who are destined to be **Preeclamptic,** there is a **loss of Refractoriness**

due to down regulation of Angiotensin receptors in the presence of persistently elevated levels.

PATHOPHYSIOLOGICAL CHANGES:

It involves multiple organ systems described as follows.

1) CARDIOVASCULAR SYSTEM:

In Preeclampsia, due to increased peripheral resistance[18], there is decreased cardiac output that results in Hyperdynamic ventricular function. Pulmonary Edema results from Alveolar Endothelial-Epithelial leak.

Generalised Vasoconstriction causes increased vascular permeability and leakage of plasma into interstitial space that results in reduced plasma volume and **HAEMOCONCENTRATION.**

2) COAGULATION:

Coagulation abnormalities seen in Severe Preeclampsia and Eclampsia patients, It includes Thrombocytopenia, Reduced levels of clotting factors, evidence of platelet activation, Intravascular coagulation and Haemolysis. Thrombocytopenia defined by platelet count less than 1 lakh indicates severe disease. Haemolysis demonstrated by increase in LDH levels, peripheral smear showing schistocytosis, spherocytosis,

reticulocytosis[19].These abnormalities results from Microangiopathic Haemolysis. The association of Thrombocytopenia, Haemolysis along with Elevated Liver Enzymes is referred as **HELLP SYNDROME.**

3) RENAL CHANGES:

Due to increased afferent arteriolar resistance there is reduced renal blood flow and reduced GFR. This results in **elevated plasma Uric Acid.**

Urine sodium concentration is increased and urinary excretion of calcium is decreased due to increased tubular reabsorption. **PROTEINURIA** is the hallmark of preeclampsia. ACUTE RENAL FAILURE due to tubular necrosis is rare and it is usually induced by Hypotension and Hypovolaemia in severe disease.

Preeclampsia produce a characteristic changes in kidneys termed as **'GLOMERULAR CAPILLARY ENDOTHELIOSIS'**, and **'EARLYFOCAL SEGMENTAL GLOMERULAR SCLEROSIS[20,21]'** in some patients. These lesions usually resolves completely after pregnancy.

4) LIVER:

Excessive fibrin deposition in hepatic sinusoids obstructs blood flow and hepatic vasoconstriction causes the release of hepatic enzymes

(AST, ALT, LDH) in circulation. Characteristic lesions in liver are **PERIPORTAL HAEMORRHAGES IN THE LIVER PERIPHERY**.

Hepatic vasculature in the subcapsular region is particularly susceptible resulting in subcapsular haemorrhages which becomes larger and forms **SUBCAPSULAR HAEMATOMAS** and liver rupture.

5) BRAIN:

Both intense vasospasm of cerebral arterioles and over-dilatation of vessels are implicated in the pathogenesis of Eclampsia. In hypertension, as a part of auto regulatory mechanism, cerebral vasoconstriction occurs which leads to Ischaemia, Edema, Infarction. When the regulatory mechanisms fails at some point, dilatation of vessels occurs resulting in Hyperperfusion and '**VASOGENIC EDEMA**[22]**'**

The Pathognomic finding in preeclampsia is EDEMA with FOCI OF INFARCTION.

CEREBRAL HAEMORRHAGE should be suspected in older gravida with Chronic Hypertension and patients presents with Hemiplegia, focal deficits, coma following eclampsia. CT/MRI should be done to confirm the diagnosis.

BLINDNESS[23] can occur due to:

- Severe Papilloedema
- Retinal Detachment
- Occipital lobe lesions

6) PLACENTA:

Placenta of Hypertensive patients shows increased evidence of Infarct, Congested chorionic villi, Haematoma, and Proliferative endarteritis.

Microscopic examination shows increased syncytial knots, fibrinoid necrosis, cytotrophoblastic cellular proliferation, calcified and hyalinised villous spots[24], endothelial proliferation.

COMPLICATIONS OF PREECLAMPSIA:

- **MATERNAL**
- **FETAL**

	MATERNAL		**FETAL**
1)	Abruptio Placenta(Most common)	1)	IUGR
2)	HELLP Syndrome	2)	Prematurity
3)	Pulmonary Edema	3)	Antepartum and Intrapartum Asphyxia
4)	Thrombocytopenia/DIC	4)	Intrauterine Death
5)	Acute Renal Failure		
6)	ARDS(Adult Respiratory Distress Syndrome)		
7)	ECLAMPSIA		
8)	Hepatic Rupture		
9)	Cerebral Haemorrhage		
10)	Sudden Postpartum Collapse		

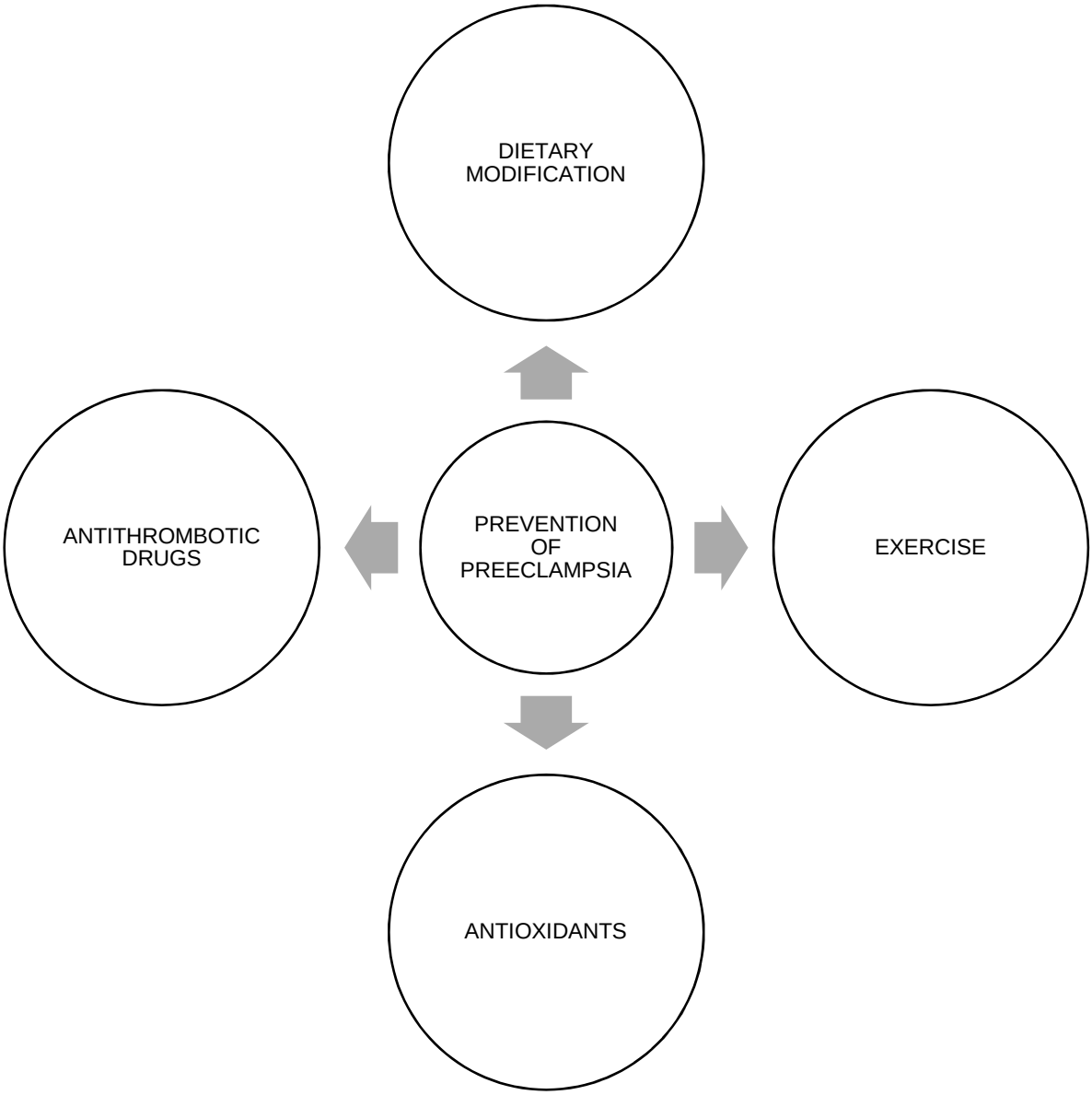
PREDICTIVE TESTS FOR THE DEVELOPMENT OF PREECLAMPSIA SYNDROME:

TESTING RELATED TO:	TESTS:
Placental perfusion/ Vascular Resistance	Roll-over test[25],Isometric handgrip test, pressor response to Angiotensin-II infusion[25],Midtrimester mean arterial blood pressure[26], 24 hour ambulatory BP monitoring, Uterine artery Doppler velocimetry, pulse wave analysis[26].
Fetoplacental unit Endocrine dysfunction	αFetoprotein, HCG[26], Estriol, PAPP-A, inhibin A, Activin A, placental protein 13,CRH.
Renal Dysfunction	**Serum URIC ACID[26]**, Microalbuminuria, Urinary Calcium[26], microtransferrinuria, Cystatin C.
Endothelial dysfunction / oxidative stress	Platelet count and activation,LDH,Fibronectin[27],PG's , prostacyclins, Thrombaxane, CRP, Cytokines, Endothelins, Homocysteine, APLA, VEGF, PIGF, sFlt-1.
Others	AntithrombinIII, ANP, β2microglobulin, haptoglobin, cell free fetal DNA, serum and urine proteomics, Hepatic aminotransferases.

UTERINE ARTERY DOPPLER VELOCIMETRY:

In normal pregnancy, impedance to uterine artery blood flow is reduced. In preeclampsia, failure of trophoblastic invasion into vessels is reflected by High impedance to uterine blood flow. **Increased resistance to flow** and **presence of Diastolic Notch** is indicative of PREECLAMPSIA. Whereas in Chronic HTN, it is predictive of superimposed Preeclampsia. Other indices like PULSATALITY INDEX, RESISTANCE INDEX are noted**.** Recent studies shows combined use of Doppler studies and biochemical markers in 1st trimester have shown improved rates of prediction for preeclampsia[26,28,29..]

PREVENTION OF PREECLAMPSIA:



1) DIETARY MODIFICATION:

- **LOW SALT DIET**: Earliest researches found that salt restriction is useful in preventing preeclampsia. However recent trial (Knuist,1998) proved that salt restricted diet is ineffective in preventing preeclampsia[30].
- **CALCIUM SUPPLEMENTATION** : Calcium supplementation of 1.5 – 2 gms reduces the incidence of preeclampsia by half[31.]
- **ZINC SUPPLEMENTATION**: Low serum Zinc levels associated with suboptimal outcomes of pregnancy including preeclampsia. However, Cochrane review (2012) does not reveal any evidence of improved pregnancy outcome with Zinc supplementation[32].
- **FISHOIL SUPPLEMENTATION**: Supplementation of common dietary sources such as EPA (Eicosapentaenoic acid), ALA (Alphalinoleic acid), DHA (Docosahexaenoic acid) would prevent inflammatory mediated Atherogenesis. But no trials conducted so far have shown to prevent preeclampsia
- **L-ARGININE**: Nitric oxide, potent vasodilator produced from L-arginine by endothelial cells. Supplementation of L-Arginine does not shown to prevent preeclampsia.

2) EXERCISE:

Exercise and physical activity have shown to prevent Hypertension in non-pregnant women.But studies have not shown to proven benefit in preeclampsia[33].

3) ANTITHROMBOTIC DRUGS:

Aspirin being an Antiplatelet aggregator improves the blood flow by preventing the formation of microthrombi within the blood vessels. A large RCT '**Collaborative Low Dose Aspirin Study in Pregnancy**' (**CLASP TRIAL**[34]) shows non-significant reduction of 12% in Preeclampsia, but there was a significant reduction of proteinuric preeclampsia in women prone to develop early onset preeclampsia. A recent metaanalysis shows earlier the aspirin started in pregnancy, greater was the benefit in reducing preeclampsia**. NICE recommends 75mg of Aspirin daily fo**r **all women who are at High risk for preeclampsia from 12 weeks until Birth of the baby**[35].

4) ANTIOXIDANTS :

A small RCT using vitamin C and E in women at 20 weeks of gestation shows significant decrease in incidence of preeclampsia in treated group. However, a second study does not show a significant difference.

INDICATORS OF SEVERITY OF PREECLAMPSIA:

ABNORMALITY	NON-SEVERE(MILD)	SEVERE PREECLAMPSIA[36]
Systolic BP	140 to <160mmHg	≥160mmHg
Diastolic BP	90 to <110mmHg	≥110mmHg
Proteinuria	Persistent 1+ to 2+ in dipstick,>0.3gm to <5gm in 24 hours	3+ or more on dipstick >5g in 24 hours
Headache	Absent	Present
Visual Disturbances	Absent	Present
Upper Abdominal Pain	Absent	Present
Convulsions	Absent	Present
Oliguria	Absent	Present
Serum Creatinine	Normal	Elevated(>1.2mg/dl)
Serum Transaminase	Minimal	Marked
Thrombocytopenia (< 100,000/µl)	Absent	Present
IUGR	Absent	Obvious
Pulmonary edema	Absent	Present

MANAGEMENT OF PRE-ECLAMPSIA:

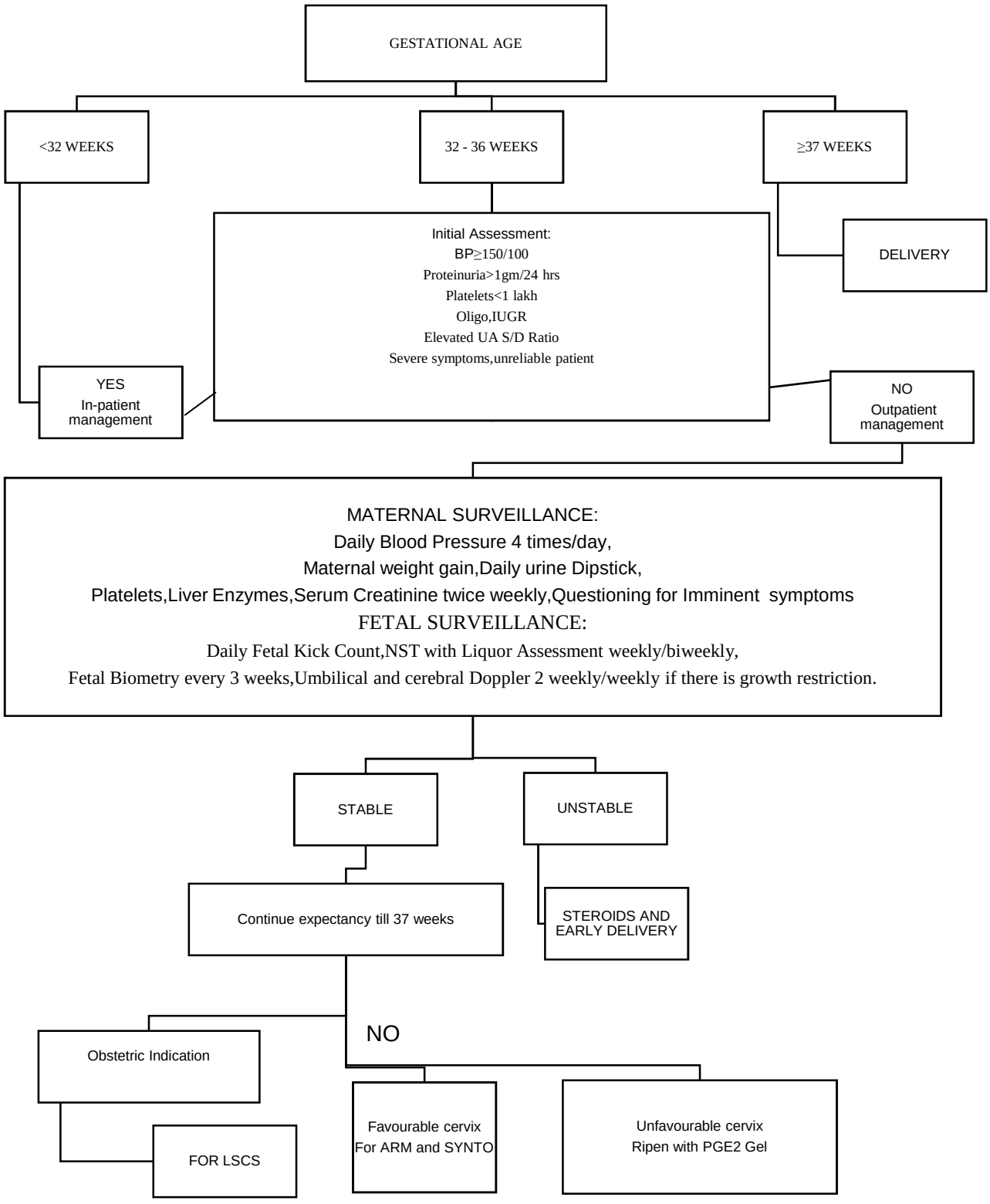
The only Effective definitive treatment of Preeclampsia is **DELIVERY.** Although delivery is always beneficial for the mother, it may not be optimal for the premature fetus. Once the diagnosis of Preeclampsia is made, the Management depends upon,

- Severity of Preeclampsia
- Gestational Age of the Fetus
- Maternal and Fetal status at the time of initial evaluation
- Presence or absence of Labour
- Level of specialized Neonatal Services

MILD PREECLAMPSIA:

The recent NICE guidelines[37] suggests that all patients initially diagnosed with Preeclampsia must be admitted to the hospital for Evaluation. The first step in the management is Assessment of Gestational Age. The Goal of management in Mild Preeclampsia is Early detection of progression to severe Preeclampsia and organ dysfunction. Antihypertensive drugs use in mild Preeclampsia is Questionable. NICE Clinical guidelines[37] suggest treating moderate Hypertension of BP 150/100 – 159/109 mmHg with Antihypertensives to keep BP < 150/80-100 range. First line AntiHypertensive in this situation is Oral Labetalol,

given orally in doses of 100-400mg every 8-12 hours. Alternatives are MethylDopa or Nifedipine.



MANAGEMENT OF SEVERE PREECLAMPSIA:

The Management of Severe Preeclampsia depends upon the Gestational Age

- <24 weeks = Seizure prevention, Blood Pressure control, and Immediate Delivery.
- 25 – 33 weeks = Expectant Management by Maternal and Fetal Surveillance, AN steroid therapy for fetal Lung Maturity, Deliver if there is maternal and fetal indication.
- > 34 weeks= Seizure prevention, Blood pressure control, immediate delivery.

MATERNAL SURVEILLANCE:

- ✓ Blood Pressure 4 times/day
- ✓ Daily Input and Output
- ✓ Urine Albumin once a day,24 Hour urinary protein
- ✓ Daily Maternal weight
- ✓ Platelet count, RFT, LFT Biweekly
- ✓ Coagulation Profile
- ✓ AntiHypertensive treatment, Steroids
- ✓ Questioning for Imminent symptoms

- ✓ Fundoscopy

FETAL SURVEILLANCE:

- ✓ Daily Fetal Kick Count
- ✓ Non stress Test Biweekly
- ✓ Biophysical profile Biweekly
- ✓ USG To assess Gestational Age and Fetal Growth every 2 weeks
- ✓ Umbilical Artery and Middle cerebral Doppler Biweekly

CRITERIA TO INTERRUPT EXPECTANT MANAGEMENT AND MOVE TO DELIVERY:

1) MATERNAL INDICATION FOR TERMINATION:

- ✓ Persistent severe Headache
- ✓ Visual Disturbances
- ✓ Eclampsia
- ✓ Shortness of breath with rales,

  SpO2<94% at room air,PULMONARY EDEMA
- ✓ Uncontrolled severe Hypertension inspite of treatment
- ✓ Persistent Platelet count < 1 lakh
- ✓ Oliguria < 500 ml in 24 hours
- ✓ Serum Creatinine ≥ 1.2 mg/dl

- ✓ Suspected Abruption,progressive labour,or ruptured membranes.

2) FETAL INDICATION FOR TERMINATION:

- ✓ Severe Growth Restriction < 5 percentile for Gestational Age
- ✓ Reverse or End Diastolic Flow in Umbilical Artery Doppler
- ✓ Persistent Severe Oligohydramnios(AFI < 5 cm)
- ✓ Biophysical profile ≤ 4 done 6 hours apart
- ✓ Fetal Death.

MODE OF DELIVERY IN SEVERE PREECLAMPSIA:

Preferred Mode of Delivery in Preeclampsia is **VAGINAL DELIVERY.**

Caesarean Section is indicated in cases of

- Fetal Distress,Malpresentation
- Placental Abruption,Placenta Praevia
- If vaginal delivery cannot be achieved in reasonable time usually 24 hours from the decision to induce
- Or the condition of patient deteriorates.

In case of Severe preeclampsia remote from term ,Caesarean section is better than vaginal due to prolonged and unsucessfull induction and fetal compromise.

INTRAPARTUM MANAGEMENT:

1) Hourly Monitoring of Blood pressure to maintain Systolic BP < 160 mmHg, Diastolic BP < 110 mmHg with AntiHypertensives.
2) Hourly Urine Output monitoring
3) To monitor Signs of Impending Eclampsia,
4) Eclampsia prophylaxis for those patients with Impending Eclampsia
5) Continuous Fetal Heart Rate Monitoring
6) Adequate Pain Releif during labour which cut downs catecholamine release and Hypertensive response. Epidural Analgesia is preferred as it is effective in control of Blood pressure and maintaining Cerebral Blood flow[38].
7) If Caesarean section becomes necessary,REGIONAL(EPIDURAL) Anaesthesia avoids the risk of aspiration and difficult intubation due to airway edema
8) Do not overload with intravenous fluids

9) Third stage should be managed with Oxytocin 10 U im and 10 U in drip to prevent PPH.Ergometrine should not be given as it causes intense vasoconstriction that may lead to Hypertensive Crisis.

ANTIHYPERTENSIVE THERAPY:

Antihypertensive therapy to a pregnant woman results in exposure of fetus to these drugs, hence the potential short term maternal benefits have to be balanced against possible short and long term benefits and risks to the fetus. There is lack of agreement regarding the blood pressure levels at which to initiate AntiHypertensive therapy. But starting AntiHypertensive therapy for Systolic BP ≥ 160mmHg or Diastolic BP ≥ 110mmHg is accepted universally.

According to Current Guidelines,AntiHypertensive treatment for Non -Severe HTN(140-159/90-109 mmHg) should target to maintain systolic BP at 130 – 155 mmHg and Diastolic at 80 – 105 mmHg in a woman without any comorbid condition. In those with comorbidities, AntiHypertensive drug therapy should be used to keep systolic BP at 130 – 139 mmHg and Diastolic BP at 80 – 89 mmHg[38].

FIRST LINE ORAL ANTIHYPERTENSIVE DRUGS:

- α and β Blocker - Labetalol
- Centrally Acting- MethylDopa

SECOND LINE ORAL ANTIHYPERTENSIVE DRUGS:

- Calcium channel blocker – Nifedipine
- BetaBlockers – Metaprolol,Acebutol,propranolol.

Drugs that are Absolutely Contraindicated in pregnancy are Angiotens in Converting Enzymes (**ACE Inhibitors**) due to its teratogenicity. In utero exposure of fetus to these drugs cause growth restriction, Oligo, hypotension, anuria, limb contractures.

A. LABETALOL:

It has both α and β blocking actions ratio being 1:3 in oral form and 1:7 in intravenous form. Its becoming first line drug because of its high effectiveness, low incidence of side effects. Beta Blockers mainly Atenolol is associated with IUGR, Hypoglycaemia, Hyperbiliribinaemia in fetus and hence not recommended.

DOSAGE: 100 to 400mg every 8-12 hours, Maxm Dose = 1200mg/day.

SIDE EFFECTS:

- Bradycardia
- Hypotension
- Dizziness

- Nausea,Vomiting
- Insomnia
- Fatigue
- Depression
- Masks the symptoms of Hypoglycaemia in Diabetic patients on insulin.

It is cautiously used in patients of Asthmatics and Heart Failure due to its beta blocking action.

B) ALPHA METHYLDOPA:

It is a centrally acting Alpha Adrenergic agonist,which acts primariliy on Central Nervous System with some effect peripherally to stimulate α2 receptors. This Decreases sympathetic tone and Arterial Blood Pressure.

DOSAGE: 250 – 500 mg bd/tds. Maximum Dose upto 2 gms/day. Onset of action starts within 4 – 6 hours and persists for 10 – 12 hours.

SIDE EFFECTS:

- Postural Hypotension
- Headache
- Dryness of mouth

- Swelling of feet
- Depression
- Rarely Haemolytic anaemia and
- Drug induced Hepatitis

It crosses placenta and secreted in Breast Milk,But no Teratogenecity reported till now.

C) CALCIUM CHANNEL BLOCKERS:

Nifedipine, the calcium channel blocker is the most commonly used drug for acute hypertension which is orally effective, easy to administer, as well as to store.

DOSAGE : 10 to 20 mg bd/tds.Maximum dose = 180 mg/day

ONSET OF ACTION : Within 10 to 15 minutes.Blood pressure is monitored every 15 mins and repeat oral dose of 10 mg can be administered every 30 to 60 mins until adequate response is achieved.

ROUTE OF ADMINISTRATION: Oral/sublingual. Oral route is preferred because of the precipitous fall in blood pressure with sublingual route.

CAUTION : Nifedipine when used along with magnesium sulphate will result in exaggerated hypotension because of their

synergistic action in blocking calcium channels.and also there is high chance of postpartum haemorrhage.

SIDE EFFECTS:

- Headache
- Dizziness
- Flushing
- Palpitation
- Heartburn
- Nasal congestion
- Hypotension
- Ankle edema

D)DIURETICS:

The main indication of diuretics use in pregnancy are as follows:

- Congestive cardiac failure
- Acute pulmonary edema
- Cerebral Intracranial tension
- Renal failure

Diuretics causes depletion of intravascular volume which can be deleterious in case of preeclampsia which already has a contracted plasma

volume. Since the placenta does not have any autoregulatory mechanism, placental perfusion is directly linked to the systemic pressure. so the reduction of plasma volume will result in reduced uteroplacental flow and placental Insufficiency. Hence diuretic use is not recommended in cases of preeclampsia with IUGR or Doppler evidence of reduced uteroplacental perfusion.

INTRAVENOUS PREPARATIONS:

These are used in Hypertensive emergencies with systolic BP > 160 mmHg, Diastolic BP > 110 mmHg to avoid complications like cerebrovascular haemorrhage, cardiac failure, placental abruption, eclampsia, Hypertensive encephalopathy.

A) LABETALOL:

It lowers the blood pressure smoothly and rapidly without tachycardia, which occurs characteristically in hydralazine.

DOSAGE : Administered at the dose of 10 to 20 mg intravenous initially followed by 20 to 30 mg every 30 mins to the maximum dose of 300mg.

Alternatively for continuous IV use,500 mg of labetalol added to 400 ml of Normal saline and administerd at the initial rate of 20 mg/hour.

If the BP does not fall into expected range(systolic < 160/diastolic 80 to 95 mmHg) in 20 mins,the dose is continued to be doubled every 20 mins until expected range is obtained.

ONSET OF ACTION : Within 5 mins and peak effect within 10 to 20 mins.

SIDE EFFECTS : Neonatal Bradycardia, Maternal Hypotension and bradycardia.

B) HYDRALAZINE:

It acts directly on arteriolar smooth muscle to reduce Peripheral vascular resistance.

It can be given as intermittent bolus of 5 mg intravenously every 20 to 30 mins or As an infusion at a rate of 0.5 to 10 mg/hour upto maxm of 30 mg.

ONSET OF ACTION : Within 10 mins

It initially causes increase in intracranial pressure by dilating the capacitance vessels in the cerebral circulation resulting in headache which mimics impending eclampsia. subsequently cerebral resistance vessels dilates and cerebral vascular flow increases.

The sympathetic effect of hydralazine causes marked tachycardia due to increased cardiac output.

SIDE EFFECTS[39]:

- Anxiety, Restlessness, Hyperreflexia (mimics impending eclampsia)
- Hypotension
- Abruption
- Oliguria
- Adverse effects on Fetal Heart Rate
- Low APGAR at 1 min

Hydralazine releases Nor adrenaline which is a potent vasoconstrictor of uteroplacental circulation. Hence continuous fetal heart rate monitoring is essential. Abnormal fetal heart rate patterns can be prevented by correction of hypovolemia and intermittent use of small doses.

C) SODIUM NITROPRUSSIDE:

It is a short acting vasodilator of both arterial and venous smooth muscle. It is given in Refractory severe Hypertension as an intravenous

infusion, started at the rate of 0.25 µg/kg/min and increased to a maximum dose of 8 µg/kg/min.

ONSET OF ACTION : Immediate(< 1 min),Duration of action is 1 to 3 mins.

It causes cyanide toxicity to the fetus.

ECLAMPSIA:

DEFINITION:

Development of seizures that cannot be attributed to other causes or unexplained coma during pregnancy or puerperium in a woman with preeclampsia. It can occur during Antepartum (38-53%), Intrapartum (18-36%), Postpartum(11-44%),Late postpartum.

It occurs more common in teenage primi.

Eclamptic Seizures are self limiting and lasts for 3 to 4 mins.It includes 4 stages.

1) Premonitory stage

2) Tonic stage

3) Clonic stage

4) Coma

PATHOPHYSIOLOGY

Seizures occurs as a result of abnormal autoregulatory response which consists of exaggerated vasoconstriction and ischaemic changes with rupture of vascular endothelium and pericapillary haemorrhages with development of foci of abnormal electrical discharges that generalize and cause convulsions.

Autopsy finding shows cerebral edema, cortical and subcortical white matter microinfarcts, pericapillary parenchymal bleeding and vascular bleeding in predominantly occipital and watershed areas.

MATERNAL COMPLICATIONS:

1) HELLP (9.7 – 20%)
2) DIC (7 – 11%)
3) Placental Abruption (7 – 10%)
4) Acute Renal Failure (5 – 9%)
5) Pulmonary edema (3 – 5%)
6) Aspiration Pneumonia (2 – 3%)
7) Cerebral Haemorrhage, Cardiopulmonary Arrest (2 – 5%).

Most common cause of maternal death is Intracranial Bleeding and Acute Renal failure secondary to placental abruption.

FETAL COMPLICATIONS:

1) Fetal distress
2) Hypoxic Ischaemic Encephalopathy(HIE)
3) Intrauterine death.

Most common cause of perinatal death is due to prematurity and Fetal asphyxia.

MANAGEMENT: It includes,

1) Control of convulsions
2) Control of Hypertension
3) Delivery of fetus

1) Control of convulsions:

- CALL FOR HELP,2 IV lines.
- To put the patient in left lateral position and clearing of airway by suctioning to prevent aspiration.
- Elevate the bedside rails to prevent maternal injury
- Give O2 by mask @ 8 – 10 L/min
- Pulse oximeter to monitor hypoxemia
- MgSO4 is the drug of choice in treatment of eclampsia.

MAGNESIUM SULPHATE:

It has central anticonvulsant and Neuroprotective effect.

PRITCHARD'S REGIMEN:

- **Intravenous Loading Dose:** Give 20 ml of 20% MgSO4 (4 gm) slow i.v for 20 mins.
- **Intramuscular Loading Dose:** Give 10 ml of 50% MgSO4 (5 gm) deep intramuscular in upper outer quadrant of each buttock using 3 inch and 20 gauge needle.
- **Maintanence Dose:** Give 5 gm of MgSO4 (10 ml of 50% solution) deep i.m in alternate buttock every 4 hours.
- **MONITORING FOR MAGNESIUM TOXICITY:**
  - Urine output should be atleast 30ml/hour or 100ml in 4 hours.
  - Deep tendon Reflexes should be present
  - Respiratory rate should be > 14/min
  - Pulseoximetry should be ≥ 96%

MgSO4 is discontinued 24 hours after delivery or after last convulsion.

Therapeutic Range of MgSO4 is 4 – 7 mEq / L.

First sign of toxicity is loss of patellar reflex.

In case of MgSO4 toxicity,give Calcium Gluconate 1gm(10ml of 10% solution) slow i.v.

2) CONTROL OF BLOOD PRESSURE:

Persistent and severe elevation in blood pressure should be treated with parentral antihypertensives to prevent Cerebrovascular accidents, Pulmonary edema, and Renal Failure.

3) DELIVERY OF FETUS:

The Definitive treatment is Delivery of baby, irrespective of gestational age in eclampsia. Patient must Deliver within 24 hours in severe preeclampsia and 12 hours in eclampsia. If the patient is stable, vaginal examination is done to assess the cervical status, If the cervix is favourable, induction of labour / amniotomy and synto acceleration is done. If unfavourable cervix, for LSCS.

HELLP SYNDROME:

It is a acronym coined by Louis Weinstein denoting

1) Haemolysis
2) Elevated Liver Enzymes
3) Low Platelets

It contributes 0.2 – 0.6 % in all pregnancies and 10 – 20 % in severe preeclampsia.

CRITERIA FOR DIAGNOSIS OF HELLP SYNDROME:

1) **HAEMOLYSIS**:

- Abnormal peripheral blood smear(Burr cells,schistocytes)
- Elevated Bilirubin > 1.2 mg/dl
- Low serum Haptoglobin
- Increased LDH(Twice the upper limit of normal >600U/L)

2) **ELEVATED LIVER ENZYMES:**

- Elevated AST and ALT Twice the upper limit of normal(≥ 72U/L)

3) **LOW PLATELET COUNT**:

- Platelet < 1,00,000/mm^3

MISSISIPPI CLASSIFICATION[40]:

1) CLASS I (Severe thrombocytopenia) = Platelet count < 50,000
2) CLASS II(Moderate thrombocytopenia) = Platelet count 50,000 to 1,00,000
3) CLASS III(Mild thrombocytopenia) = Platelet count 1,00,000 to 1,50,000

TENNESSEE CLASSIFICATION:

1) Complete HELLP = All 3 parameters are abnormal.

2) Incomplete/Partial HELLP = When 1 or 2 parameters are abnormal.

DIFFERENTIAL DIAGNOSIS: It needs consideration for

- Acute Fatty Liver Of Pregnancy
- Thrombotic Thrombocytopenic Purpura
- Haemolytic uraemic syndrome

MATERNAL MORBIDITY IN HELLP SYNDROME:

- ✓ Abruptio Placenta => 10 -15%
- ✓ DIC = >10 – 15%
- ✓ Subcapsular liver haematoma
- ✓ Hepatic rupture(Severe complication)

- ✓ Pulmonary edema => 6-8%
- ✓ Acute Renal Failure => 5-8%
- ✓ ARDS => 1-2%
- ✓ Death = >1%

Women with history of HELLP syndrome carry an increased risk of 20% in developing some form of Gestational Hypertension in subsequent pregnancy[41.]

MANAGEMENT OF HELLP:

Termination of pregnancy is the treatment of choice. When Gestational age is > 34 weeks => Stabilise the condition and deliver the baby. When Gestational age is between 27 – 34 weeks => Antenatal steroids for fetal maturity and delivery. The potential benefits has to be weighed against the risks of expectant management which include abruptio placenta, acute renal failure, pulmonary edema, DIC, perinatal and maternal death.

High dose Corticosteroids has been proposed to improve maternal prognosis of HELLP. In recent COCHRANE review, comparing corticosteroids with placebo, there was no difference in the risk of maternal death. The only clear effect on individual was improved platelet count.

Follow up is done with measurement of Platelet count and LDH, which becomes normal 72 hours following delivery. Other treatment modalities includes Platelet transfusion, plasmapheresis.

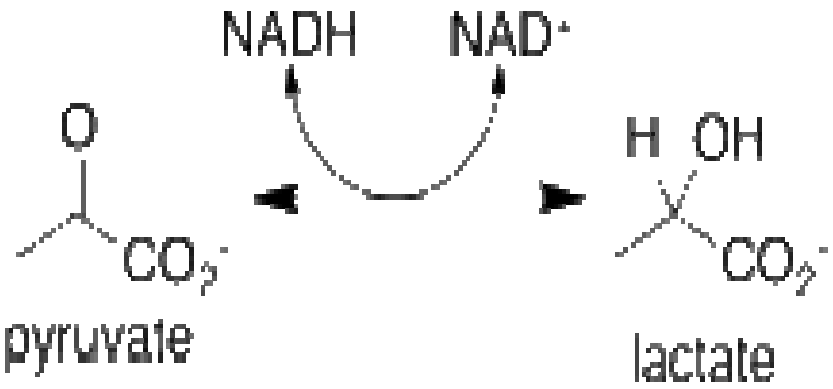
LACTIC ACID DEHYDROGENASE:

Lactate Dehydrogenase (LDH) is mainly an intracellular enzyme Which is responsible for interconversion of pyruvate and lactate in the cells. LDH levels are several times greater inside the cells than in the plasma. So its levels are increased in situations of increased cell leakiness, hemolysis and cell death.Preeclampsia is a multisystem disorder that leads to a lot of cellular death. So, serum LDH levels can be used to assess the extent of cellular death and thereby the severity of disease[42.]Serum LDH Levels can further be used to help in making decision, regarding the management strategies to improve the maternal and fetal outcome.

Lactate dehydrogenase catalyzes the interconversion of pyruvate and lactate with concomitant interconversion of NADH and NAD^+. It converts pyruvate, the final product of glycolysis, to lactate when oxygen is absent or in short supply, and it performs the reverse reaction during the Cori cycle in the liver. At high concentrations of lactate, the enzyme exhibits feedback inhibition, and the rate of conversion of pyruvate to

lactate is decreased. It also catalyses the dehydrogenation of 2-Hydroxybutyrate, but it is a much poorer substrate than lactate.

Reaction catalysed by LDH Enzyme



ISOENZYMES IN MAMMALS:

Lactate dehydrogenase is composed of four subunits (tetramer). The two most common subunits are the LDH-M and LDH-H protein, encoded by the *LDHA* and *LDHB* genes, respectively. These two subunits can form five possible tetramers (isoenzymes): 4H, 4M, and the three mixed tetramers (3H1M, 2H2M, 1H3M). These five isoforms are enzymatically similar but show different tissue distribution and electrophretic mobility.

The major isoenzymes of skeletal muscle and liver, M_4, has four muscle (M) subunits, while H_4 is the main isoenzymes for heart muscle in most species, containing four heart (H) subunits.

- LDH-1 (4H)—in the heart and in RBC (red blood cells), as well as the brain.
- LDH-2 (3H1M)—in the reticuloendothelial system
- LDH-3 (2H2M)—in the lungs
- LDH-4 (1H3M)—in the kidneys, placenta, and pancreas
- LDH-5 (4M)—in the liver and striated muscle.

Usually **LDH-2** is the predominant form in the **serum**. A LDH-1 level higher than the LDH-2 level (a "flipped pattern") suggests myocardial infarction(damage to heart tissues releases heart LDH, which is rich in LDH-1, into the bloodstream).

PREECLAMPSIA RESULTS IN INCREASE IN TOTAL LDH.

NORMAL VALUES OF LDH:

- Non pregnant adult = 115 – 211 IU/L
- First Trimester = 78 – 433 IU/L
- Second Trimester = 80 – 447 IU/L
- Third Trimester = 82 – 524 IU/L

CONDITIONS CAUSING LDH ELEVATION ARE AS FOLLOWS:

PHYSIOLOGICAL:

- Strenuous Exercise
- Pregnancy

PATHOLOGICAL:

- Myocardial Infarction
- Leukemia
- Haemolysis
- Muscular Dystrophy
- Hepatitis
- Pancreatitis

STUDIES BASED ON LDH IN PREGNANCY:

1) A prospective study conducted at 2002, by Qublan et al At King Hussein Medical Centre Jordan, 111 preeclampsia women (29 with mild and 62 with severe preeclampsia) and 60 normotensive controls were studied and demonstrated a significant association of serum LDH levels with severe preeclampsia. Increase in the incidence of neonatal deaths was observed in patients with increasing levels of serum LDH levels. IUD was seen in 4.8% of

cases, IUGR in 33.9% and premature in 77.9%. Neonatal deaths were reported in 95.2% patients with severe preeclampsia. Severely pre-eclamptic women with LDH levelsof >800 IU/l showed a significant increase in complications

2) A study done in 2008 by Rubin Aziz et al at Karachi ; 100 pregnant women with 50 as normal pregnant women as control and 50 preeclampsia women as study group , found that mean serum LDH was significantly higher in preeclampsia patients &thereby concluded that preeclampsia is characterized by vascular endothelial dysfunction & Higher levels Serum LDH can be a useful marker to identify the occurrence of complications of preeclampsia in early pregnancy which may reduce the risk of occurrence of disease.

3) A prospective comparative study conducted in 2008-09 & published in 2011 by Jaiswar S.P ^{et} al at Lucknow for 1 year. Total 146 patients were studied, out of which 26.7% were normal pregnant women which served as control group; remaining 73.3% cases included pregnancy with eclampsia and preeclampsia. Out of these 107 cases 32.7% were mild Out of these 107 cases 32.7% were mild preeclampsia, 33.6% were severe preeclampsia and 33.6% cases were of eclampsia clearly observed that there is significant rise in the LDH levels with increasing severity of the

disease. The occurrence of neonatal complications, stillbirths and perinatal deaths were significantly higher in mothers who had increased serum levels of LDH.

URIC ACID:

Uric acid is the end product formed from Metabolism of Purines.

Its level is elevated in preeclampsia due to its decreased renal clearance or by its increased production by breakdown of purines in placenta. Decreased renal clearance is due to altered renal tubular function.

This uric acid impairs the generation of Nitric Oxide from endothelial cells causing endothelial cell dysfunction which is the main pathophysiology in Preeclampsia. Hence it is used as the predictive marker for Preeclampsia. Various studies have been done on Uric acid levels in Preeclamptic patients and correlation with severity of disease, maternal and fetal complications. Some studies are as follows.

1) A Study was done by Disha et al at Civil Hospital,Ahemadabad in 2012 where 80 Hypertensive women were selectedrandomly and retrospectively studied.Birth weight,Gestational age at delivery,Complications like HELLP,Eclampsia,IUD,abnormality in

platelet count,creatinine,bilirubin were noted.Group were divided into 2 based on uric acid levels as <6 and >6mg% and all variables correlated.In this study, increase in maternal,fetal complications($p<0.05$) were noted in group with uric acid >6mg%.Mean gestational age at delivery and mean birth weight were reduced in group with uric acid>6mg%'

2) A prospective study conducted in department of O&G,ESIMC,PGIMSR Bangalore from Jan to Aug 2014 in which 80 pregnant women were included(mild and severe PIH).Uric acid and LDH were estimated. The women were followed up till delivery and early postpartum. Gestational age at delivery, birth weight, mode of delivery, maternal and fetal complications were noted. Significant association was found between LDH and uric acid with severity of preeclampsia, maternal morbidity, birth weight of babies. Gestational age at delivery and neonatal outcome was not statistically significant in this study.

MATERIALS AND METHODS

STUDY DESIGN:

Observational Study

METHODOLOGY:

This study involves estimation of serum LDH and Uric acid in normotensive and Hypertensive Antenatal woman in third trimester attending Antenatal OPD and Labour ward at Govt R.S.R.M Lying in Hospital, Stanley Medical College, during the period of January 2015 to September 2015.Patients were selected based on Inclusion and Exclusion Criteria. After obtaining their consent, detailed history, clinical examination and necessary investigations done accordingly.

The study population is divided into

1) CONTROLS = 50

2) SUBJECTS = 115

SUBJECTS are further subdivided into 3 groups based on Blood Pressure as Mild, Severe Preeclampsia and Eclampsia according to NHBPEP Classification.

1) MILD PREECLAMPSIA: Blood Pressure of ≥140/90 to <160/110mmHg

2) SEVERE PREECLAMPSIA: Blood Pressure of ≥160/110 mmHg

3) ECLAMPSIA: Preeclamptic patients with 1 or more episode of Generalised Tonic Clonic Seizures.

Study Population is also divided according to LDH and Uric Acid Levels as follows:

- According to Serum LDH levels:

  A) <600 IU/L

  B) 600 – 800 IU/L

  C) >800 IV/L

- According to serum Uric Acid levels:

  A) <6 mg

  B) >6mg

Patients were followed till delivery and early postpartum. Maternal complications like Abruption, HELLP, Eclampsia, Pulmonary edema, Intracranial haemorrhage, Maternal death and Fetal complications like IUD, IUGR were noted and correlated with serum LDH and Uric acid values.

INCLUSION CRITERIA:

All Normotensive and Hypertensive Antenatal woman in third trimester.

EXCLUSION CRITERIA:

1) Mothers with Hypertension < 20 weeks of gestation(Chronic Hypertension)

2) Preexisting Diabetes Mellitus

3) Liver disorder

4) Renal disorder

5) Epilepsy

6)Thyroid disorder

7) Heart Disease

8) Leukemia

9) Haemolysis

10) Hepatitis

11) Pancreatitis

METHOD OF LDH ESTIMATION:

Under aseptic precautions, 1 ml venous blood taken.

Sample allowed to clot and then centrifuged for serum to be separated.

By **International FederationOf Clinical Chemistry(IFCC)** method, estimation of serum LDH done.

PRINCIPLE:

Reduction of pyruvate with NADH forms NAD.This reaction is catalysed by Lactate Dehydrogenase.Temperature for this reaction to occur is of **30±0.05^{0}C** and pH of **9.40±0.05**.

340 nm is the absorbance maximum for NADH, Which after a period of time,it is used up and there is decrease in absorbance which is proportional to the enzyme activity that is detected by spectrophotometer.

SAMPLE MATERIAL:

The sample should be serum that is free from haemolyis. Total LDH is found to be stable in serum at 2 – 8^{o}C for about 1 – 3 days. Freezing causes inactivation of Liver isoenzyme.

PROCEDURE:

Under 30^0C at 340nm=> First,Substrate start Assay is done by adding the sample to Buffer and Starter reagent, initial absorbance is noted and absorbance values are noted every 1,2,3 mins.Mean Absorbance change/min is calculated. Then Sample start Assay is done by adding working reagent to sample and Mean Absorbance Change/min(A/min) is calculated.

CALCULATION:

LDH Activity in U/L (30^oC) = ▲A / min X 3333

ESTIMATION OF SERUM URIC ACID:

Uric acid is the catabolite formed from Purine Metabolism.

Uric acid estimation can be done by 2 methods.

1) Colorimetric Method(Phototungstic method) or
2) Enzymatic method(Uricase Method).

Enzymatic method is the most commoly used method. It involves oxidation of uric acid by uricase enzyme which convert the substrate to Allantoin. It is Quantified based on Differential Absorbance at 293 nm for these substances.

OBSERVATION AND RESULTS

A total of 165 Antenatal women attending OPD / Labour ward at Stanley Medical College from January 2015 to September 2015 were included in the study.

Study population were taken from third trimester. Both Normotensives and Hypertensives were included. They were selected irrespective of age, parity. Based on NHBPEP Classification, The study had 4 separate groups , one being a normotensive control with 50 women, and the rest three being patients with mild pre-eclampsia, severe pre-eclampsia and eclampsia amounting to 48, 53 and 14 respectively. Patients were divided further according to serum LDH values as < 600, 600 – 800, > 800 IU/L and based on serum uric acid values as < 6 mg and > 6 mg%. LDH and Uric Acid values were compared with Maternal and Fetal outcomes and studied using appropriate statistical test.

The results were compared based on One Way Analysis of Variance, chi-square test and differences were considered as significant when $p<0.05$.

The observations and results from this study are as follows.

AGE DISTRIBUTION AMONG GROUPS

In our study, age distribution among study population which included 11 patients (6.7%) of age <19 years,110 patients(66.7%) from 20-25 years, 30 patients(18.2%) from 26-30 yrs and 14 patients(8.5%) of > 30 yrs

Age in years		Group			
		Control	Mild Preeclampsia	Severe Preeclampsia	Eclampsia
<= 19	% within Age in years	.0%	27.3%	27.3%	45.5%
20-25	% within Age in years	33.6%	25.5%	33.6%	7.3%
26-30	% within Age in years	30.0%	43.3%	23.3%	3.3%
> 30	% within Age in years	28.6%	28.6%	42.9%	.0%

Out of 11 patients in age <19 years,3(27.3%) belong to mild preeclampsia,3(27.3%) belong to severe preeclampsia,5(45.5%) belong to Eclampsia, and none of the patients in normotensive group. Among 20-25 yrs age group,37(33.6%) are normotensives,28(25.5%) belong to mild preeclampsia,37(33.6%) belong to severe preeclampsia and 8(7.3%) belong to eclampsia. Among 26-30 yrs age group,9(30%) belong to controls,13(43.3%) belong to mild preeclampsia,7(23.3%) belong to

severe preeclampsia and 1(3.3%)patient in eclampsia group. Among age >30 years,4(28.6%) belong to controls,4(28.6%) belong to mild preeclampsia,6(42.9%) in severe preeclampsia and none of the patients in Eclampsia.

In Extremes of age group(<19yrs &>30 yrs) higher percentage of individuals belong to severe preeclampsia and eclampsia.

DISTRIBUTION OF PARITY AMONG STUDY POPULATION:

Out of 165 patients, 91(55.2%) are primigravida,59(35.8%) were G2,11(6.7%) are G3,4(2.4%) are G4 and above. High percentage of patients were Primi group.

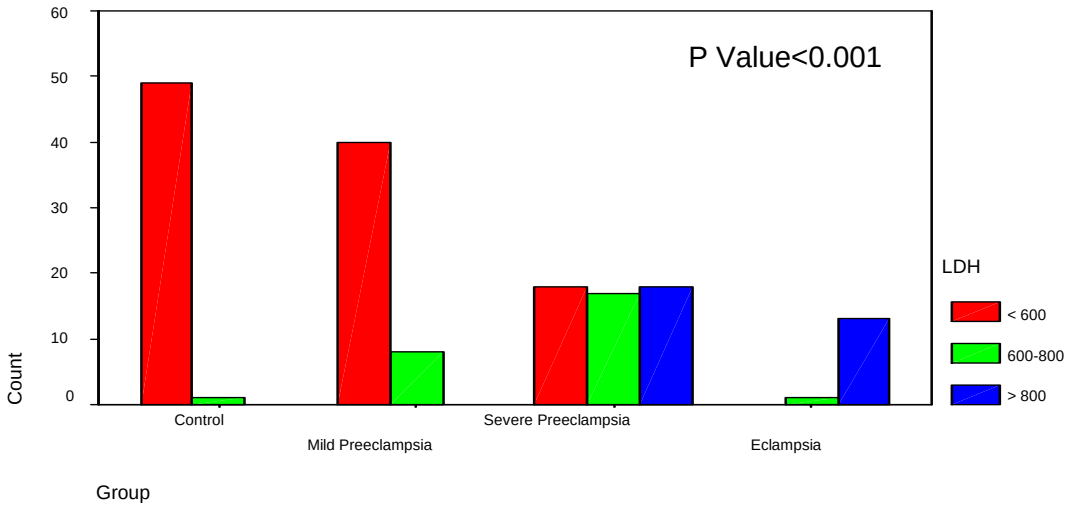
DISTRIBUTION OF PARITY AMONG CASES:

Obstetrics Score		Group				
		Control	Mild Preeclampsia	Severe Preeclampsia	Eclampsia	
Primi	% within Obstetrics Score	24.2%	30.8%	34.1%	11.0%	P Value< 0.187
G2	% within Obstetrics Score	42.4%	25.4%	25.4%	6.8%	
G3	% within Obstetrics Score	18.2%	45.5%	36.4%	.0%	
G4 and above	% within Obstetrics Score	25.0%	.0%	75.0%	.0%	

Out of 165 women in study group,91 patients are primigravida,and 74 are G2 and above. Parity distribution among different groups were analysed by chisquare test and the **P Value is 0.18. There is no statistically significant difference in distribution of parity among groups**.

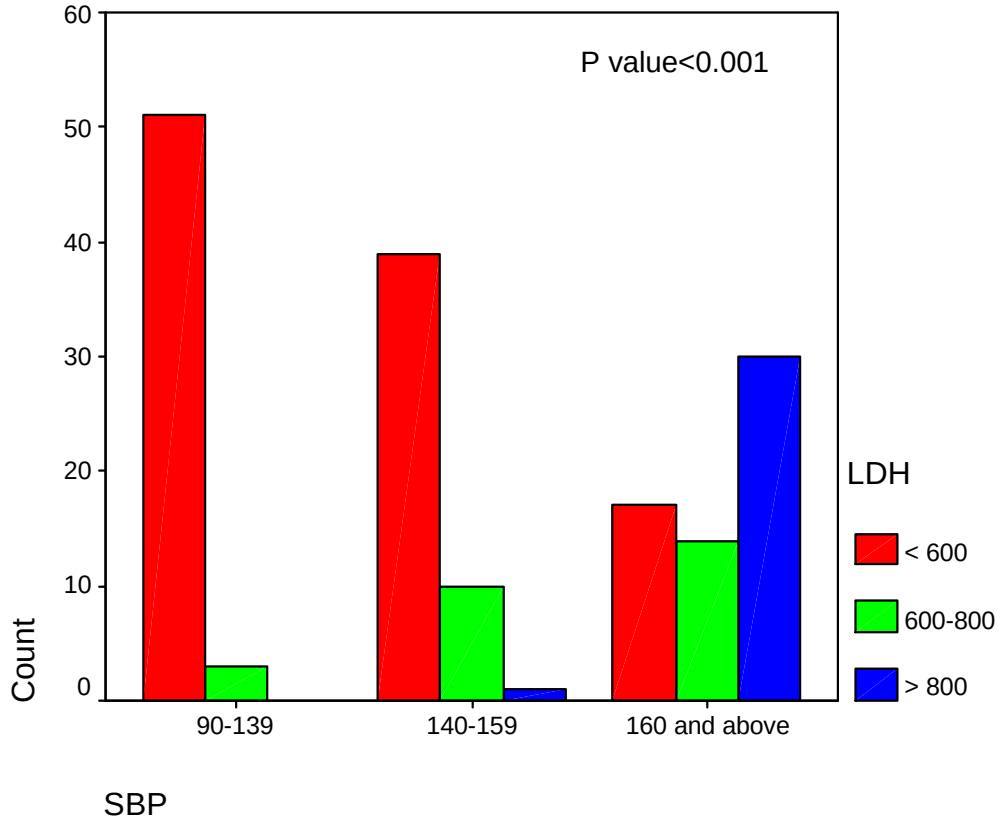
LDH AMONG DIFFERENT GROUPS:

Group	% patients with LDH <600 U/L	% patients with LDH 600-800	% patients with LDH >800 U/L	P value
Control	95	2	0	
Mild pre-eclampsia	83.3	16.7	0	
Severe pre-eclampsia	34	32.1	34	< 0.001
Eclampsia	0	7.1	92.9	



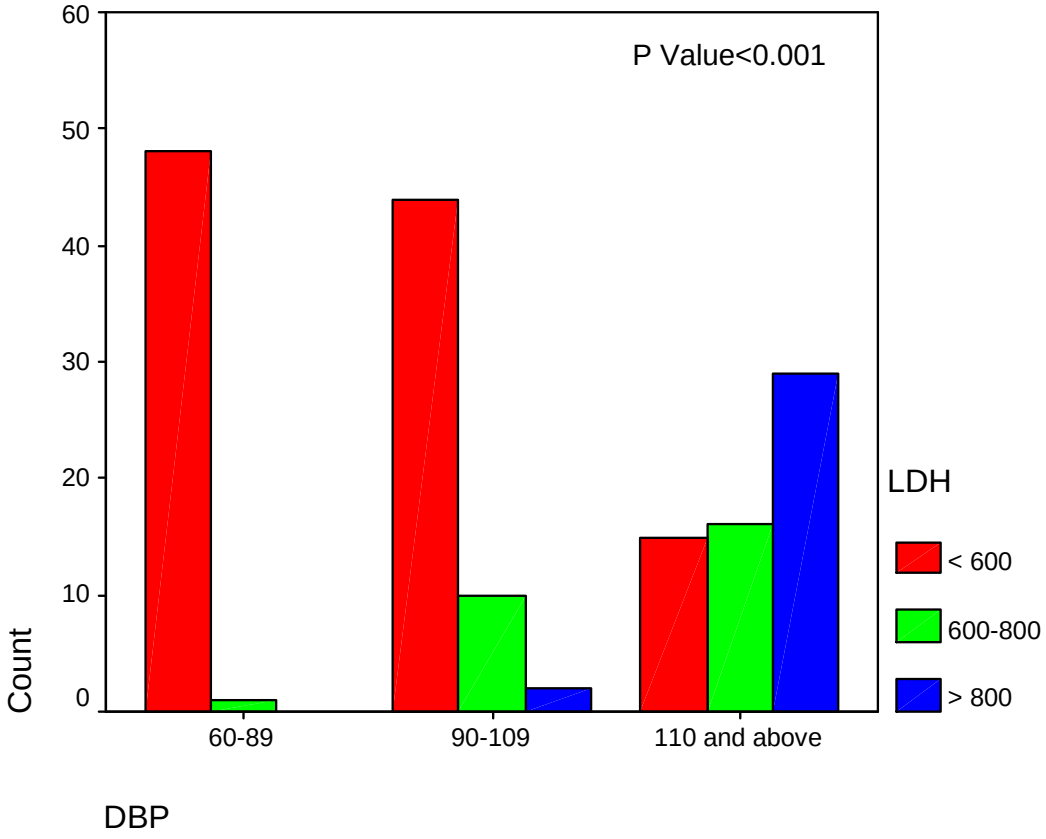
92.9% of the patients who had eclampsia had higher LDH levels more than 800 U/L; levels were equally split up in the 3 LDH ranges in patients with severe pre-eclampsia ($p<0.001$). However normal patients or those with mild pre-eclampsia had LDH levels <600 IU/L.

ASSOCIATION BETWEEN LDH AND SYSTOLIC BP:



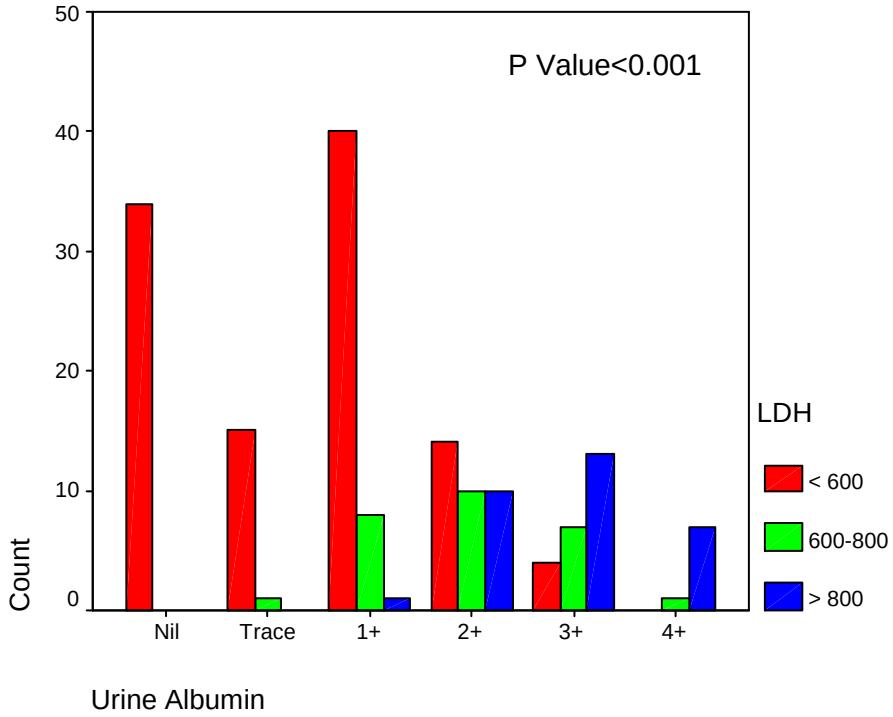
Among 107 patients with LDH<600 IU/L, majority (47.7%) were normotensive. Among 27 patients with LDH 600-800IU/L, 51.9% had SBP 160 and above. Out of 31 patients with LDH>800IU/L, none were normotensive, and 98.8% had SBP 160 and above **(p<0.001).Serum LDH and Systolic BP found to have significant association.**

ASSOCIATION BETWEEN LDH AND DIASTOLIC BLOOD PRESSURE:



Out of 107 patients with LDH <600IU/L, 44.9 had normal Diastolic BP. Out of 27 patients with LDH 600-800IU/L, majority(59.3%) had DBP 110 and above. Out of 31 patients with LDH>800IU/L, 93.5 had DBP 110 and above **(P Value <0.001).There was significant Association between serum LDH and DBP.**

ASSOCIATION BETWEEN LDH AND PROTEINURIA:



34 patients without proteinuria had LDH<600IU/L and 94% of trace excretion had LDH<600.

Out of 49 patients with 1+ proteinuria, majority (81.6% had LDH <600 IU/L.

Out of 34 patients with 2+ oteinuria,14(41%),10(29%),10(29%) had LDH <600, 600-800,>800 IU/L respectively.

Among 24 patients with 3+ proteinuria,4(17%),7(29%),13(54%) had LDH <600,600-800,>800 IU/L respectively. Out of 8 patients with 4+ proteinuria, none had LDH<600 and 87% had LDH >800IU/L (p<0.001).**Increasing LDH values isassociated with increasing severity of proteinuria.**

SERUM LDH AND GESTATIONALAGE IN WEEKS:

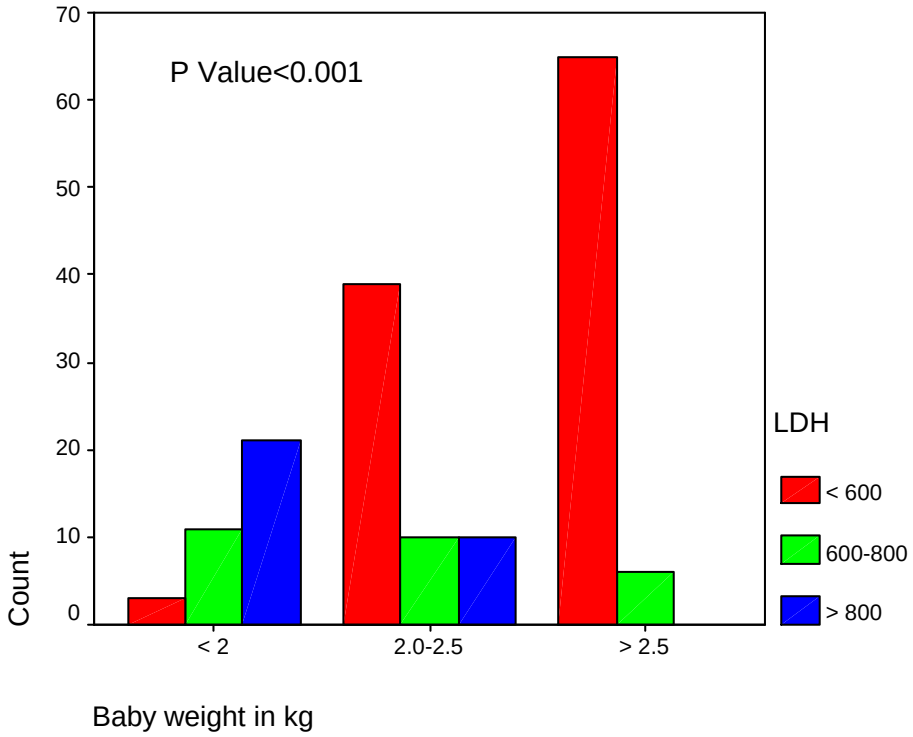
Group	% patients with LDH <600 U/L	% patients with LDH 600-800	% patients with LDH >800 U/L	P value
<34	0.9	3.7	6.6	P < 0.05
34-36	7.6	33.3	58.1	
>36	91.6	63	35.6	

Among 107 patients with LDH<600IU/L,0.9 % delivered at <34 weeks,8% delivered between 34-36 weeks,92% delivered at >36 weeks. Among 27 patients with LDH 600-800IU/L, 3.7%,33%,63% delivered at <34, 34-36,>36 weeks respectively. Among 31 patients with LDH>800IU/L, 6.6%, 58%, 35.6% delivered at <34, 34-36,>36 weeks respectively. There is significant difference in Gestational age of delivery between each groups. **There was a reduction inmean gestational age with increase in LDH**. **Propably due to more pretermdeliveries.**

SERUM LDH AND MODE OF DELIVERY:

There was **no statistical difference** between the mode of delivery and serum LDH values. But there is **higher percentage of Operative deliveries**(LSCS) in all groups ,that is more significant in groups with LDH 600-800 and >800IU/L.

SERUM LDH AND BIRTH WEIGHT :



Out of 107 patients with LDH<600 IU/L,61% of babies had birth weght>2.5kg,39% had birth weight 2-2.5kg,2.8% had birth weight<2 kg. Out of 27 patients with LDH 600-800 IU/L,22%,37%,41% had birth weight >2.5kg,

2-2.5kg,<2kg respectively. Among patients with LDH>800IU/L,68% of babies had birth weight<2kg,32% of babies had birth weight between 2-2.5kg and none of the babies had birth weight >2.5kg**. There is Significant Association between LDH and birth weight of baby. With Higher values of LDH, there was significant reduction in the birth weight (p<0.001).**

ASSOCIATION OF LDH WITH MATERNAL AND FETAL COMPLICATIONS:

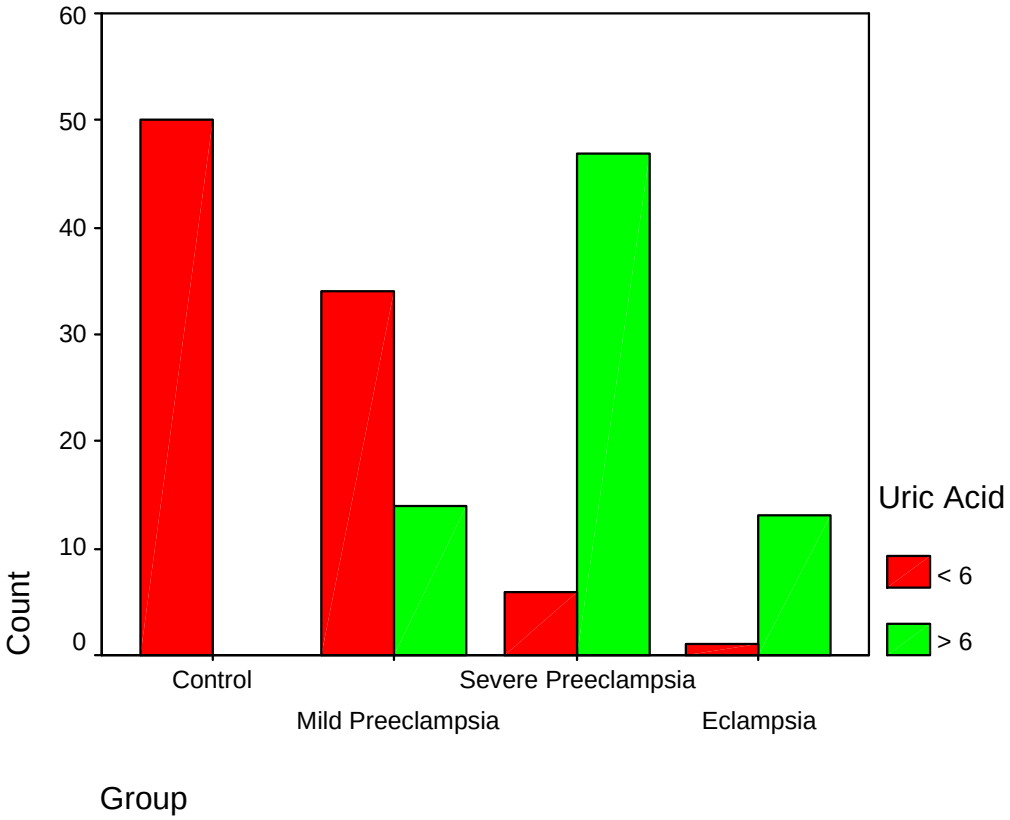
The levels of LDH were compared with various maternal and fetal complications as depicted in table below.

Complications	patients with LDH <600 U/L	patients with LDH 600-800	Patients with LDH >800 U/L	P value
IUD	1	4	4	0.001
IUGR	1	10	23	0.001
Intra cranial hge	0	0	1	NS
Pulmonary edema	0	1	0	NS
HELLP	0	1	4	0.02
Abruption	4	9	6	0.001
Eclampsia	0	1	13	0.001
Maternal death	0	0	1	NS

There was a higher number of IUDs and infants with IUGR who were born to mothers who had LDH levels > 800 IU/L(p=0.001). Among the maternal complications, 1 mother had intra cranial haemorrhage (>800IU/L), 1 had pulmonary edema (600-800IU/L), 1 mother died post partum(>800IU/L) due to intra cranial hemorrhage (p NS). However, patients with abruption(15/19) had LDH more than 600 IU/L and majority of patients with HELLP(4/5) and eclampsia(13/14) had LDH more than 800IU/L.

URIC ACID LEVELS AMONG STUDY GROUPS:

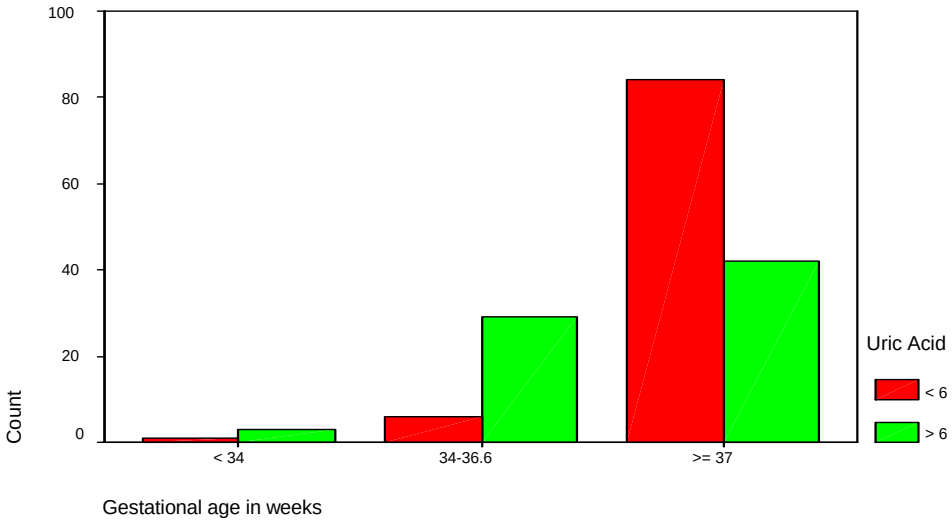
Group	% of patients with uric acid <6mg	% patients with uric acid >6mg	P value
Control	100	0	< 0.001
Mild pre-eclampsia	70.8	29.2	
Severe pre-eclampsia	11.3	88.7	
Eclampsia	7.1	92.9	



In control and mild preeclampsia group,100% and 71% respectively had uric acid <6mg .89% of severe preeclamptic women had uric acid>6mg and 92% of the Eclamptic women had uric acid>6mg. **There was Statistically significant association of serum uric acid and severity of preeclampsia(P value <0.001)**

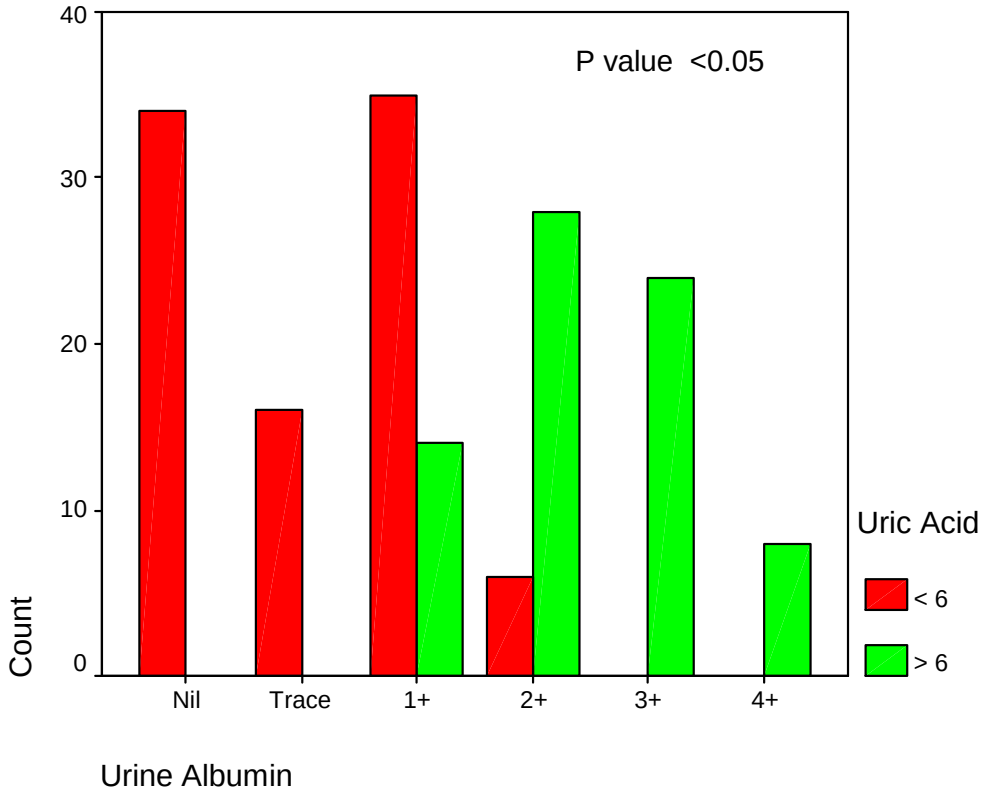
ASSOCIATION BETWEEN SERUM URIC ACID AND GESTATIONAL AGE AT DELIVERY:

Group	% patients with Uric acid<6mg	% patients with Uric acid>6mg	P value
<34	25	75	P < 0.05
34-36	17.1	82.9	
>36	66.7	33.3	



As depicted in the diagram above, Occurrence of preterm delivery is more common in women with serum uric acid >6mg% probably due to earlier termination of pregnancies in view of preeclampsia.

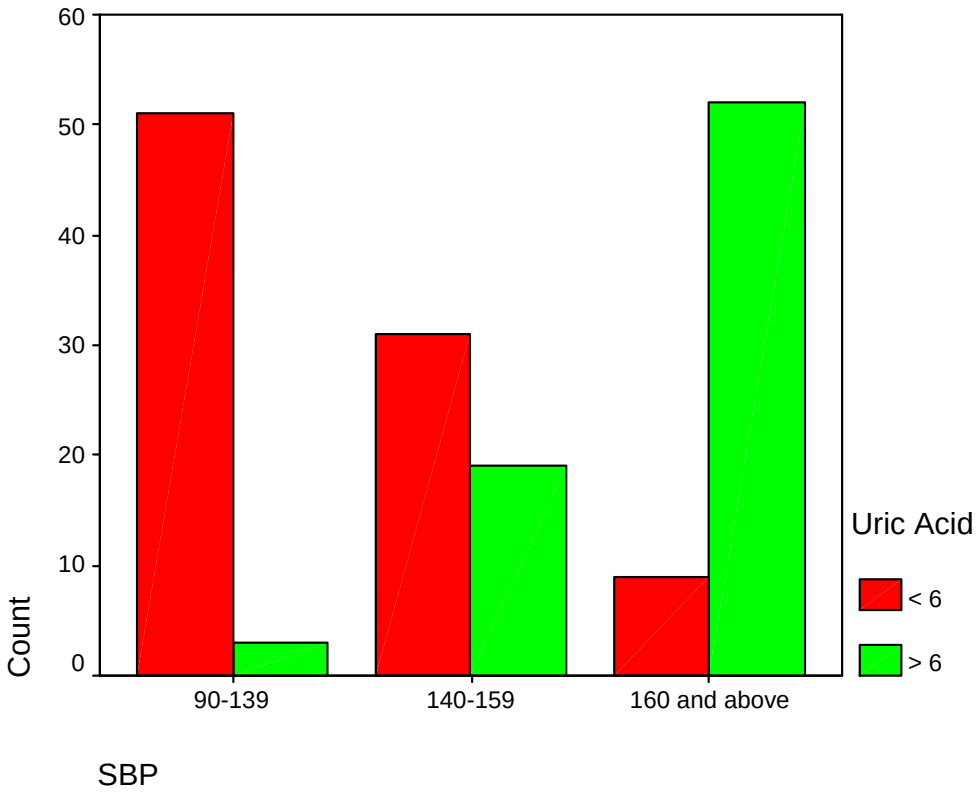
ASSOCIATION BETWEEN SERUM URIC ACID AND PROTEINURIA:



As depicted in the diagram above**, Increasing Proteinuria is significantly associated with Higher uric acid levels(P value <0.05)**

ASSOCIATION OF SERUM URIC ACID AND SYSTOLIC BP:

Systolic BP mmHg	% patients with Uric acid<6mg	% patients with Uric acid>6mg	P value
90-139	94.4	5.6	P < 0.001
140-159	62	38	
160 and above	14.8%	85.2%	



As shown in the table above,Majority(85.2%) of the patients with systolic BP of >160mmHg had uric acid levels>6mg.(**P Value<0.001)**

ASSOCIATION OF URIC ACID WITH DIASTOLIC BP:

Diastolic BP mmHg	**% patients with Uric acid<6mg**	**% patients with Uric acid>6mg**	**P value**
60-89	100	0	P < 0.001
90-109	62.5	37.5	
110 and above	11.7%	88.3%	

88.3% of the patients with DBP >110mmHg had uric acid levels >6mg but not so in those patients with DBP <90mmHg**.(P value <0.001**).

ASSOCIATION OF URIC ACID WITH BIRTH WEIGHT:

Birth weight in Kg	**% patients with Uric acid<6mg**	**% patients with Uric acid>6mg**	**P value**
<2	8.6	91.4	P < 0.001
2-2.5	52.5	47.5	
>2.5	80.3	19.7%	

As depicted in the table above, 91% of the babies with birth weight <2Kg were born to mothers who had uric acid levels >6mg%. **(P value<0.001).**

ASSOCIATION OF URIC ACID WITH MATERNAL AND FETAL COMPLICATIONS

Complications	Uric acid <6mg%	Uric acid >6mg%	P value
IUD	1	8	0.007
IUGR	3	31	0.001
ICH	0	1	NS
Pulmonary edema	0	1	NS
HELLP	0	5	0.02
Abruption	4	15	0.002
Eclampsia	1	13	0.01
Maternal death	0	1	NS

There was a higher number of IUDs and infants with IUGR who were born to mothers who had uric acid >6 mg%(p=0.001). Among the maternal complications, 1 mother had intra cranial haemorrhage >6 mg%)), 1 had pulmonary edema (>6mg%), 1 mother died post partum(>6mg%)) due to intra cranial hemorrhage (p NS). However, patients with abruption(15/19) had uric acid more than 6 mg% and majority of patients with eclampsia(13/14) and all patients with HELLP had LDH more than 6 mg%.

ASSOCIATION BETWEEN LDH AND URIC ACID:

As both LDH and uric acid had similar associations with th parameters assessed, a comparison was done between LDH and uric acid. As in the table, majority of patients(40.5%) who had LDH >800 IU/L also had high uric acid levels >6 mg% which was **statistically significant (p<0.001)**

Group	**% patients with LDH <600 U/L**	**% patients with LDH 600-800**	**% patients with LDH >800 U/L**	**P value**
Uric acid <6mg%	95.6	3.3	1.1	< 0.001
Uric acid > 6mg%	27	32.4	40.5	

DISCUSSION

Our study was conducted in the Department of Obstetrics and Gynecology, RSRM Hospital, Stanley Medical College. A total of 165 antenatal women were recruited from Outpatient department/ Labour Ward at Stanley Medical College & Hospital from Jan2015 - September 2015 All patients were of gestational age 28 weeks and above.

Patients were selected based on the inclusion and exclusion criteria irrespective of the age and parity and they were divided into three groups based on NHBPEP classification as 50 normotensives, 48 mild pre-eclamptics, 53 severe pre-eclamptics & 14 eclamptics. Patients were also divided into three groups based on their S. LDH (less than 600, 600 to 800, and more than 800 IU/l) and two groups based on uric acid levels (<6mg% and >6mg%)

All the diagnostic components and the possible maternal and fetal complications of pre-eclampsia were compared with their LDH and uric acid levels.

This study was similar to the study done by S.P Jaiswar et al and Disha et al.

Discussion on LDH :

The distribution of age & mean age between LDH groups were almost similar. No significant difference was observed in terms of parity between groups and moreover they did not influence S.LDH in contrast to Qublan et al and Jaiswar et al. Qublan et al stated that the majority were young primigravida in the affected population.

S. LDH levels consistently increased with increasing systolic & diastolic blood pressure, with a P value of <0.001 similar to Jaiswar & Amrit et al (p=0.01).

Most of the women with severe preeclampsia & eclampsia had severe proteinuria and S. LDH significantly increased with the severity of proteinuria (P<0.001). Results were comparable to Qublan et al who showed a significant increase in S. LDH with severity of proteinuria (P value of <0.05).

In the study done by S.P.Jaiswar et al, only 1 case had abruptio Placenta and 1 had HELLP but the incidence was high with 19 cases of abruption and 5 cases of HELLP in this study.LDH levels were significantly elevated in patients with these maternal complications(P <0.001) which was comparable to Jaiswar et al who showed significant increase in maternal morbidity with the increasing LDH levels

1 maternal death occurred in the study population and had LDH levels more than 800IU/L and died of intra cranial haemorrhage.

Higher LDH levels were associated with increased number of pre-term deliveries probably because of the severity of pre-eclampsia.

The incidence of operative delivery was elevated with increased LDH levels though did not reach statistical significance.

Women with LDH <600 IU/L gave birth to babies with adequate birth weight more than 2.5 kg. However those who had >800IU/L had LBW <2kg ($p<0.001$)

This fact could be explained by the increased preterm deliveries and the need for early termination of pregnancy to improve the maternal outcome in view of severity of disease.

Complications like growth restriction & late intrauterine fetal demise are well known complication of pre-eclampsia. He S , Bremme K, Kallner et al studied the S. LDH levels in pre-eclamptic women with small for gestational age infants and found a significant correlation between both. Incidence of IUGR and IUD were significantly higher in pre-eclamptic women and their S. LDH levels compared to the controls were abnormally high (P value < 0.00) similar to He. S et al.

Discussion on uric acid :

S. uric acid levels consistently increased with increasing systolic & diastolic blood pressure, with a P value of <0.001. The results of our study were similar to the study by Roberts et al, wherein uric acid was elevated in 75% of patients with diagnosed PIH.

Most of the women with severe preeclampsia & eclampsia had severe proteinuria and uric acid levels significantly increased with the severity of proteinuria (P<0.001) similar Hawkin's et al where 59% 0f patients with proteinuria had high uric acid levels.

1 maternal death occurred in the study population and had uric acid more than 6mg% which is similar to the results of Patel et al where there was only 1 maternal mortality in patients with high uric acid levels >6 mg%

Higher uric acid were associated with increased number of pre-term deliveries probably because of the severity of pre-eclampsia, the results of which was similar to that of Disha et al, where there were more number of patients high uric acid who were delivered pre term than with low uric acid levels.

The incidence of operative delivery was elevated with increased uric acid levels (p=0.02) probably due to the severity of the disease.

Patients with Uric acid <6mg% gave birth to babies with adequate birth weight more than 2.5 kg. However those who had >6mg%had LBW <2.5kg ($p<0.001$), results being similar to that of Disha et al where 17/23 children who had BW < 2kg were born to mothers who had high uric acid levels (>6.5 mg%)

This fact could be explained by the increased preterm deliveries and the need for early termination of pregnancy to improve the maternal outcome in view of severity of disease.

Our study reported 9 IUD, of which 8 had uric acid levels more than 6mg%. Similar study done by Patel et al, showed similar results where all 8 IUD was associated with uric acid levels > 6 mg% .

19 cases of abruption were reported in our study among which 15 cases had uric acid levels>6mg%(p value<0.001),similar study done by disha et al were 3 out of 4 cases of abruptio placenta had uric acid>6mg%.

SUMMARY

Ours was a comparative observational study done on 165 patients attending Outpatient department/ Labour Ward at Stanley Medical College & Hospital from Jan 2015 - September 2015 Our study was done in search of a valuable marker for preeclampsia and Eclampsia which would reflect the severity of the disease and would predict the maternal and fetal outcome so that such markers can help in decision making and can influence the current management protocols in order to achieve a better maternal and perinatal outcome. Lactate dehydrogenase and uric acid has been suggested by various authors as a promising marker and the inferences made out of this study are as follows.

1. Extremes of age was associated with elevated LDH but not uric acid
2. Parity does not affect the levels of either LDH or uric acid
3. Patients with high S. LDH and uric acid levels also had high SBP and DBP($p<0.001$)
4. Proteinuria by itself is a marker of severity of the disease and was associated with high LDH and uric acid ($p<0.001$), hence LDH and uric acid, may be used as similar markers with high significance and hence the need for management strategies based on S. LDH and uric acid.

5. Patients with elevated LDH and uric acid had increased numbers of pre-term deliveries especially between 34-36 weeks
6. High uric acid levels was associated with increased chances of operative deliveries probably to reduce maternal or fetal morbidity and mortality
7. High LDH and uric acid levels were associated with low birth weight less than 2 kg, probably as a result of increased risk of IUGR and pre-term deliveries
8. High uric acid and LDH levels were significantly associated with more number of IUDs
9. High uric acid and LDH levels were associated with high chances of abruption, HELLP, eclampsia.
10. Though rare complications like pulmonary edema, intracranial haemorrhage and maternal deaths were associated with high LDH and uric acid levels, it did not reach statistical significance.

CONCLUSION

1. S. LDH and uric acid values were significantly high in pre-eclamptic patients depending on the severity of the disease indicating the increased cellular turnover in them.

2. Higher LDH and uric acid levels was associated with diagnostic components of preeclampsia like SBP, DBP, Proteinuria, maternal morbities like abruption, HELLP, eclampsia, intracranial haemorrhage, pulmonary edema or death and fetal morbidities like IUGR or sometimes IUD

3. Hence diagnostic and management strategies may be considered based on S.LDH and uric acid levels and further studies on a larger sample can be done to substantiate our observations on the utility of this parameter as a diagnostic and prognostic component of preeclampsia.

4. Development of new management strategies based on S. LDH and uric acid levels may help in appropriate decision making thereby avoiding unwanted maternal & fetal deaths.

BIBLIOGRAPHY

1. James PR, Nelson-Piercy C.Management of Hypertension before, during, and after pregnancy.Heart.2004;90:1499-1504.
2. Khan KS, Wojdyla D,Say L,et al.WHO analysis of causes of maternal death : a systematic review.Lancet.2006;367:1066-1074.
3. Conde - Agudelo A, Romero R,Lindheimer MD:Tests to predict preeclampsia. In Lindheimer MD, Roberts JM,Cunningham FG(eds).

   Chesley's Hypertensive Disorders of Pregnancy,3rd ed.New York: Elseiver,2009:191.
4. Jaiswar S.P et al2011,Lactic acid dehydrogenase, a biochemical marker for preeclampsia-eclampsia. Gupta Amrit. Sachan Rekha. The Journals Of Obstetrics and Gynaecology of India.
5. Sreelatha S, Bharathi A,Ramya S,Shwetha Sharau (2015). Estimation of serum LDH and uric acid in Preeclampsia and its correlation with maternal and perinatal outcome. International Journal Of Advances in Case Reports, 447-449.
6. NHBPEP (National High Blood Pressure Education Program) Working Group on High Blood Pressure. Report of the NHBPEP Working Group on High Blood Pressure in pregnancy. Am J Obstet Gynecol.2000; 183:S1-22.

7. American College of Obstetricians and Gynaecologists. Diagnosis and Management of Preeclampsia and eclampsia. Practice Bulletin No.33.Washington, DC:ACOG, January 2002.
8. National Institute Of Health and Clinical Excellence.2010. Hypertension in pregnancy: The Management of Hypertensive disorders during pregnancy.CG no 107.London: National Institute of Health and Clinical Excellence.
9. Sibai B,Dekker G,Kupferminc M:Preeclampsia. Lancet.2005; 365; 785-799.
10. Redman CWG, Sargent IL, Roberts JM.Immunology of abnormal pregnancy and preeclmpsia. In Lindheimer MD, Roberts JM, Cunningham FG(eds).Chesley's Hypertensive Disorders of Pregnancy,3rd ed. New York:Elseiver,2009:129.
11. Madazli R,Budak E, Calay Z,et al.Correlation between placental bed biopsy findings, vascular cell adhesion molecule and fibronectin levels in preeclampsia.Br J Obstet Gynecol 2000; 107:514
12. Granger JP, Alexander BT, Llinas MT, Bennett WA, Khalil RA.Pathophysiology of hypertension during preeclampsia linking placental ischaemia with endothelial dysfunction. Hypertension 2001Sep;38(3 Pt 2):718-22.

13. Redman CWG, Sargent IL, Roberts JM.Immunolgy of abnormal pregnancy and preeclampsia. In : Lindheimer MD, Roberts JM, Cunningham FG(eds). Chesley's Hypertensive Disorders in Pregnancy,3rd edition.Elsevier,2009,p129
14. Ward K, Lindheimer MD.Genetic factors in the etiology of preeclampsia / eclampsia. In: Lindheimer MD, Roberts JM, Cunningham FG(eds). Chesley's Hypertensive Disorders in Pregnancy, 3rd edition. Elsevier, 2009, p51.
15. Maynard SE, Min J-Y,Merchan J et al. Excess placental soluble Sms-like tyrosine kinase 1 9sFlt1) may contribute to endothelial dysfunction, hypertension and proteinuria in preeclampsia.J Clin Invest 2003; 111(5):649.
16. Levine RJ, Lam C, Qian C et al. Soluble endoglin and other circulating antiangiogenic factors in preeclampsia. N Eng J Med 2006; 355:992
17. Gant NF, Chand S, Worley RJ, Whalley PJ, Crosby UD, Mcdonald PC.A clinical test useful for predicting the development of acute Hypertension in pregnancy. Am J Obstet Gynecol 1974 sep; 120(1):1-7
18. Hibbard JU, Shroff SG, Lang RM.Cardiovascular changes in preeclampsia. Semin Nephrol.2004;24:580-587.

19. Cunningham FG, Lowe T, Guss S et al. Erythrocyte morphology in women with severe preeclampsia and eclampsia. Am J Obstet Gynecol 1985;153:358

20. Strevens H, Wide Swensson D,Hansen A, Horn T, Ingemarsson I, Larsen S, Willner J,Olsen S.Glomerular endotheliosis in normal pregnancy and preeclampsia. BJOG 2003 Sep;110(9):831-836.

21. Gaber LW, Spargo BH, Lindheimer MD .Renal pathology in preeclampsia. Baillieres Clin Obstet and Gynecol 1994 june;8(2): 443-68.

22. Sibbai BM.Diagnosis prevention and management of eclampsia. Obstet Gynecol 2005 feb; 105(2)402-10.

23. Cunningham FG, Fernandes CO, Hernandes C.Blindness associated with preeclampsia and eclampsia. Am J Obstet Gynecol 1995; 172:1291

24. Majumdar S, Das Gupta H, Bhattacharya K, Bhattacharya A.A study of placenta in normal and hypertensive pregnancies. J Anat Soc India 2005; 54(2):1-9

25. Gant Nf,S Chand, RJ Worley et al 1974.A clinical test useful for predicting the development of acute Hypertension in pregnancy. Am J Obstet Gynecol 120:1

26. Williams Obstetrics 23rd edition Page 725,726,733.

27. Halligan A ,J Bonnar,B Sheppard et al 1994. Haemostatic, fibrinolytic and endothelial variables in normal pregnancy and preeclampsia. BR J Obstet Gynecol 101:488
28. D.C.Dutta's Textbook of Obstetrics by Hiralal Konar 7th edition pg227
29. Irion O, J Masse JC Forest and JM Moutquin.1998.Prediction of preeclampsia, low birth weight for gestation and prematurity by uterine artery blood flow velocity waveform analysis in low risk nulliparous women.Br J Obstet Gynecol 105:422-29
30. Duley L, Henderson – Smart D,Meher S.Altered dietary salt for preventing preeclampsia, and its complications. Cochrane Database Syst rev 2005 oct 19;(4) : CD005548.
31. Hofmeyr GJ, Lawrie TA,Atallah AN, Dulie L.Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Syst rev 2010 aug 4;(8) : CD001059.
32. Mori R,Ota E,Middleton P, Tobe-Gai, R Mahomed K,Bhutta ZA.Zinc supplementation for improving pregnancy and infant outcome. Cochrane Database Syst rev 2012 july 11;(7) : CD000230
33. Osterdal ML, Strom M,Klemmensen AK,Knudson VK,Juhl M, Halldorsson TI, Nibo Anderson AM, Magnus P, Olsen SF. Does

leisure time physical activity in early pregnancy protect against preeclampsia? Prospective cohort in Danish Women. BJOG 2009 January;116(1):98-107

34. CLASP : A Randomized trial of Low Dose Aspirin for the Prevention and Treatment of preeclmpsia among 9364 pregnant woman. CLASP (Collaborative Low Dose Aspirin Study in Pregnancy) Collaborative group. Lancet 1994 march 12;343 (8898): 619-29

35. The Management of Hypertensive disorders during Pregnancy. NICE Clinical Guidelines 107, Jan 2011 National Institute of Clinical Excellence.

36. Wagner LK.Diagnosis and Management of Preeclampsia. Am Fam Physician 2004 dec 15;70(12):2317-24.

37. National Institute of Health and Clinical Excellence 2010.Hypertension in Pregnancy. The Management of Hypertensive disorders in pregnancy. CG No107.London; National Institute of Health and Clinical Excellence

38. Chronic Hypertension in Pregnancy. Practice Bulletin No 125.American College of Obstetricians and Gynaecologists. Obstet Gynecol 2012; 119:396-407.

39. Magee LA, Cham C, Waterman EJ, Ohlsson A, Von Dadelszen P.Hydralazine for treatment of severe hypertension in pregnancy: Meta Analysis.BMJ.2003 Oct 25;327(7421):955-60

40. Martin-JN J, Magann EF, Blake PG.Analysis of 454 pregnancies with severe preeclampsia /eclampsia /HELLP Syndrome using the 3-class system of classification. Am J Obstet Gynecol 1993; 68: 386-391

41. Haram K,Svendsen E,Abildgaard U.The HELLP Syndrome: clinical issues and management. a review.BMC Pregnancy child birth 2009 feb 26;9:8

42. Vasudevan D, Sreekumari J,Vaidyanadhan K.Textbook of Biochemistry 16th edition. New delhi, Jaypee brothers, 2011.Clinical Enzymology and Biomarkers:146-159.

ANNEXURES

INSTITUTIONAL ETHICAL COMMITTEE, STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Lactic Acid Dehydrogenase and Uric Acid- Biochemical markers for preeclampsia- Eclampsia at Stanley Medical College.

Principal Investigator : Dr. A Divya Lakshmi

Designation : PG MS (O & G)

Department : Department of O & G
Government Stanley Medical College,
Chennai-01

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 10.06.2015 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

K Vasanta

MEMBER SECRETARY,
IEC, SMC, CHENNAI

CONSENT FORM

I agree to participate in the study entitled "**LACTIC ACID DEHYDROGENASE AND URIC ACID- BIOCHEMICAL MARKERS FOR PRE ECLAMPSIA - ECLAMPSIA**"

I confirm that I have been told about this study in my mother tongue and have had the opportunity to clarify my doubts.

I understand that my participation is voluntary and I may refuse to participate at any time without giving any reasons and without affecting my benefits.

I agree not to restrict the use of any data or results that arise from this study.

Name of the participant: Sign / Thumb print:

Sign of Investigator:

ஒப்புதல் படிவம்

திருமதி.....

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என்ற விலாசத்தில் வசிக்கும் நான் எனக்கு அளிக்கப்பட்ட தகவல் படிவத்தில் உள்ள விவரங்களையும் படித்தும் கேட்டும் புரிந்து கொண்டேன்.

இந்த ஆய்விற்கு தேவையான இரத்தத்தை ஊசி மூலம் எடுத்துக்கொள்ள சம்மதிக்கிறேன்.

ஆய்வன் முடிவினை சொந்த அடையாளங்களை வெளியிடாமல் மருத்துவ ஆராய்ச்சிக்காக பயன்படுத்தி கொள்ள சம்மதிக்கிறேன்

நாள் கையொப்பம்

இடம் பெயர்

PROFORMA

DATE:

NAME: AGE: LMP:

IP NO: EDD:

D.O.A: D.O.D OBSTETRIC CODE:

ADDRESS & CONTACT NO:

PRESENTING COMPLAINTS:

MENSTRUAL HISTORY : MD SINCE:

OBSTETRIC HISTORY:

PAST HISTORY:

GENERAL EXAMINATION:

HT: WT: TEMP: PR: BP:

PALLOR: PEDAL EDEMA:

CVS: RS:

P/A:

P/V:

INVESTIGATIONS:

URINE ALBUMIN:

Hb:
PLATELETS:
RBS:
RFT:
LFT:
SERUM URIC ACID:

SERUM LACTATE DEHYDROGENASE:

USG:

TREATMENT:

STAY IN HOSPITAL:

OUTCOME:

RESULT:

தகவல் படிவம்

ஸ்டான்லி மருத்துவமனையின் ஆர்.எஸ்.ஆர்.எம். மருத்துவமனையில் மகப்பேறு மற்றும் பெண்கள் நல மருத்துவதுறையில் மேற்கொள்ளப்படும் ஆய்வு தொடர்பான தகவல் படிவம் இது. இந்த ஆய்வு மரு. டாக்டர். ஆ.திவ்யலட்சுமி அவர்களால் மற்றும் பிற அனுபவம் வாய்ந்த மருத்துவர்களின் உதவியோடு நடத்தப்படுகிறது.

இந்த ஆய்வு இரத்த கொதிப்பு உள்ள கர்ப்பிணி பெண்களிடம் இரத்தத்தில் லேக்டேட் டிஹைட்ரோஜினேஸ் (LDH) மற்றும் யூரிக்ஏசிட் (Uric Acid) அளவினை மதிப்பிட்டு தாய் மற்றும் சேய்யுக்கும் ஏற்படும் விளைவுகளை கண்டறியும் தொடர்பான ஆய்வு இது.

இந்த ஆய்வில் உட்படுத்தப்படும் பெண்களுக்கு எந்த பாதிப்பும் இல்லை. என்பதை தெரிவித்துக்கொள்கிறேன். இந்த ஆய்வு தங்கள் சுயவிருப்பத்துடன் முன்வந்தால் மட்டுமே மேற்கொள்ளப்படும்.

S. NO	NAME	AGE	I.P. NO	OBS CODE	GROUP	GA(weeks)	U/A	LDH	URIC ACID	SBP	DBP	Mode of Delivery	B.Wt(kg)	IUD	IUGR	IntracranialHge	PULM.OEDOEMA	HELLP	ABRUPTION	ECLAMPSIA	MATERNAL DEATH
1	Victoria	21	8748	Primi	Severe Preeclampsia	33	3+	317	6.2	170	100	LN	1.2	-	-	-	-	-	-	-	-
2	Vijayakumari	21	8846	Primi	Severe Preeclampsia	39	2+	1288	7.3	160	110	Emerg.LSCS	2.05	-	1	-	-	-	-	-	-
3	Dharshini	26	8848	Primi	Mild Preeclampsia	40	1+	209	7	130	100	LN	2.7	-	-	-	-	-	-	-	-
4	Reshma	20	8962	Primi	Severe Preeclampsia	40	2+	234	6.6	140	110	Emerg.LSCS	3.1	-	-	-	-	-	-	-	-
5	Vijayalakshmi	25	9406	G2P1L1	Severe Preeclampsia	36	2+	554	6.2	160	104	Emerg.Rpt LSCS	2.2		-	-	-	-	-	-	-
6	Saraswathy	32	9524	G3P2L1	Mild Preeclampsia	37	1+	141	5.8	140	96	Elect.Rpt LSCS	3.2	-	-	-	-	-	-	-	-
7	Sindhumathi	23	2053	G2P1L1	Control	37	nil	128	3.8	120	70	Emerg.Rpt LSCS	2.8	-	-	-	-	-	-	-	-
8	Kalaiarasi	21	9147	Primi	Mild Preeclampsia	38	1+	204	4.8	140	94	Emerg.LSCS	2.6	-	-	-	-	-	-	-	-
9	Shanthi	33	10106	Primi	Mild Preeclampsia	39	1+	378	2.4	140	90	LN	2.5	-	-	-	-	-	-	-	-
10	Alamelu	22	10166	Primi	Mild Preeclampsia	40	1+	456	4.2	140	96	LN	2.4	-	-	-	-	-	-	-	-
11	Nagammal	18	9696	G2A1	Eclampsia	30	1+	1257	5.1	170	110	Emerg.Hysterotomy	0.95	-	-	-	-	-	-	1	-
12	Sasirekha	24	9994	G2P1L1	Mild Preeclampsia	37	1+	428	6.2	140	100	Emerg.Rpt LSCS	2.8	-	-	-	-	-	-	-	-
13	Sangeetha	28	10130	G2P1L1	Mild Preeclampsia	36	1+	660	6.5	150	100	LN	1.8	-	-	-	-	-	-	-	-
14	Ameena	20	10221	G2P1L1	Severe Preeclampsia	38	2+	750	7.1	160	100	Emerg.Rpt LSCS	2.1	-	1	-	-	-	-	-	-
15	Seethalakshmi	18	10219	G2P1L0	Severe Preeclampsia	37	2+	580	6.8	150	110	LN	2.3	-	-	-	-	-	-	-	-
16	Sulthana	30	12312	G2P1L1	Mild Preeclampsia	36	1+	192	5.5	160	100	Emerg.Rpt LSCS	1.9	-	-	-	-	-	-	-	-
17	Nanthini	23	2020	G2P1L1	Control	39	nil	154	3.2	120	70	Emerg.LSCS	3.3	-	-	-	-	-	-	-	-
18	Latha	26	12300	G2P1L1	Severe Preeclampsia	37	2+	376	6.5	170	110	Emerg.Rpt LSCS	2.7	-	-	-	-	-	-	-	-
19	Vidhya	24	10041	Primi	Severe Preeclampsia	36	3+	1226	6.2	150	110	Emerg.LSCS	1.75		1	-	-	-	-	-	-
20	Preetha	24	12071	G3P2L0	Control	38	Trac	214	4	130	74	Emerg.LSCS	3.36	-	-	-	-	-	-	-	-
21	Sivasakthi	19	10420	G2A1	Eclampsia	28	2+	1450	6.5	170	110	Emerg.LSCS	1.25		-	-	-	-	-	1	-
22	Radhika	24	10091	Primi	Severe Preeclampsia	37	2+	1356	7.2	190	100	Emerg.LSCS	1.8		1	-	-	-	-	-	-
23	Priyadharshini	19	10871	Primi	Mild Preeclampsia	38	1+	440	5.6	140	96	Emerg.LSCS	2.7	-	-	-	-	-	-	-	-
24	Vanitha	17	11132	Primi	Mild Preeclampsia	37	1+	320	5	160	90	Emerg.LSCS	2.6	-	-	-	-	-	-	-	-
25	Sankari	35	12091	G2P1L1	Control	38	nil	156	2.7	130	80	Emerg.Rpt LSCS	3.17	-	-	-	-	-	-	-	-
26	Radhika	30	10247	Primi	Mild Preeclampsia	36	1+	224	7.2	150	100	Emerg.LSCS	2.5	-	-	-	-	-	-	-	-
27	Ramya	20	11275	Primi	Severe Preeclampsia	37	3+	414	6.1	180	100	Emerg.LSCS	2.6	-	-	-	-	-	-	-	-

28	Valli	19	11475	G2P1L0	Severe Preeclampsia	37	2+	1515	6.5	170	120	Emerg.LSCS	2.2	-	1	-	-		1	-	-
29	Nirmala	36	2082	G2P1L1	Control	39	Trac	190	3.2	110	70	Emerg.Rpt LSCS	3.1	-		-	-	-	-	-	-
30	Jayanthi	22	12012	Primi	Mild Preeclampsia	39	1+	215	3.6	140	90	LN	2.8	-	-	-	-	-	-	-	-
31	Sumaiya	23	12057	G2P1L1	Severe Preeclampsia	38	2+	820	6.3	160	110	LN	2.3	-	-	-	-	-	-	-	-
32	Mala	27	12177	G2P1L1	Mild Preeclampsia	39	1+	360	5	140	90	Emerg.LSCS	2.8	-	-	-	-	-	-	-	-
33	Pushpam	34	12204	G2P1L1	Mild Preeclampsia	38	1+	284	4.8	150	94	Emerg.Rpt LSCS	3	-	-	-	-	-	-	-	-
34	Nasilima	22	12279	Primi	Eclampsia	37	3+	820	7.2	180	112	Emerg.LSCS	2.1	-	1	-	-	-	-	1	-
35	Nadhiya	29	7221	G2P1L1	Severe Preeclampsia	38	2+	770	6.8	160	116	Emerg.LSCS	2.8	1	-	-	-	-	1	-	-
36	Sangeetha	29	12277	G2P1L0	Mild Preeclampsia	37	1+	288	5.6	150	90	LN	2.5	-	-	-	-	-	-	-	-
37	Ellamal	21	20078	G2P1L1	Control	38	nil	166	2.2	120	70	Emerg.LSCS	3.1	-	-	-	-	-	-	-	-
38	Parveen	33	7807	G2P1L1	Severe Preeclampsia	36	2+	960	7.4	160	120	Emerg.LSCS	1.9	1		-	-	-	1	-	-
39	Bhavani	19	8001	Primi	Severe Preeclampsia	36	2+	570	5.5	160	112	LN	2.5	-	-	-	-	-	-	-	-
40	Allima	28	2100	G3P2L1	Control	39	trac	201	3	110	80	Emerg.Rpt LSCS	3.02	-	-	-	-	-	-	-	-
41	Lillirani	22	9825	G2A1	Mild Preeclampsia	40	1+	700	6.1	140	108	Emerg.LSCS	3	1	-	-	-	-	1	-	-
42	Jhansi	19	10267	Primi	Eclampsia	34	3+	1376	7.2	190	120	Emerg.LSCS	1.1	1	1	-	-	-	-	1	-
43	Saritha	28	10776	Primi	Severe Preeclampsia	36	2+	1040	6.7	160	110	LN	1.4	1	1	-	-	-	1	-	-
44	Kalpana	28	2099	G2P1L1	Control	38	nil	246	2.8	130	70	Emerg.LSCS	2.6	-	-	-	-	-	-	-	-
45	Kaveri	22	2112	Primi	Control	38	Trac	224	3.2	120	80	Emerg.LSCS	2	-	1	-	-	-	-	-	-
46	Kalaiselvi	31	11069	G3P2L2	Severe Preeclampsia	34	2+	700	6.2	180	110	Emerg.Rpt LSCS	1.5	1		-	-	-	1	-	-
47	Vinnarasi	23	11909	G2P1L1	Severe Preeclampsia	38	2+	766	7.5	170	120	Emerg.Rpt LSCS	3.2	1	-	-	-	-	1	-	-
48	Muthari	23	12015	G2P1L0	Mild Preeclampsia	37	1+	380	4.1	150	90	Elective LSCS	3	-	-	-	-	-	-	-	-
49	Thilagavathy	23	1245	Primi	Severe Preeclampsia	38	3+	568	6.2	160	112	Emerg.LSCS	2.3	-	-	-	-	-	-	-	-
50	Gomathy	23	2028	G2P1L1	Control	39	nil	146	2.8	120	76	Elective LSCS	2.8	-	-	-	-	-	-	-	-
Eme	Jayalakshmi	21	2079	G2P1L1	Control	39	Trac	610	5	130	80	Elective Rpt LSCS	2.25	-	1	-	-	-	-	-	-
52	Gayathri	24	12554	G2P1L1	Mild Preeclampsia	38	1+	470	5.1	150	100	Emerg.Rpt LSCS	3.2	-	-	-	-	-	-	-	-
53	Sumalatha	31	12413	G2P1L1	Mild Preeclampsia	37	1+	520	4.8	150	90	Elective Rpt LSCS	2.6	-	-	-	-	-	-	-	-
54	Poonam	21	12653	Primi	Severe Preeclampsia	38	2+	540	5.8	160	114	Emerg.LSCS	2.75	-	-	-	-	-	-	-	-
55	ParveenBanu	22	11719	Primi	Mild Preeclampsia	37	1+	514	5.1	140	90	Emerg.LSCS	3.1	1	-	-	-	-	-	-	-
56	Selvarani	23	12351	Primi	Severe Preeclampsia	36	3+	1274	7.3	170	118	LN	1.1	1	1	-	-	-	1	-	-
57	umamaheshwari	37	2233	Primi	Control	37	nil	217	3	110	76	Emerg.LSCS	2.45	-	-	-	-	-	-	-	-
58	Shalini	23	2171	G4P1L0A	Control	38	Trac	350	3.6	130	76	Emerg.LSCS	2.4	-	-	-	-	-	-	-	-
59	Pavithra	21	2000	G2P1L1	Mild Preeclampsia	37	1+	264	4.2	140	96	LN	2.35		-	-	-	-	-	-	-
60	Jayalakshmi	24	2085	G2P1L1	Mild Preeclampsia	37	1+	640	6.8	150	100	Emerg.Rpt LSCS	2.25			-	-	-	-	-	-

61	Aaliyathabasum19	19	6484	Primi	Eclampsia	37	4+	1710	7.2	180	124	Emerg.LSCS	2.3		1	1	-	-	-	1	1
62	Vaishnavi	22	2292	G2P1L1	Control	38	Trac	209	2.6	120	70	Emerg.Rpt LSCS	3.1	-	-	-	-	-	-	-	-
63	Suganthi	24	1719	G2P1L0	Control	37	nil	196	3.2	110	80	Emerg.LSCS	2.6	-	-	-	-	-	-	-	-
64	Mohana	27	2068	G2P1L1	Severe Preeclampsia	37	3+	1056	6.6	170	108	Emerg.LSCS	1.7	-	1	-	-		1	-	-
65	Anitha	22	2335	Primi	Severe Preeclampsia	37	2+	540	6	156	110	Emerg.LSCS	2.2	-	-	-	-	-	-	-	-
66	Sandhya	28	2065	Primi	Mild Preeclampsia	38	1+	412	5.8	140	90	Emerg.LSCS	3.2	-	-	-	-	-	-	-	-
67	Sumathy	35	2635	G6P2L2A	Severe Preeclampsia	40	2+	450	4.5	160	112	Emerg.LSCS	4.3	-	-	-	-	-	-	-	-
68	Anitha	20	2427	Primi	Mild Preeclampsia	37	1+	670	6.2	140	106	Emerg.LSCS	2.3	-	-	-	-	-	-	-	-
69	Yasodha	20	2301	G2P1L1	Control	40	nil	154	2.8	130	70	Emerg.Rpt LSCS	3.01	-	-	-	-	-	-	-	-
70	Soundarya	25	2306	Primi	Control	40	nil	176	3.1	120	80	Emerg.LSCS	3.2	-	-	-	-	-	-	-	-
71	Pushpa	34	6152	Primi	Severe Preeclampsia	34	3+	1096	7	170	110	Emerg.LSCS	900g		1	-	-	-	-	-	-
72	Nagalakshmi	20	2461	Primi	Mild Preeclampsia	39	1+	593	6.3	150	96	Emerg.LSCS	2.4	-		-	-	-	-	-	-
73	Kalaivani	29	2436	G2P1L1	Control	39	Trac	317	4.7	120	70	Emerg.Rpt LSCS	2.6	-	-	-	-	-	-	-	-
74	Suseela	24	2465	Primi	Control	40	nil	162	3.2	120	76	Emerg.LSCS	2.8	-	-	-	-	-	-	-	-
75	Sugi	22	2291	Primi	Severe Preeclampsia	36	3+	880	7.1	170	120	Emerg.LSCS	1.2	-	1	-	-	-	-	-	-
76	Sajitha	22	2388	Primi	Mild Preeclampsia	38	1+	424	5.6	160	106	Emerg.LSCS	2.75	-	-	-	-		1	-	-
77	Jayanthi	21	2556	Primi	Severe Preeclampsia	37	2+	410	6.6	160	110	Emerg.LSCS	2.4	-	-	-	-	-	-	-	-
78	Jeevitha	22	2782	G2P1L1	Control	39	nil	170	2.6	120	80	Emerg.Rpt LSCS	2.9	-	-	-	-	-	-	-	-
79	Ramya	24	2577	Primi	Severe Preeclampsia	35	3+	740	6.8	180	120	Emerg.LSCS	1.75	-	-	-	-	-	-	-	-
80	Sujatha	23	2599	G2P1L1	Control	40	Trac	212	4	120	74	Emerg.Rpt LSCS	3.5	-	-	-	-	-	-	-	-
81	Maheshwari	24	7101	Primi	Eclampsia	34	4+	1296	7.1	170	120	Emerg.LSCS	2.3	-	-	-	-	-	-	1	-
82	Shanthi	20	2757	Primi	Mild Preeclampsia	36	1+	620	5.7	150	108	Emerg.LSCS	1.5	-	1	-	-	-	-	-	-
83	Lakshmi	21	2754	G5P3L2A	Severe Preeclampsia	36	2+	770	6.5	180	100	Emerg.LSCS	1.5	-	1	-	-	-	1	-	-
84	Rekha	28	2846	G3P1L2	Mild Preeclampsia	39	1+	556	6.6	156	106	Emerg.LSCS	3.2	-	-	-	-	-	1	-	-
85	Valli	20	2609	G2P1L1	Control	38	trac	317	5.2	130	80	Elective LSCS	2.45	-	-	-	-	-	-	-	-
86	Premalatha	22	2834	Primi	Mild Preeclampsia	37	1+	280	4.8	150	90	Emerg.LSCS	2.75	-	-	-	-	-	-	-	-
87	Victoria	25	2825	G2P1L1	Severe Preeclampsia	37	3+	750	7.2	176	112	Emerg.LSCS	1.96	-	1	-	-		1	-	-
88	Vijayalakshmi	20	2920	Primi	Mild Preeclampsia	40	1+	280	5	140	102	Emerg.LSCS	2.4	-		-	-	-	-	-	-
89	Anbarasi	21	2600	Primi	Control	39	nil	135	2.6	120	76	Emerg.LSCS	3	-	-	-	-	-	-	-	-
90	Jayashree	23	2663	Primi	Control	40	nil	196	3	126	82	Emerg.LSCS	3.1	-	-	-	-	-	-	-	-
91	Thenmozhi	31	7211	G2A1	Severe Preeclampsia	35	3+	1050	6.9	170	110	Emerg.LSCS	1.8	-	-	-	-	1	-	-	-
92	Shanthi	21	2880	Primi	Mild Preeclampsia	38	1+	350	5	150	90	Elective LSCS	2.75	-	-	-	-	-	-	-	-
93	Deepalakshmi	21	3479	G3A2	Severe Preeclampsia	37	2+	617	6.1	156	112	Emerg.LSCS	2.6	-	-	-	-		1	-	-

94	Ramya	25	38416	Primi	Mild Preeclampsia	37	1+	280	4.2	160	100	Emerg.LSCS	2.75	-	-	-	-		1	-	-
95	Rajeshwari	24	2015	G2P1L0	Eclampsia	37	2+	780	6.8	170	114	Emerg.LSCS	2.75	-	-	-	1	-	-	1	-
96	Priya	20	3515	Primi	Control	39	nil	192	2.8	110	80	LN	2.5	-	-	-	-	-	-	-	-
97	Vanishree	25	3814	Primi	Control	40	nil	205	3.1	120	82	Emerg.LSCS	3	-	-	-	-	-	-	-	-
98	Suganthi	30	3816	Primi	Control	40	nil	217	3.2	112	74	LN	2.5	-	-	-	-	-	-	-	-
99	Ezhilarasi	24	3377	Primi	Mild Preeclampsia	39	1+	550	6.4	156	90	Emerg.LSCS	2.4	-	-	-	-	-	-	-	-
100	Banupriya	22	3227	Primi	Mild Preeclampsia	38	1+	406	5	140	96	Emerg.LSCS	2.6	-	-	-	-	-	-	-	-
101	Kanchana	26	7325	Primi	Eclampsia	36	3+	978	6.2	180	110	Emerg.LSCS	2	-	1	-	-	-	-	1	-
102	Sandhiya	23	3421	G2P1L1	Mild Preeclampsia	39	1+	318	5.2	140	100	Emerg.LSCS	3.2	-	-	-	-	-	-	-	-
103	Asha	26	3439	Primi	Mild Preeclampsia	38	1+	340	4.9	130	94	Emerg.LSCS	3	-	-	-	-	-	-	-	-
104	Sumithra	20	3639	Primi	Severe Preeclampsia	38	2+	580	6.9	150	110	Emerg.LSCS	2.5	-	-	-	-	-	-	-	-
105	Vasanthi	21	3688	Primi	Severe Preeclampsia	36	3+	702	6.6	107	110	Emerg.LSCS	1.8	-	-	-	-	-	-	-	-
106	Mariammal	26	3595	Primi	Control	37	Trac	217	4.2	120	84	Emerg.LSCS	2.4	-	-	-	-	-	-	-	-
107	Anitha	26	3767	Primi	Control	39	nil	180	2.2	120	76	LN	3.1	-	-	-	-	-	-	-	-
108	Saranya	24	3831	Primi	Mild Preeclampsia	39	1+	320	4.2	150	106	Emerg.LSCS	3	-	-	-	-	-	1	-	-
109	Hemavathy	22	3970	Primi	Mild Preeclampsia	38	1+	412	5.4	162	100	Emerg.LSCS	2.45	-	-	-	-	-	-	-	-
110	Malini	25	3838	Primi	Control	40	nil	145	2.6	120	80	LN	3.1	-	-	-	-	-	-	-	-
111	Sudharsana	19	7825	Primi	Eclampsia	34	4+	1150	6.3	170	114	Emerg.LSCS	1.4	-	1	-	-	1	-	1	-
112	Vasantha	28	3995	G2P1L1	Severe Preeclampsia	36	4+	1260	7.2	180	110	Emerg.LSCS	1.5	-	1	-	-	1	-	-	-
113	Nasreenbanu	19	1384	Primi	Mild Preeclampsia	38	1+	634	6.2	156	108	Emerg.LSCS	2.3	-	-	-	-	-	-	-	-
114	Kuppammal	24	3868	G2P1L1	Control	39	nil	180	2.2	110	76	LN	2.7	-	-	-	-	-	-	-	-
115	Rajeshwari	23	3842	G2P1L1	Control	39	Trac	204	3.6	120	84	Emerg.Rpt LSCS	2.5	-	-	-	-	-	-	-	-
116	umamaheshwari	20	1623	Primi	Severe Preeclampsia	36	3+	620	6.5	170	112	Emerg.LSCS	1.8	-		-	-	-	-	-	-
117	Nalini	28	1923	G2P1L1	Mild Preeclampsia	37	1+	470	5.8	140	106	Emerg.Rpt LSCS	2.3	-	-	-	-	-	-	-	-
118	Easwari	21	3833	Primi	Control	39	nil	156	3.1	120	70	Emerg.LSCS	2.8	-	-	-	-	-	-	-	-
119	Annapoorani	20	1822	Primi	Severe Preeclampsia	38	2+	1256	6.7	160	120	Emerg.LSCS	2.5	-	-	-	-	1		-	-
120	Sathyabama	27	3869	G2P1L1	Control	39	nil	317	4	130	70	Emerg.Rpt LSCS	2.8	-	-	-	-	-	-	-	-
121	Nirosha	25	3754	Primi	Control	40	nil	194	2.8	120	76	LN	2.8	-	-	-	-	-	-	-	-
122	Vasanthi	21	3882	G2P1L1	Control	40	nil	172	2.6	110	74	LN	3.5	-	-	-	-	-	-	-	-
123	Vijaya	25	1844	G2P1L1	Eclampsia	36	4+	986	6.8	184	114	Emerg.LSCS	2.2	-	-	-	-	-	-	1	-
124	Nandhini	27	1928	G3P1L1A	Mild Preeclampsia	37	1+	360	5.5	146	94	Emerg.Rpt LSCS	2.3	-	-	-	-	-	-	-	-
125	Deepalakshmi	21	3479	G3A2	Mild Preeclampsia	37	1+	626	5.2	156	104	Emerg.LSCS	2.6	-	-	-	-		1	-	-
126	Gayathri	21	2039	G2A1	Control	37	Trac	354	4.4	130	80	LN	2.3	-	-	-	-	-	-	-	-

127	Pushparani	28	3658	G2P1L1	Severe Preeclampsia	36	3+	440	6.1	160	110	Emerg.Rpt LSCS	1.9	-	-	-	-	-	-	-
128	Nadhiya	26	3640	Primi	Mild Preeclampsia	37	1+	317	5.4	150	94	Emerg.LSCS	2.4	-	-	-	-	-	-	-
129	Sumathy	25	3881	G2P1L1	Control	38	nil	166	2.8	110	70	LN	2.7	-	-	-	-	-	-	-
130	Shridevi	24	3636	Primi	Severe Preeclampsia	38	2+	745	6.5	160	112	Emerg.LSCS	2.1	-	1	-	-	-	-	-
131	Poongodi	26	3847	Primi	Control	40	nil	150	2.7	126	76	LN	3.3	-	-	-	-	-	-	-
132	Shrividhya	26	3671	Primi	Severe Preeclampsia	39	2+	420	6.1	160	112	Emerg.LSCS	3.75	-	-	-	-	-	-	-
133	Naviselvi	25	3495	G3P2L2	Severe Preeclampsia	32	4+	780	6.7	130	110	LN	1	-		-	-	-	-	-
134	Nagavalli	20	3848	G2P1L1	Control	38	Trac	226	3.2	130	70	LN	2.5	-	-	-	-	-	-	-
135	Nagalakshmi	28	3987	G3P12L1	Mild Preeclampsia	37	1+	510	6.8	150	96	Emerg.Rpt LSCS	2.1	-	-	-	-	-	-	-
136	Arunadevi	25	3884	Primi	Control	36	nil	194	2.1	120	90	Emerg.LSCS	2.1	-	-	-	-	-	-	-
137	Umadevi	23	14956	Primi	Severe Preeclampsia	35	3+	710	6.2	140	110	Emerg.LSCS	1.2	-	1	-	-	-	-	-
138	Samandhi	24	3791	Primi	Mild Preeclampsia	38	1+	752	6.3	150	104	Emerg.LSCS	1.75	-	1	-	-	-	-	-
139	Navamani	33	3740	G2P1L1	Control	38	Trac	260	2.8	130	76	Emerg.Rpt LSCS	2.45	-	-	-	-	-	-	-
140	Najumunisha	22	3890	Primi	Control	39	nil	162	2.5	120	70	LN	2.9	-	-	-	-	-	-	-
141	Gayathri	22	3802	G2P1L0	Mild Preeclampsia	37	1+	380	4.7	150	94	Emerg.Rpt LSCS	2.6	-	-	-	-	-	-	-
142	ParveenBanu	24	3032	G4P2L1A	Severe Preeclampsia	34	3+	940	7.1	160	110	LN	1.5	-	1	-	-	-	-	-
143	Ramani	30	3748	G2P1L1	Control	37	nil	240	3.1	120	72	Emerg.Rpt LSCS	2.5	-	-	-	-	-	-	-
144	Varnalatha	24	3914	Primi	Eclampsia	34	3+	1120	6.3	176	112	Emerg.LSCS	1.75	-	1	-	-	-	1	-
145	Kasinabegum	34	12142	Primi	Severe Preeclampsia	35	2+	755	6.6	170	112	Emerg.LSCS	2	-	-	-	-	-	-	-
146	Vasanthi	21	12764	Primi	Eclampsia	37	4+	1350	7	180	120	Emerg.LSCS	1.75	-	1	-	-	-	1	-
147	Suseela	23	3416	G2P1L1	Control	39	Trac	405	5.1	130	86	LN	2.5	-	-	-	-	-	-	-
148	Dilshath	22	14068	G3P1L1A	Severe Preeclampsia	36	3+	1226	6.5	160	120	Emerg.LSCS	1.9	-	1	-	-		1	-
149	Jothika	20	3924	Primi	Control	40	nil	312	2.8	112	74	LN	3.2	-	-	-	-	-	-	-
150	Sangeetha	25	3939	Primi	Control	39	nil	270	3.2	118	80	LN	2.7	-	-	-	-	-	-	-
151	umamaheshwari	21	13286	Primi	Eclampsia	38	4+	1359	7.2	190	116	Emerg.LSCS	1.6	-	1	-	-	-	1	-
152	Sathya	24	14216	Primi	Severe Preeclampsia	34	2+	1056	6.6	166	110	Emerg.LSCS	1.5	-	1	-	-	-	-	-
153	Komala	24	3932	Primi	Control	39	nil	220	2.2	120	74	Emerg.LSCS	2.6	-	-	-	-	-	-	-
154	Revathy	21	8283	Primi	Severe Preeclampsia	38	3+	770	6.8	160	120	Emerg.LSCS	2.2	-	1	-	-	1		-
155	Angelchristy	24	14197	Primi	Eclampsia	38	2+	866	6.8	170	110	Emerg.LSCS	2.1	-	1	-	-	-	1	-
156	Vijayashree	22	3971	Primi	Control	37	nil	366	3.6	130	76	Emerg.LSCS	2.4	-	-	-	-	-	-	-
157	Kirija	24	8330	Primi	Severe Preeclampsia	36	2+	468	6	150	110	LN	2.3	-	-	-	-	-	-	-
158	Santhanamary	21	8413	Primi	Mild Preeclampsia	37	1+	376	5.2	156	90	Emerg.LSCS	2.25	-	-	-	-	-	-	-
159	Maragatham	21	2080	Primi	Mild Preeclampsia	39	1+	334	6.2	150	100	Emerg.LSCS	3	-	-	-	-	-	-	-

160	Monika	20	3973	Primi	Control	38	nil	245	3.2	120	80	LN	2.5	-	-	-	-	-	-	-	-
161	Maha	23	2418	Primi	Severe Preeclampsia	38	2+	716	7.3	166	112	Emerg.LSCS	2.2	-	1	-	-	-	-	-	-
162	Divya	24	2654	Primi	Severe Preeclampsia	35	3+	1026	7.2	170	120	Emerg.LSCS	1.4	-	1	-	-	-	-	-	-
163	Indhu	21	2808	Primi	Severe Preeclampsia	39	2+	509	6.4	160	110	Emerg.LSCS	3.5	-	-	-	-	-	-	-	-
164	Sundaravalli	21	3450	Primi	Severe Preeclampsia	36	2+	527	5.8	150	116	Emerg.LSCS	2.3	-	-	-	-	-	-	-	-
165	Kanagavalli	22	836	G2A1	Severe Preeclampsia	37	3+	720	6.4	162	110	Emerg.LSCS	2.3	-	-	-	-	-	1	-	-

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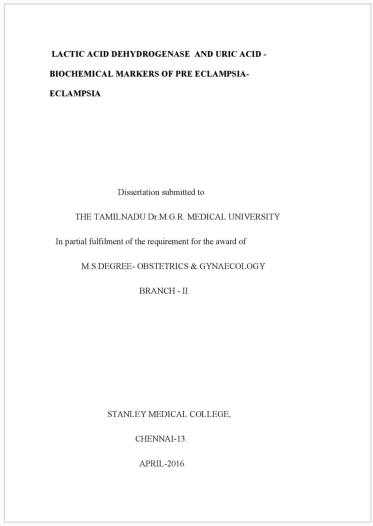

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In partial fulfilment of the requirement for the award of

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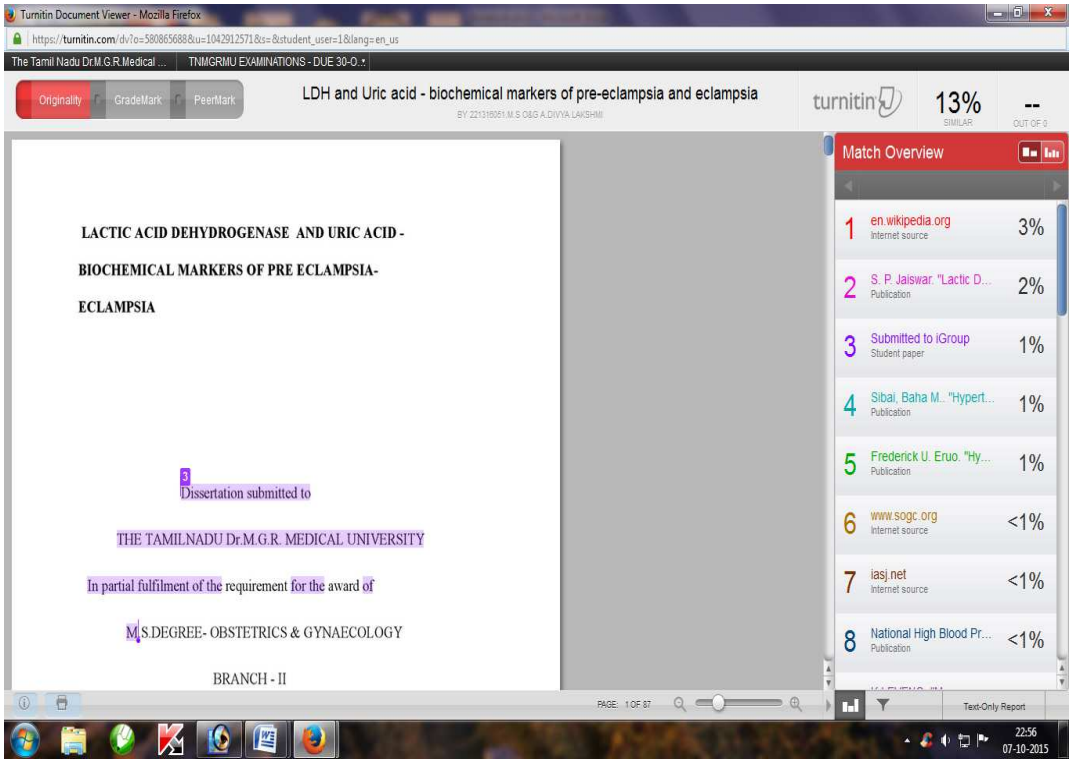
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