CORRELATION OF SERUM PROLACTIN LEVEL WITH SEVERITY OF PREECLAMPSIA AND ITS OUTCOME

Dissertation submitted to

The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfilment of the regulations for the award of the degree of

M.S (Branch II)

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DEPARTMENT OF OBSTETRICS AND GYNECOLOGY

GOVERNMENT THENI MEDICAL COLLEGE

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CERTIFICATE

This is to certify that this dissertation titled **"CORRELATION OF SERUM PROLACTIN LEVEL WITH SEVERITY OF PREECLAMPSIA AND ITS OUTCOME"** is a bonafide work done by **Dr.B.ANITHA**,**D.G.O.,** at the department OBSTETRICS and GYNECOLOGY, Government Theni medical college, during her postgraduate study for MS Branch II OBSTETRICS and GYNECOLOGY (2017-2019) from October 2017 to September 2018.This dissertation is submitted to DR. MGR Medical University in partial fulfilment of the University rules and regulations for the award of MS degree in OBSTETRICS and GYNECOLOGY.

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DECLARATION

I hereby declare that this dissertation entitled "**CORRELATION OF SERUM PROLACTIN LEVEL WITH SEVERITY OF PREECLAMPSIA AND ITS OUTCOME ”** was prepared by me under the direct guidance and supervision of **Prof. DR.M.THANGAMANI, MD., DGO., and Dr.C. SHANTHADEVI. MD,DGO.** The dissertation is submitted to the Dr. M.G.R. Medical University in partial fulfilment of the University regulations for the award of MD degree in Obstetrics and Gynaecology, Examination to be held in May 2019.

This record of work has not been submitted previously by me for the award of any degree or diploma from any other university.

Place: Theni **Dr. B. ANITHA**

Date:

ACKNOWLEDGEMENT

At the outset, it is with a sense of accomplishment and deep gratitude that I dedicate this dissertation to all those who have been instrumental in its completion.

First and foremost I express my heartful thanks to my esteemed and respected HOD, Department of Obstetrics and Gynaecology GTMCH, and my guide **Prof. Dr.M.Thangamani, MD, DGO, and Chief, Professor Dr.C. Shanthadevi, MD, DGO, DNB.** had it not been for their whole hearted support throughout the period of this study, extending from their vast knowledge, invaluable advice and constant motivation, I truly would not have been able to complete this dissertation topic in its present form.

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I am deeply indebted to all the teaching staff and my fellow postgraduates for their helpful attitude and valuable suggestions in every stage of my study. Lastly, I thank the ethical committee for permitting me to do this study and more importantly

I thank all my patients involved for their kind help and cooperation.

CONTENTS

INTRODUCTION

“Fighting the fear in pregnancy – BP”

Is still a mystery

Cause is obscure

Preeclampsia is a multi system disorder which affects the vascular system and manifests by hypertension and proteinuria after 20weeks of gestation and returns to normal by 12 weeks in the postnatal period.

Every day, 830 women die due to Pregnancy associated disease and childbirth.

WHO estimates maternal death about 216.

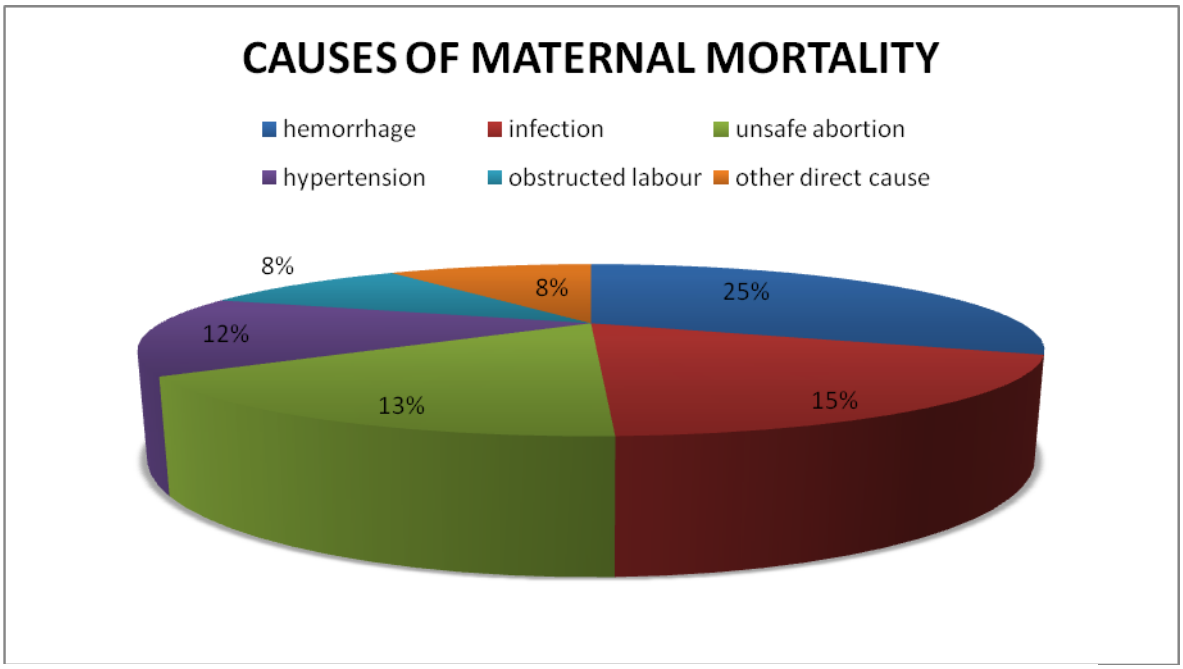
Most of the death occurs in the developing Countries about 98-99%.Preeclampsia and eclampsia is main contributable and preventable cause of maternal death. Maternal mortality which is higher in rural areas and among poorer communities. Now trend is changing, it also occurs in urban population.

Clear protocols for early detection and managing the hypertension in pregnancy in all levels of health care by skilled personnel before, during and after childbirth are needed for good maternal and neonatal outcome. Between year 1990 and 2015, maternal

mortality worldwide declined about 44%.This translates into an average annual rate of reduction of 2.3 percent. According to the Sustainable Development Goals, global maternal mortality ratio has to be reduced by 2016-2030 to a level less than 70% in 1,00,000 live births.

CAUSES OF MATERNAL DEATH WORLDWIDE

- Obstetric haemorrhage 25%
- Infection 15%
- Unsafe abortion 13%
- Hypertensive disorders of pregnancy 12%
- Obstructed labour 8%
- Other direct causes 8%
- Indirect causes 20%



EPIDEMIOLOGY

Preeclampsia is a significant public health threat in both developed and developing countries contributing to maternal and perinatal morbidity and mortality globally. India's third National Family Health Survey says factors responsible for the prevalence of preeclampsia that are socio-demographic, maternal, lifestyle and dietary determinants. The incidence of preeclampsia is reported to be 8-10% in India. The prevalence of hypertensive disorders of pregnancy was 7.8% of with preeclampsia. The recent World Bank data says MMR for India reported in 2015 at 174 per 100,000 live birth, which is declined from215reported in 2010

AIMS OF STUDY

- My study is about whether prolactin has a role in pathogenesis of preeclampsia and its severity, whether it can be used as a predictor of preeclampsia .
- STUDY DESIGN-PROSPECTIVE STUDY.

OBJECTIVES

- To find if prolactin has a role in pathogenesis of preeclampsia.
- To compare serum prolactin level in all preeclampsia patients with normal healthy pregnant women
- To correlate serum prolactin levels with severity of preeclampsia and its outcome.

REVIEW OF LITERATURE

Timalsina et al did a case control study of which54 cases and 60 controls. The median level of Prolactin was significantly higher in pre eclamptic women when compared to normal pregnant women according to this study.

Alfredo ullareo et al conducted a studied the relationship between the serum and urinary prolactin levels among preeclamptic women and also excretion of antiangiogenic prolactin fragments in urine. According to his study the level of urinary prolactin excretion was significantly higher among hypertensive patients.

Alfredo Leaños-Miranda et al., conducted a randomised study of Circulating Factors and serum Prolactin level. They are used as Predictors in Women With Preeclampsia, to deal about the adverse outcomes. They assessed whether these biomarkers are involved in the adverse maternal and perinatal outcomes in preeclamptic women. They conducted study in 501 women with preeclampsia who attended the tertiary care hospital.

THEORIES OF PREECLAMPSIA

21ST CENTURY RECENT THEORY 0F DISEASE CAUSATION.

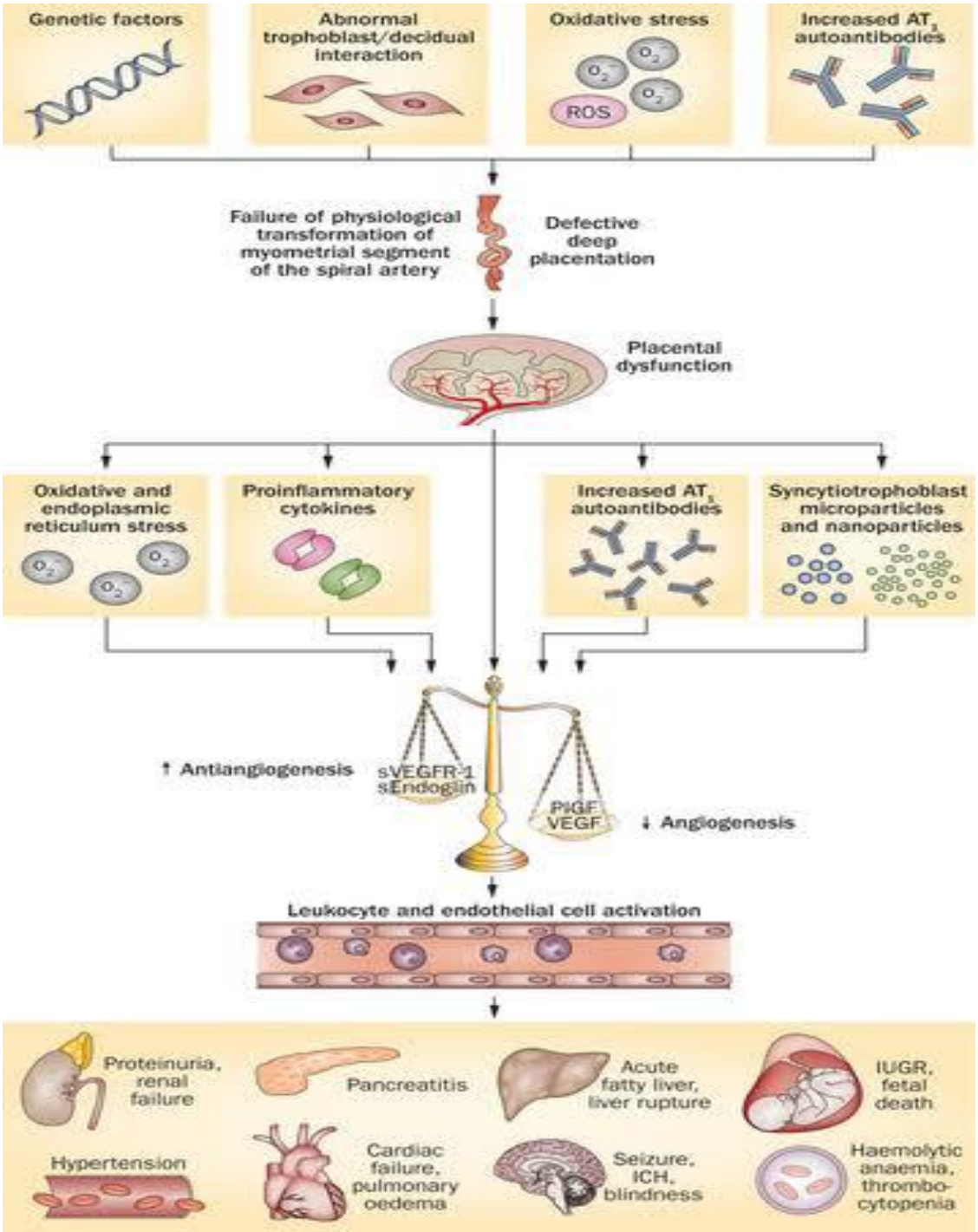
At present many theories are suggested to explain etiogenesis, some are;

1. **IMMUNOGENIC INTOLERANCE THEORY:**
    - Intolerance between fetoplacental unit and maternal tissue.
    - Put forth by Leeman and Fontaine in 2008

2. **TWO STAGE MODEL PREECLAMPSIA:**
    - Proposed by Roberts and Hubel in 2009.
    - **STAGE 1:** abnormal location of placenta and subsequent remodeling leads to placental hypoperfusion causing maternal syndrome.
    - **STAGE 2:**Occlusivemicro thrombi affecting multiple organs, leads on to hypertension, proteinuria and Oedema.

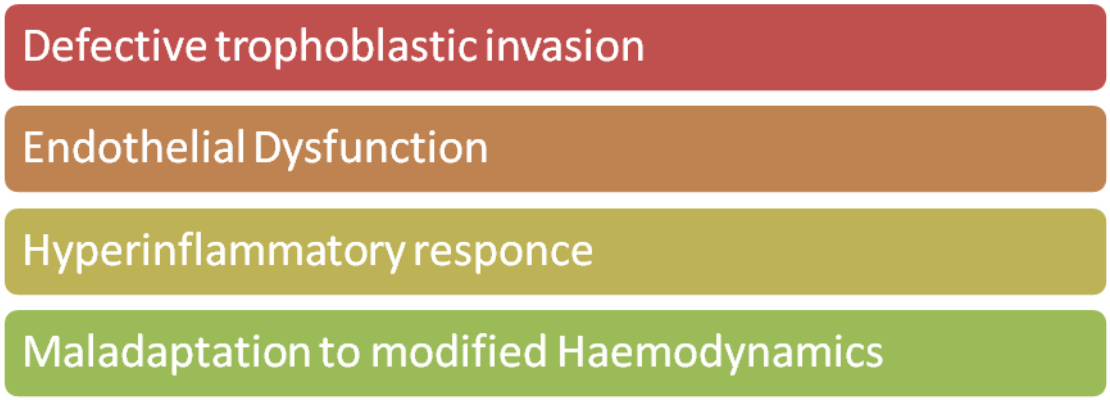
      This is the pathognomonic feature of preeclampsia.

3. **PLACENTAL TOXINS** (cytokines, angiogenic factors, VEGF, free placental growth factors etc) are not tolerated by some women leading to preeclampsia.


Genetic factors
Abnormal trophoblast/decidual interaction
Oxidative stress
ROS
Increased AT1 autoantibodies
Failure of physiological transformation of myometrial segment of the spiral artery
Defective deep placentation
Placental dysfunction
Oxidative and endoplasmic reticulum stress
Proinflammatory cytokines
Increased AT1 autoantibodies
Syncytiotrophoblast microparticles and nanoparticles
↑ Antiangiogenesis
sVEGFR-1
sEndoglin
PlGF
VEGF
↓ Angiogenesis
Leukocyte and endothelial cell activation
Proteinuria, renal failure
Pancreatitis
Acute fatty liver, liver rupture
IUGR, fetal death
Hypertension
Cardiac failure, pulmonary oedema
Seizure, ICH, blindness
Haemolytic anaemia, thrombo-cytopenia

AETIO PATHOGENESIS OF PRE ECLAMPSIA

The main characteristic feature of preeclampsia is abnormal trophoblastic invasion of uterine vessels, in appropriate endothelial activation, exaggerated inflammatory response, maladaptation to cardiovascular changes of normal pregnancy.



It is hypothesized as two stage disorder

PRIMARY STAGE-

Defective Physiological changes

↓

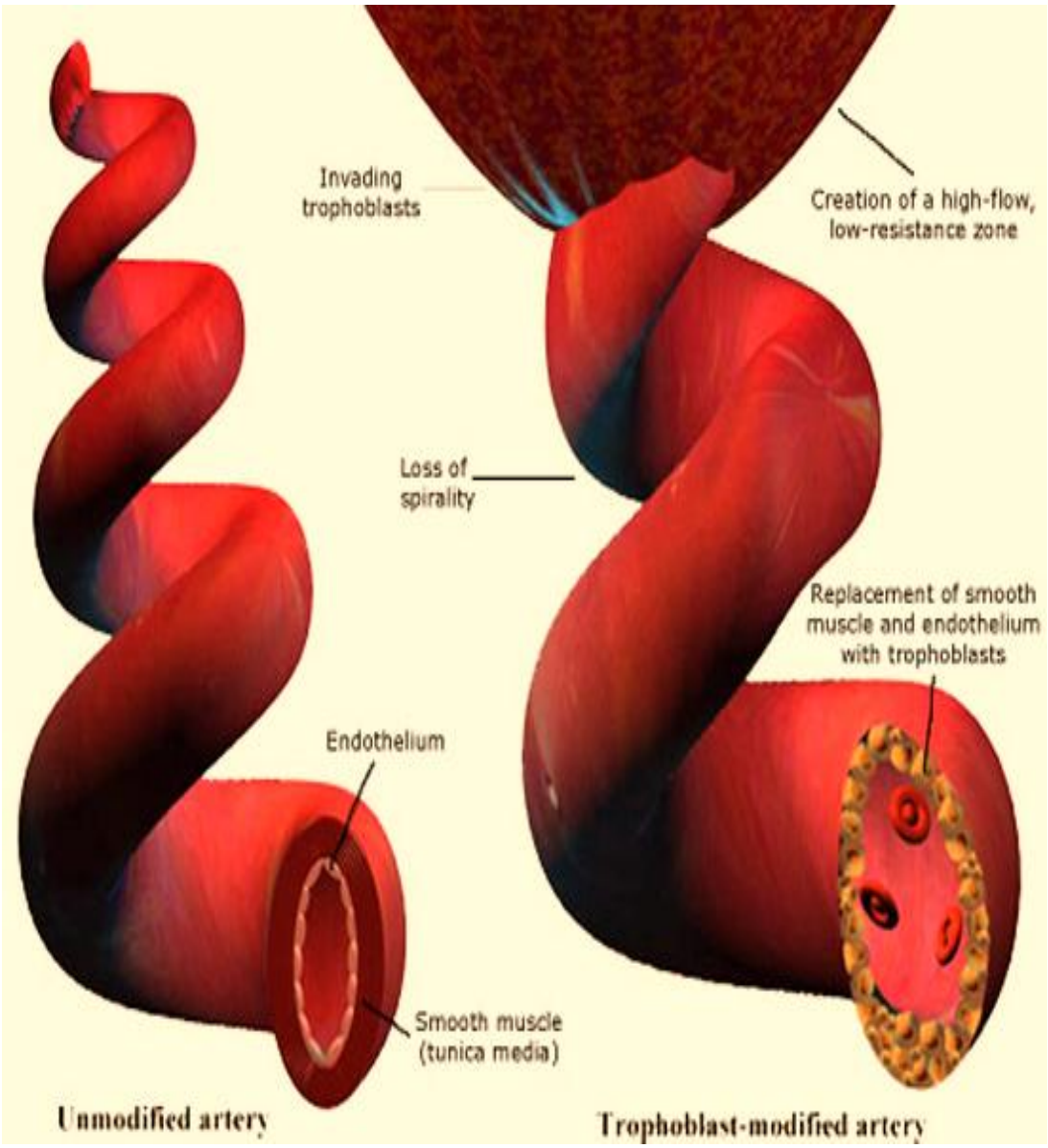
Incomplete Trophoblastic invasion of the myometrial part of spiral arteries

↓

Vasospasm

↓

Uteroplacental Hypoperfusion


Invading trophoblasts
Creation of a high-flow, low-resistance zone
Loss of spirality
Replacement of smooth muscle and endothelium with trophoblasts
Endothelium
Smooth muscle (tunica media)
Unmodified artery
Trophoblast-modified artery

SECONDARY STAGE

ABNORMAL IMMUNE RESPONSE BY ENDOTHELIAL ACTIVATION

There is release of toxins into maternal circulation due to the placental hypoxia which is later followed by reperfusion at that site, this released toxins leads to many inflammatory reactions in the body of the patient , leads onto exagarrated immune response which leads onto signs and symptoms suggestive of multi organ failure.

ACTIVATION OF THE VASCULAR ENDOTHELIUM

Placental factors like VEGF, free placental growth factors leading to oxidative stress, activation of leucocytes, formation of free radicals and lipid peroxides. This causes activation of nitric synthetase enzyme in endothelium that leads to increased vascular permeability and edema.

ANGIOGENIC FACTORS

Imbalance between angiogenic and anti angiogenic substance associated with severity of disease. Some are;soluble fms like tyrosine receptors, free placental like growth factors, angiotension etc.

GENETIC FACTORS

Some genes have possible associations with preeclampsia syndrome like genes involved in FactorV, Angiotensinogen, Methylene tetrahydrofolate reductase, Human leukocyte antigens, Lipoprotein lipase, decreased methylation.

EXAGGERATED PRESSOR RESPONSE

Preelamptic patients, when exposed to substances like angiotensin2, deoxycortisone and nor epinephrine, have an exaggerated vascular response.

NITRIC OXIDE

It is a potent vasodilator, synthesized from L-ariginie. It is secreted by endothelium. In preeclampsia, there is decreased endothelial nitric oxide synthesis which leads to diffuse vasospasm.

PROSTOGLANDINS

The prostanoids have important role in the pathogenesis of pre eclampsia. In NORMAL PREGNANCY the decreased response to pressor agents due to production of prostacyclin.

In PREECLAMPSIA- there is less production of PGI2 and there is more production of thrombaxne A2 from the platelet . Alteration in prostacyclin to thromboxane A2 ratio leads to increased sensitivity to these substances.

DIAGNOSIS OF HYPERTENSION:

Defined as systolic BP>140mm Hg and diastolic BP >90mm Hg on two occasions at least 6 hours apart ,taken in the same arm.

Instead of relaying single high value ,average value of BP for a week or high BP during booking visit or preconceptional visit has increased risk or maternal and perinatal outcome.

Measurement of blood pressure

- In sitting posture with arm at the level of heart.
- Appropriate cuff size to be used (length of 1.5 times the circumference of arm)
- Korottoff phaseV is taken as diastolic BP
- .If diastolic BP less than 40mmHg, then phase IV is taken

Measurement of Proteinuria:

Urinary dipstick testing (automated reagent strip)reading device is recommended.It may be used for screening the patients for proteinuria It has many advantages like easy availability, rapid and low cost, so can be used in all most all pregnant women who are at risk of developing pre eclampsia.

Grading for proteinuria is

TRACE - 0.1mg/dl

1+ - .3mg/dl

2+ - 1mg/dl

3+ - 3mgdl

4+ - 10mg/dl

The automated reagent strips is recommended to reduce interobserver variations and to reduce false positivity.

What is Clinically Significant Proteinuria:

Urinary excretion of 300mg or more of protein in 24 hours urine collection or persistent 30mg/dl in random clean catch sample on atleast 2 occasions collected 6 hours apart.

This corresponds to protein /creatinine to 30nmol.

This is clinically Significant Proteinuria.

URINE SPOT PCR

This is an alternative and rapid method for 24 hours urine protein, spot protein to creatinine ratio of more than 0.3 denotes significant proteinuria .

DIFFERENT TYPES OF CLASSIFICATION OF PREGNANCY

National High Blood Pressure Education Program (NHBPEP) Working Group, the classification is as follows :

- Gestational hypertension
- Chronic hypertension
- Preeclampsia
- Eclampsia
- Super imposed preeclampsia (on chronic hypertension)

Gestational hypertension:

The characteristics to diagnose a patient as gestational hypertension is by the recording the BP of 140/90 mm Hg or more for the first time after 20 weeks of gestation measured on two occasions. And also the Blood pressure returns to normal in less than 12 weeks' postpartum

Chronic hypertension:

Chronic Hypertension is the one which is diagnosed before 20 weeks of gestation and also which remains persistent after 12 weeks of post partum period. Before labeling some one as chronic hypertension, Molar pregnancy and other secondary cause of hypertension has to be ruled out.

DEFINITION FOR PREECLAMPSIA

It is defined as BP>140/90 with proteinuria more than *1 and who have protein in 24 hr urine collection >0.3g beyond 20 weeks of gestation.

SUPERIMPOSED PREECLAMPSIA:

Criteria for superimposed preeclampsia;

(1) Known case of hypertension with a New onset proteinuria (≥300 mg/24 h)

(2) A sudden increase in proteinuria or blood pressure or thrombocytopenia less than 100,000/mm^3or renal changes(elevated creatinine level)in a woman with hypertension and proteinuria before 20 weeks of gestation.

ECLAMPSIA.

It is the Severe form of pre eclampsia.

Literally means “flash of lights”.

It is clinically characterized by sudden onset of generalized tonic and clonic form of seizures during pregnancy or childbirth.

National Institute for Health and Care Excellence (NICE, UK:

CLASSIFICATION OF HYPERTENSION

- Mild: systolic BP 140 to 149mmHg and /or diastolic BP 90 to 99mmHg
- Moderate: : systolic BP 150 to 159mmhg and /or diastolic BP> 100 to 109 mmHg
- Severe: : systolic BP >160mm/hg and /or diastolic BP >110mm/hg

AMERICAN CONGRESS OF OBSTETRICIANS AND GYNECOLOGISTS (ACOG)

INDICATORS OF SEVERITY OF GESTATIONAL HYPERTENSIVE DISORDERS

- ***Non severe***
- ***Severe***

ABNORMALITY	***NONSEVERE***	***SEVERE***
• ***DIASTOLIC BP***	***<110 mmHg***	***≥ 110mmHg***
• ***SYSTOLICBP***	**<160 mm Hg**	***≥ 160 mm Hg***
• ***PROTEINURIA***	**None to positive**	***None topositive***
• ***HEADACHE***	**Absent**	***Present***
• ***VISUAL DISTURBANCES***	**Absent**	***Present***

• ***EPIGASTRIC PAIN***	**Absent**	***Present***
• ***OLIGURIA***	**Absent**	***Present***
• ***SERUM CREATININE***	**Normal**	***Elevated***
• ***THROMBO -CYTOPENIA***	**Absent**	***Present***
• **SERUM TRANSAMINASE ELEVATION**	**Minimal**	***Marked***
• **FGR**	**Absent**	***Present***
• **PULMONARY EDEMA**	**Absent**	***Present***
• **GESTATIONAL AGE**	**Late**	***Early***

RISK FACTORS

Risk factors for pre-eclampsia include more and complexity of the disease. . These can be classified based on familial factors, demographic factors, past medical or obstetric history, pregnancy-associated factors, paternal factors and miscellaneous factors. The placenta plays a vital role in the pathogenesis of pre-eclampsia, thus implying that both maternally and paternally derived fetal genes may play a role in the development of the disease .

Demographic factors

Age

Extremes of maternal age is an important factor. Maternal age more than 35 years has more risk for preeclampsia though not for eclampsia. However, women less than19 years of age were at high risk for eclampsia, but not a diagnosis of pre-eclampsia. This may be due to under diagnosis of preeclampsia and inadequate antenatal care.

Ethnicity

South Asian and African population have higher incidence of preeclampsia, while American women more prone for HELLP (haemolysis, elevated liver enzymes and low platelet) syndrome.

Stature and pre-pregnancy body mass index

Short stature women of 145 cm are predisposed to have increased risk of severe preeclampsia

Women who are overweight or obese are known to have increased risk for preeclampsia due to maternal adiposity. BMI 21 to 30 kg/m2 have greater risk of developing preeclampsia.

Pre-existing medical conditions

Pre-gestational diabetes (type 1 and type 2) is an important contributor of new onset of preeclampsia. Women with chronic hypertension were at risk of getting superimposed preeclampsia. Preeclampsia chances are more with chronic kidney disease, lupus nephropathy, as well as diabetic nephropathy. Especially women with diabetes, proteinuria of either190–499 mg/day or □+2 on urine dipstick at Booking visit is having higher risk of preeclampsia. High levels of total cholesterol and low levels of High density lipoprotein level has associating factor for preeclampsia.

THROMBOPHILIA

Testing for inherited thrombophilias (such as factor V Leidenmutation, prothrombin gene mutation, protein C or S deficiency, or antithrombin III deficiency) or acquired thrombophilia (such antiphospholipid antibodies) are very important. Factor V Leiden was more significant. The antiphospholipid syndrome (APS) is a systemic autoimmune disorder which is characterized by arterial and venous thrombosis, has poor pregnancy outcomes. Routine screening is not recommended.

Parity

Preeclampsia is recognised to more commonly complicate first pregnancy and increases the risk of late-onset pre-eclampsia when compared with early-onset disease.

Interval between pregnancies

The risk of pre-eclampsia is generally lower in the second pregnancy .Birth interval more than 4years with no prior history of preeclampsia have higher risk.

previous miscarriages

women who had recurrent spontaneous abortions and infertilitytreatment, a three-fold increased risk of pre-eclampsia

previous pre-eclampsia

The risk of recurrent pre-eclampsia was **12%** for those who previously delivered at term and increased to **40%** for those who delivered before 28 weeks of gestation.

Pregnancy-associated factors

Multiple pregnancy

Twin pregnancy had higher rates of gestational hypertension and pre-eclampsia due to increased placental mass. This leads to increased circulating levels of soluble fms-like tyrosinekinase-1 (sFlt1), which is a circulating antiangiogenic marker of placental origin, and may play an important role in pathophysiology of, especially early-onset of pre-eclampsia.

Fetal gender

Male gender have preponderance to preeclampsia than that of females.

Infections

Women with UTI and periodontal disease are more likely to develop pre-eclampsia. There was some association between the other maternal infections like chlamydia, malaria, treated or untreated HIV and group B streptococcal colonisation and risk of pre-eclampsia are noted

Paternal factors

Paternal age

Epidemiological studies shows that the risk for pre-eclampsia increases in the woman has a partner aged>45 years, because spermatozoa had genetic mutation due to ageing or environmental factors such as exposure to radiation and heat.

Primipaternity and sperm exposure

Increased risk of preeclampsia if women conceives within 4 months or less. This risk decline every month delay in conception. Repeated intercourse with the same partner leads to maternal mucosal tolerance to paternal antigens, which maybe mediated by seminal vesicle-derived transforming growth factor. This is not a significant factor.

Paternal medical history

Higher lipid profile, myocardial infarction and high BMI are some additive factors.

MISCELLANEOUS FACTORS

SMOKING

Cigarette smoking is known to have adverse effects on all organ systems. But smoking decrease the risk.This is protective effect was not well established. But smoking have effects on angiogenicfactors, endothelial function and the immune system, which may contribute to the lowered risk of pre-eclampsia.

physical activity

Exercise and physical activity is advised during pregnancy to improve maternal health. These people less likely to develop preeclampsia

micronutrient deficiencies

Vitamin D deficiency is associated with pre-eclampsia. Level of vitamin D <30 nmol/L, was associated with the risk of pre-eclampsia

Mental health

Depression and anxiety in the first trimester of pregnancy are found to increase the risk of pre-eclampsia . Any lifetime stress and perceived stress during pregnancy may cause pre-eclampsia. It may be mediated by the neuropsychoimmunological pathway.

Socioeconomic status

In developing countries, rural people were more likely to get pre-eclampsia when compared with urban people. Furthermore, women with concurrent anemia and poor intake of fruits and vegetables were at higher risk of pre-eclampsia.

MATERNAL CHANGES OF PRE ECLAMPSIA

HEART CHANGES

NONSEVERE PREECLAMPSIA

This would mainly increase the cardiac output rather than increase in peripheral vascular resistance

SEVEREPREECLAMPSIA-

There is decrease in cardiac output and elevated peripheral vascular resistance which leads to rise in BP.

This result in traumatic intravascular haemolysis (microangiopathic haemolytic anemia)

WATER AND ELECTROLYTES CHANGES

Relative hypovolemia in preeclampsia causes depletion of intracellular space. The fluid shift into extracellular space leads to edema. Proteinuria in these women creates reduced oncotic pressure and further causes fluid shift.

Thus hypovolemia can be identified by hemo concentration, which in turn may affect the birth weight of the baby and also lead on to perinatal mortality and prematurity in the babies born to them.

PHYSIOLOGICAL EDEMA

In pregnancy is due to raised intracapillary hydrostatic pressure.

PATHOLOGICAL OEDEMA

It is mainly due to

- increased permeability to plasma proteins
- reduction in plasma colloid oncotic pressure.

SIGNS AND SYMPTOMS OF EDEMA

- Sudden appearance of pathological swelling around periorbital regions and in the face.
- Rapid increase in the weight>1kg/week for 2 – 3 weeks or >2 kg/week in 1 week, mainly in last trimester

INTRAVASCULAR VOLUME CHANGES

HEMOCONCENTRATION

This is the main hallmark of severe preeclampsia and eclampsia.

The physiological expansion of blood volume in normal pregnancy is about 4500ml.

This is mainly by 40% increase in plasma volume, blood volume in a normal person is only about 3000ml.

The generalized vasospasm and leakage of plasma proteins into interstitial space in case of pre eclampsia leads to loss of this extra 1500ml of blood. After delivery, vasoconstriction reverses, blood volume reexpands, causes fall in the hematocrit and hemoglobin, so even small blood loss during delivery should be managed carefully**.** The Preeclamptic patient have increased sensitivity to both fluid therapy and blood loss .

CHANGES IN PERIPHERAL VASCULAR RESISTANCE:

Normotensive women during pregnancy show resistance to pressor agent ANGIOTENSIN II AND CATECHOLAMINE throughout gestation, in contrast preeclampsia.

HEMATOLOGICAL CHANGES

MILD THROMBOCYTOPENIA (7% - 10% of cases).is the most common abnormality .

OVERT THROBOCYTOPENIA i.e. platelet count <1,00,000/μl- severity of disease

In most cases, the platelet count continues to decrease first day of delivery then it reaches normal level by 3-5 days postpartum in 90% cases and it does not affect the neonatal platelet count.

COAGULATION CHANGES

1. There is found to be a decrease in the level of clotting factor, factor viii.
2. Pre eclamptic patients also shows an Increases fibrinogen levels and D-dimers.
3. Reduced level of antithrombinIII, proteinC and proteins.

But investigations like partial and activated thromboplastin time are not routinely required, can be used only in case of abruption placenta.

CEREBRAL CHANGES

Acute and severe hypertension

⬇

1ST-Overregulation of cerebral perfusion

⬇

Vasospasm-cytotoxic edema

2nd-forced vasodilation and vasoconstriction

⬇

High hydrostatic pressure, hyperperfusion

⬇

Vasogenic edema

Loss of autoregulation-eclamptic seizures.

SIGNS AND SYMPTOMS:

- Hyperreflexia and clonus
- Eclamptic seizures are found to be grand mal in nature.
- Frontal headache - It is due to vasospasm of frontal cortex

It is not relieved by analgesics.

- Visual disturbances and cortical blindness can also occur

PRES. (POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME) –

Constriction in visual field of the cortex**.** Maternal mortality is most commonly found to be due to cerebrovascular accidents.

RENAL CHANGES:

In normal pregnancy , it is very well known that there is increase in the Renal perfusion and glomerular filtration rate, Lets see the changes in the pre eclamptic patients.

In preeclampsia:

resistance in renal afferent arterioles increased

renal hypoperfusion

reduced glomerular filtration rate

PATHOLOGY:

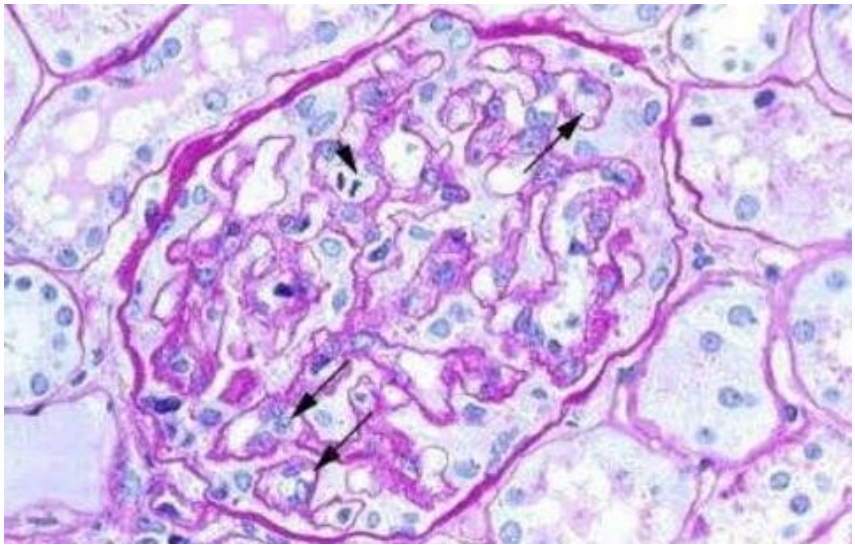
It is characterized by swollen glomerular intracapillary endothelial cells and called as GLOMERULAR ENDOTHELIOSIS.

ELECTRON MICROSCOPY

Shows deposition of osmophilic material in the cytoplasm of endothelial cell. This is reacted with antibodies against fibrinogen and fibrin seen in immunoflourescence.

Preeclamptic patients have high level of uric acid and they also show diminished excretion of urinary calcium, which is mainly due to altered GFR in these patients.

Glomerular Endotheliosis



Swollen endothelial cells in pre eclamptic patients is leading on to partial obstruction in many of the capillary lumens this is indicated in the figure by large arrows. Mitosis indicates cellular repair taking place in the preeclamptic patients, which is shown by small arrow.

Acute renal azotemia is a rare in these patients.

COMPLICATIONS OF PRE ECLAMPSIA

Most common is acute tubular necrosis This is mainly due to bilateral cortical necrosis.

LIVER CHANGES:

hepatic sinusoids shows fibrin deposition

⬇

hypoperfusion to liver

⬇

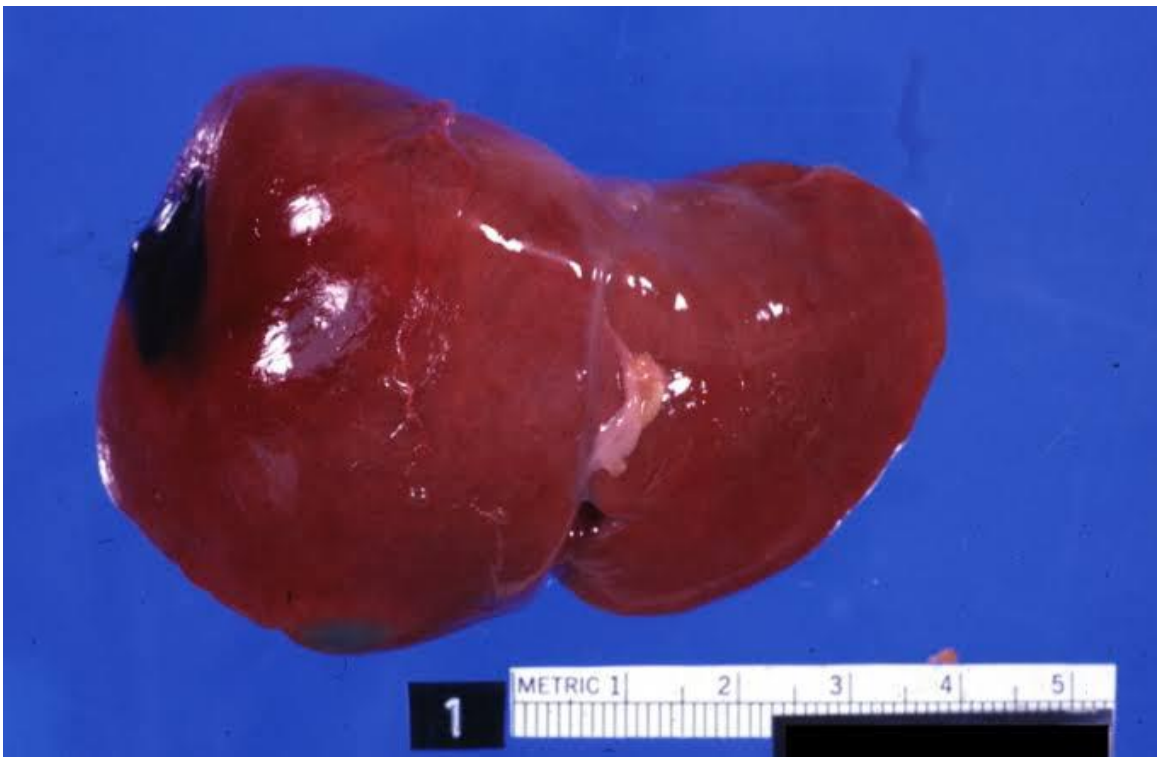
vasospasm mediated hypoxemia

⬇

liver enzymes released into circulation

⬇

- subcapsularedema and stretching
- Hepatocellular necrosis
- Periportalhaemorrhages
- Sub capsular hematoma



HELLP SYNDROME:

This is the most serious complications of preeclampsia, which is characterized by:

- **H**aemolysis
- **E**levated **L**iver enzymes
- **L**ow **P**latelets count

PATHOGENESIS:

Due to endothelial disruption with platelet adherence and fibrin deposit leads to micro angiopathic haemolysis.

The HELLP syndrome precedes to consumptive coagulopathy and DIC.

HEMOLYTIC ANEMIA:

Hemolysis is diagnosed by:

- IN SERUM: elevated lactate dehydrogenise and low haptoglobin level.
- IN PERIPHERAL SMEAR:will showschizocytosis, spherocytosis and reticulocytosis

DIAGNOSIS:

1.Confirmation of hemolysis by elevated LDH or peripheral smear findings.

1. AST or ALT >70 IU/L.
2. Platelet count below 100000 /ɱl

UTERUS AND PLACENTAL CHANGES

- The major cause of perinatal morbidity and mortality was diminished uteroplacental perfusion.
- Resistance was more pronounced in peripheral vessals than central-a”ring like “distribution.

SCREENING TEST FOR PRE ECLAMPSIA

Various biochemical and biophysical markers are proposed for its prediction of preeclampsia but there is no reliable valid and economical screening test available

TEST FOR VASCULAR /PLACENTAL PERFUSION

RESISTANCE;

MID TRIMESTER BLOOD PRESSURE

Normal drop in mid trimester blood pressure has been not noted in preclampsia .

If mean Arterial pressure > 90 mmHg is more risk of developing pre eclampsia.

HAND GRIP TEST .

Rise of diastolic pressure of greater than 20mmHg during this test at 28 to 32 weeks of gestation had a positive predictive value of 20 to 30%.

ANGIOTENSION II INFUSION TEST

The level of Angiotension II less than 8ng/dl minute to increase BP by 20mm Hg has a positive predictive value of 20to 40% for developing pre eclampsia.

ROLL OVER TEST

A test in which blood pressure is recorded in left lateral position. Then she rolls into the supine position and blood pressure is noted after 5 minutes .If the Diastolic BP raised to more than 20mmHg had a more positive predictive value of 33%.

DOPPLER STUDY

Uterine Artery impedence around 18 weeks is an early second trimester screening test.

TESTS FOR KIDNEY DYSFUNCTION:

URIC ACID

Level greater than 5.9 mg/dl had a positive predictive value of 33%.

CALCIUM METABOLISM.

if the level of 24 hour urinary calcium level was less than 12 mg/dl has positive value of about 91%.

URINARY KALLIKREIN EXCRETION

Diminished excretion and reduced level of Kallikrien which is an essential pressor agent is a predictor of pre eclampsia.

TESTS FOR ENDOTHELIAL DYSFUNCTION:

FIBRONECTIN

Greater than 400ng/dl of fibronectin level is important to develop preeclampsia.

PLACENTAL PEPTIDES

InhibinA, ActivinA, PAPP-A, Placental protein13 are early markers of preelampsia which are trial.

PROLACTIN AS A PREDICTOR OF PRE ECLAMPSIA

My aim of study is about whether prolactin can be used a predictor of pre eclampsia and whether it has an importance in the pathogenesis.

PROLACTIN

Prolactin (**PRL**), otherwise known as **luteotropin**, is a polypeptide protein, which has vital role in milk secretion,especially in female mammals. Prolactin is synthesized from anterior pituitary gland by lactotrophs.

The main stimulus for prolactin secretion is found to be during many of our normal activities like eating, mating , stress and ovulation, also during estrogen treatment and during nursing.

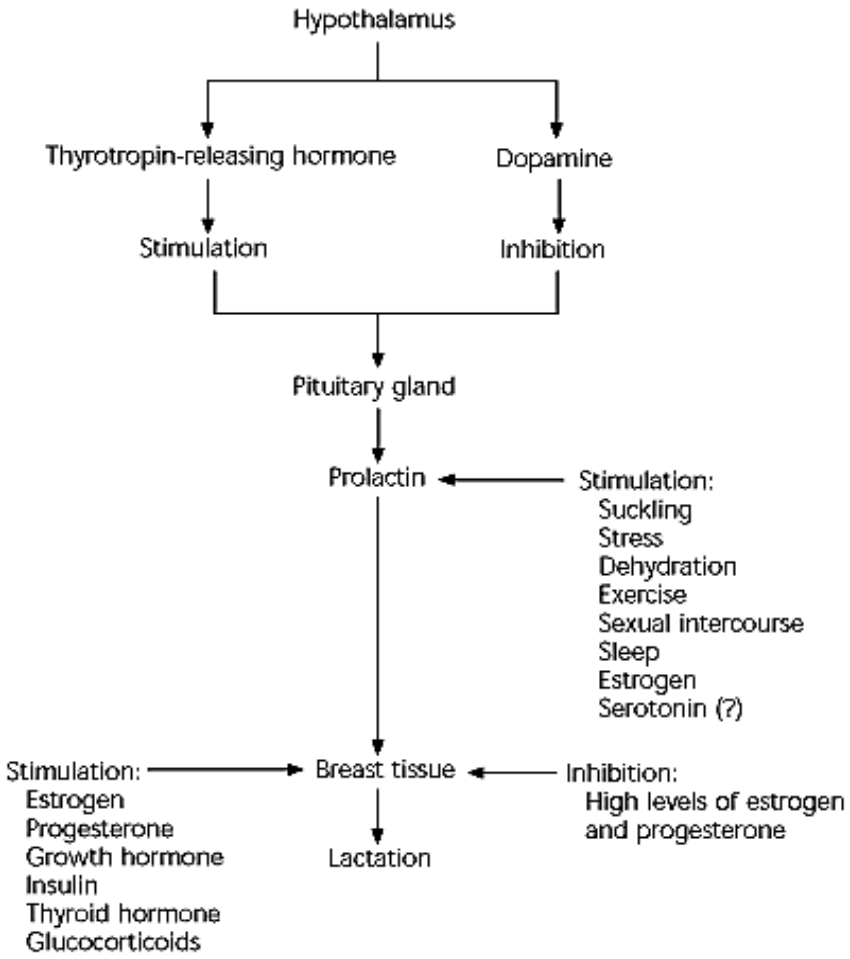
Prolactin is found to be secreted in pulsatile manner.. It also has an important role in the regulation of the immune system. The main function of prolactin in human is in milk production. It may also act as a growth factor and angiogenic factor. It acts binding to cytokine-like receptors , through which it plays a vital role in hematopoiesis, angiogenesis and is also involved in the regulation of blood clotting pathways.

The hormone acts as both in autocrine and in a paracrine manner through its prolactin receptor and a cytokine receptors.

REGULATION OF SECRETION

The hypothalamic factor that inhibits prolactin secretion is the neurotransmitter dopamine which is secreted by arcuate nucleus by acting through D2 receptors. .

Thyrotropin-releasing hormone, stimulates prolactin release, however prolactin is pitituary hormone which is mainly under inhibitory control.



The prolactin production is mainly controlled by estrogens , which directly stimulate prolactin production as well as acts by suppressing dopamine. It synthesis milk from the mammary gland by its enlargement (lactation), during pregnancy and also prepare for milk production. Lactation starts when the levels of progesterone fall by the end of pregnancy and a suckling reflex starts.

Vasoactive intestinal peptide and peptide histidine isoleucine are involved in the regulation of prolactin secretion in humans. It has diurnal and ovulatory cycles. It levels increase during REM sleep and in the early morning. High levels of estrogen and progesterone increase prolactin levels by 10- to 20-fold during pregnancy.

In vertebrates such as mice a ,similar actions with tissue specific effect is attained by a group of prolactin-like proteins .

The sudden fall in level of estrogen and progesterone levels after the delivery of baby will allow prolactin to induce lactation in the women.

MECHANISM OF ACTION

The prolactin expression is stimulated by cAMP present in decidual cells and in lymphocytes .

It is mediated by an imperfect cAMP–responsive element and two CAAT/enhancer binding proteins (C/EBP).

Prolactin synthesis is increased by progesterone in the endometrium,where as it also decreases its level in myometriumand breast glandular tissue.

Pit-1 promoter in addition to the distal promoter expressed in breast and other tissues.

SUCKLING REFLEX / MILK EJECTION REFLUX

SUCKING OF THE NIPPLE BY THE BABY

ACTIVATES MECHANO RECEPTORS AROUND THE NIPPLE

REFLUX FROM THESE RECEPTORS IS CARRIED BY NERVE FIBRES THROUGH SPINAL CORD

IT IS CARRIED TO THE HYPOTHALAMUS

THERE IS A CHANGE IN THE ELECTRICAL ACTIVITY OF NEURONS

REGULATES THE PITUATARY GLAND TO SECRETE OXYTOCIN FROM POSTERIOR PITUATARY GLAND

Prolactin controls lactogenesis but not the milk-ejection reflex, this is mainly done by oxytocin and the rise in prolactin level fills the breast with milk ,it thus prepares for the next feed.

It is found that level of prolactin rises during activities like exercise, sexual intercourse, breast examination, following minor surgical procedures or following epileptic seizures, may also increase due to physical or emotional stress, following intake of high protein meal.

OTHER FUNCTIONS OF PROLACTIN

1. Prolactin cause the sexual refractory period. The hormone counteracts the effect of dopamine, which is associated to sexual arousal.
2. Sex hormones level is regulated by change in level of prolactin in women and testosterone in men which leads to spermatogenesis.
3. It also act as a weak gonadotropin, hence it suppresses GnRH secretion. The mechanism is not understood.
4. Prolactin helps in the proliferation of oligodendrocyte precursor cells and its differentiation, which is involved in the synthesis of myelin.
5. It affects the fetal lung surfactant synthesis , it also helps in building up of the immunity level in the fetus.

6. Fetal brain and maternal neural development is also controlled to many extent by the prolactin. The site of synthesis of prolactin is not only in the anterior pituitary, but is also produced in other sites like decidua, myometrium, breast, lymphocytes, leukocytes and prostate.

ABNORMALITY IN PROLACTIN LEVEL

PROLACTINOMAS : Anterior pitituary tumour are associated with hyperprolactinemia. Prolactinomas may affects the hypothalamic – pituitary gonadal axis by suppressing the secretion of GnRH

PROLACTINOMA

SUPPRESSES THE SECRETION OF GnRH SECRETION FROM HYPOTHALAMUS

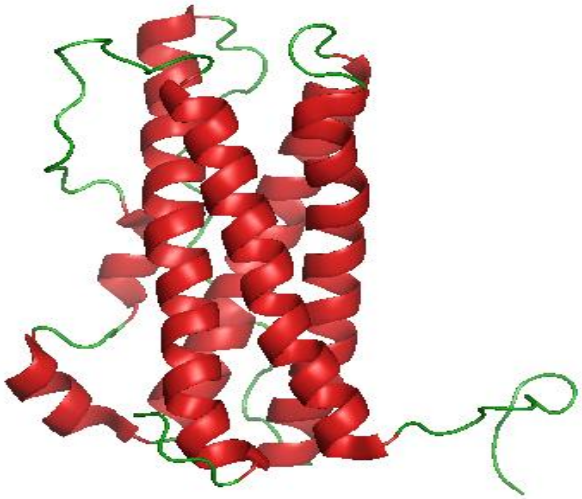
DECREASES THE SECRETION OF FSH AND LH

DISRUPTS THE OVULATORY CYCLE

AMENNORRHEA , INFERTILITY IN FEMALES

The other problems due to prolactinomas is mainly excessive lactation (galactorhea) and visual disturbances.

STRUCTURE AND ISOFORMS



Chemically prolactin appears as posttranslational form with some chemical modifications like phosphorylation or glycosylation. Placental lactogen and growth factors has a structure similar to that of the prolactin. There is three disulfide bonds in its molecular structure.

The dominant form of prolactin is non-glycosylated form which is synthesized by pitituary gland.

SIZES OF PROLACTIN:

3 different sizes are seen

1. Little prolactin -

It is the predominant form. It has a structure with a single-chain polypeptide of 198 amino acids. It has a molecular weight of about 22-kDa.[1]

2. Big prolactin

Its weight is found to be more or less 48 kDa. It is usually formed as the product of interaction of several prolactin molecules. It has little biological activity.

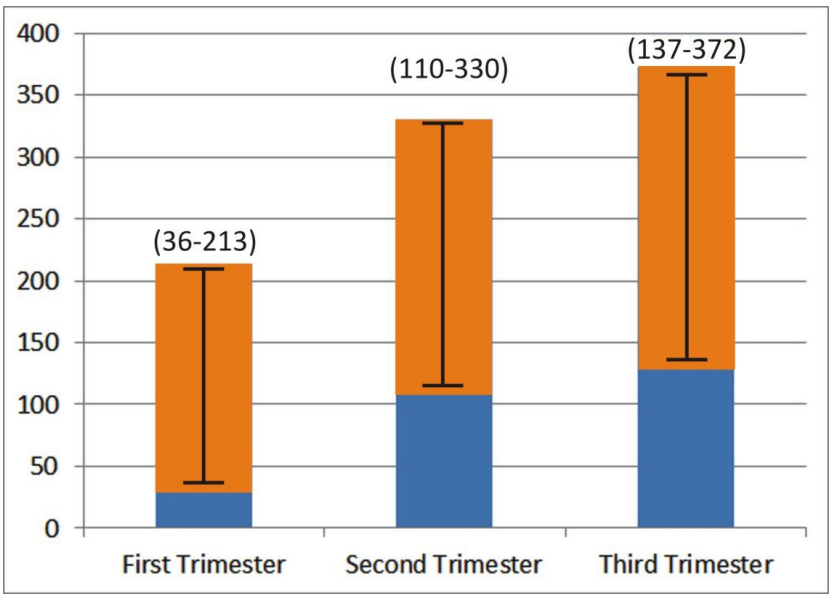
3. Big big prolactin

Its weight is about 150 kDa. It appears to have a low biological activity. In the early postpartum period there is increase in the level of larger ones.

Serum prolactin level

Units	Nonpregnant Female	First Trimester	Second Trimester	Third Trimester
ng/mL	0 – 20	36 - 213	110 - 330	137 – 372

Serum prolactin level



THE ROLE OF PROLACTIN IN THE PATHOGENESIS OF PRE ECLAMPSIA.

1. Prolactin cause an increased response to vasopressor agent.
2 There is an imbalance in angiogenesis and anti angiogenesis, this is leading on to pre eclampsia.
3. Endothelial nitric oxide is one of the important factors which controls the blood pressure, Prolactin causes elevation in the BP by decreasing the level of nitric oxide synthetase, which in turn leads on to decrease in the level of nitric oxide.
4. It causes sodium and water retention of fluids and electrolytes affecting the osmoregulation.
5. Elevation of arterial pressure during the pregnancy is directly controlled by the prolactin

AIMS OF STUDY

- My study is about whether prolactin has a role in pathogenesis of preeclampsia and its severity, whether it can be used as a predictor of preeclampsia .
- STUDY DESIGN - PROSPECTIVE STUDY.

OBJECTIVES

- To find if prolactin has a role in pathogenesis of preeclampsia.
- To compare serum prolactin level in all preeclampsia patients with normal healthy pregnant women
- To correlate serum prolactin levels with severity of preeclampsia and its outcome.

MATERIALS AND METHODS

TYPE OF STUDY : PROSPECTIVE OBSERVATIONAL STUDY.

PERIOD OF STUDY : OCTOBER 2017-SEPTEMBER 2018.

SAMPLE SIZE : 100 preeclamptic patients

100 normal pregnant women.

PLACE OF STUDY :

Antenatal outpatient department, Antenatal ward and Labor ward in the Dept of Obstetrics and Gynaecology, in Govt. Theni medical college.

METHOD OF STUDY:

- Careful history taking is done as per the proforma.
- This is followed by Complete clinical examination which is done Under aseptic precaution, this is followed by sampling , which is done by venipuncture of 6ml of blood. The blood is drawn out ,of which 4ml of blood will be used for routine investigation and TSH 2ml of blood for serum prolactin which is done by ELIZA clear method. The patients were then followed up until delivery.

INCLUSION CRITERIA

- All pregnant patients with BP 140/90mmHg and urine albumin 1+ after 20 weeks of gestation.
- All preeclamptic patients will be cases and all normal patients will be control.

EXCLUSION CRITERIA

- Chronic hypertension,
- Type 1&2 diabetes mellitus.
- Multiple pregnancy.
- Thyroid disorders.
- h/o galactorrhea.
- H/o drug intake affect serum prolactin such as neuroleptics.

MATERIALS:

SERUM PROLACTIN LEVEI.

- Non-pregnant- 0-20 ng/ml
- 1st trimester - 36-213 ng/ml.
- 2nd trimester - 110-330 ng/ml.
- 3rd trimester - 137-372 ng/ml.

BP MONITORING

- At booking visit.
- 2nd trimester - every fortnight.
- 3rd trimester - every week.

URINE ALBUMIN

- Grading of proteinuria.

DISCUSSION

- The preeclampsia is mainly characterized by hypertension, edema and increased protein excretion.
- Blood vessels in preeclamptic patients shows hyper response to pressor agents.
- Normally Prolactin was elevated in large amounts in pregnancy.
- Prolactin is involved in osmoregulation that leads to sodium and water retention.
- It causes increased vasoreactivity to angiotensin. Angiogenic process in preeclampsia is affected by high level of preeclampsia.

STATISTICAL ANALYSIS

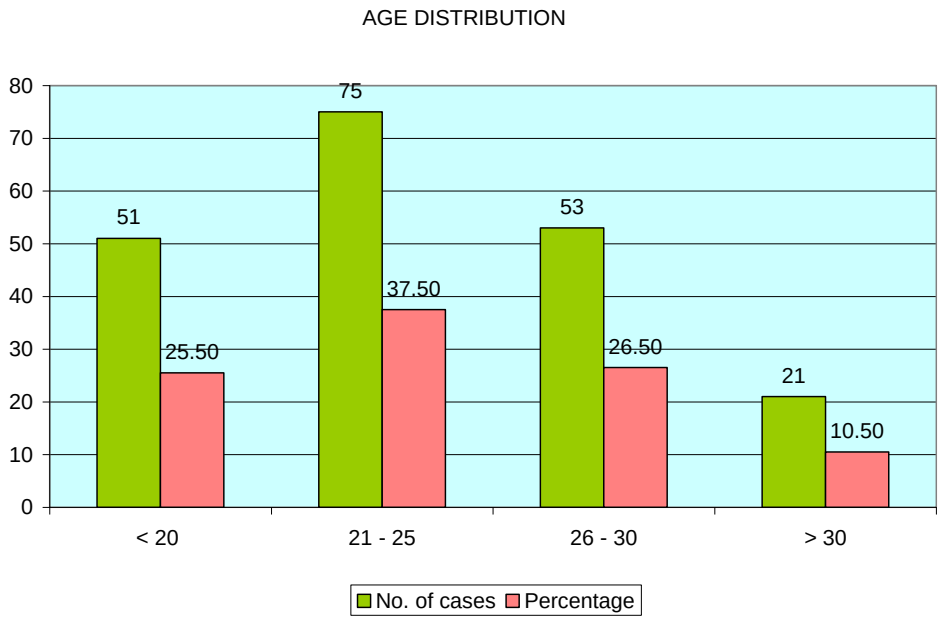
The mean and standard deviation of the serum prolactin will be calculated and student 't' test is used to compare mean.

STATISTICAL ANALYSIS

Prolactin was taken as the primary outcome variable. Presence or absence of Preeclampsia was considered as primary exposure variable. Different Age groups, parity, gestational age at which prolactin was taken were considered as other explanatory variables. Descriptive analysis of all the variables was done using mean, median and standard deviation for quantitative variables, frequency and percentage for categorical variables. The association between Preeclampsia and primary outcome variables was assessed by Independent Sample T-Test. Mean differences; standard deviation and p-value were calculated and presented. P value 0.001 was considered as statistically significant.

TABLE 1.Distribution of age in the study group

Age	No. of cases	Percentage
≤ 20	51	25.50
21 – 25	75	37.50
26 – 30	53	26.50
> 30	21	10.50
Total	200	100.00



In study group 25.5%were in the age group less than 20 years and 37.5%were in the age group 21to 25 years 26.5% in the age group between 26 to30 years 10.50 %were in the age group between >30 years.

TABLE 2.Distribution of parity in study group

Parity	No. of cases	Percentage
Primi	98	49.00
Multi	102	51.00
Total	200	100.00

In this study 49% were primi 51% were multigravida

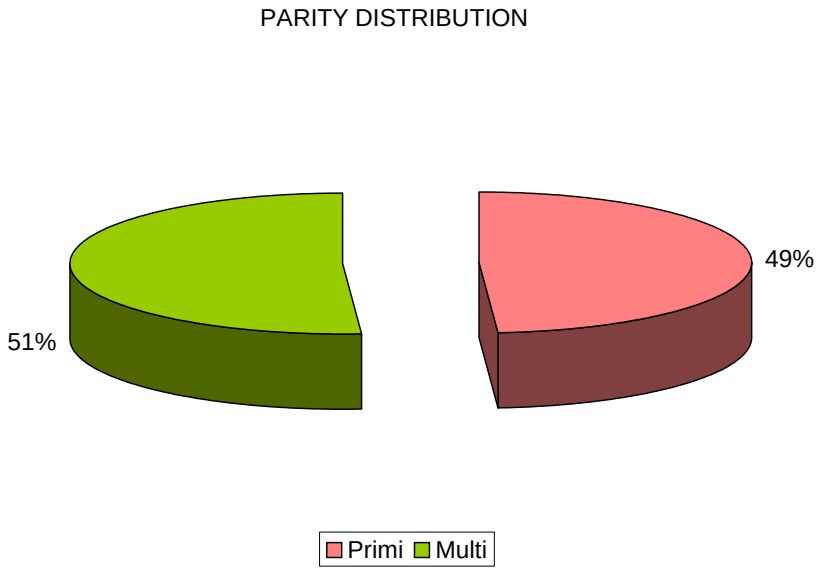
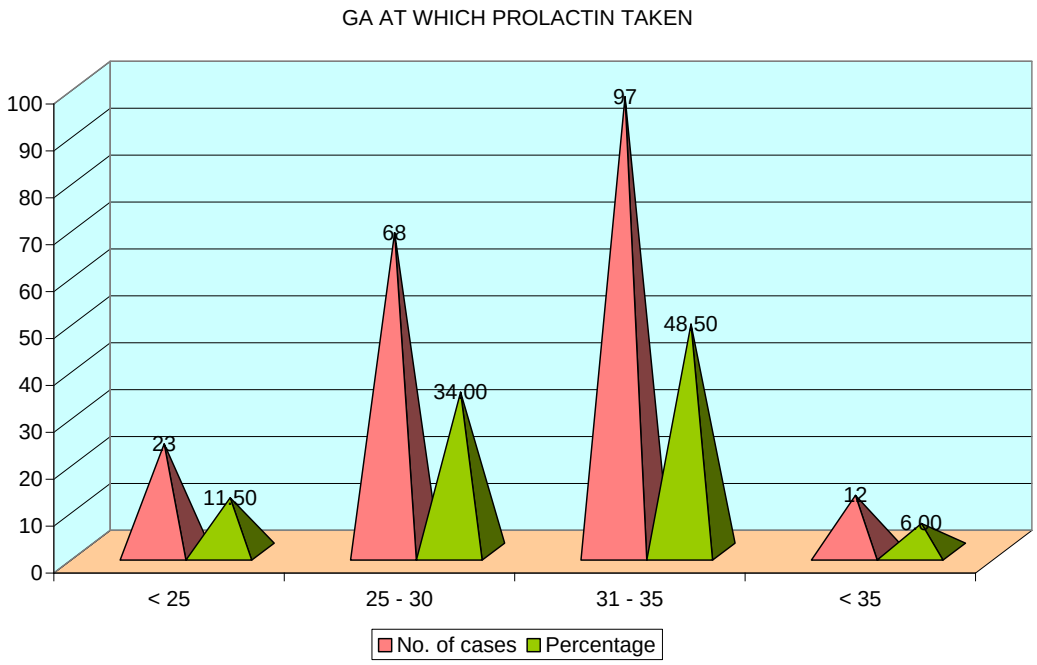


TABLE3 : Gestational age at which prolactin level taken



GA at Which Prolactin taken	No. of cases	Percentage
< 25	23	11.50
25 - 30	68	34.00
31 - 35	97	48.50
< 35	12	6.00
Total	200	100.00

This table shows that, serum prolactin has taken maximum in the week of 31wk-35wk of gestation is about 48.5%,

TABLE 4 Pre Eclampsia

Preeclampsia	No. of cases	%
Yes	91	45.50
No	109	54.50
Total	200	100.00

Among the study group 45.5% are preeclampsia remaining 54.5% remain normotensive.

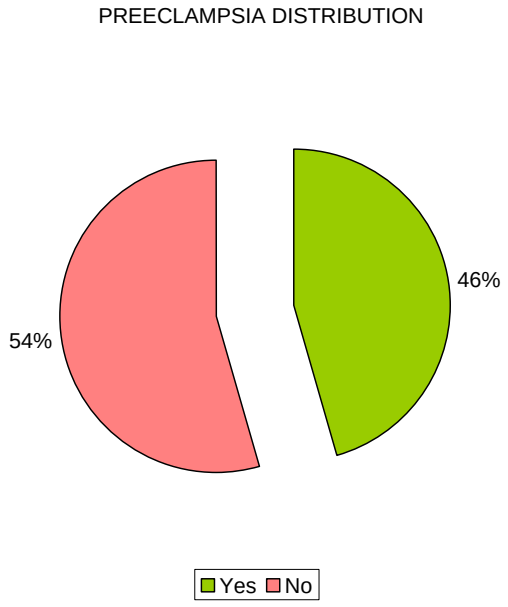


TABLE 5. Non Severe& Severe preeclampsia

PREECLAMPSIA	No. of cases	%
Severe	44	22.00
Non severe	47	23.50
Total	91	45.50

Among the study group 54.5% remain normotensive ,23.50% are nonsevere pre eclampsia and 22% severe preeclampsia.

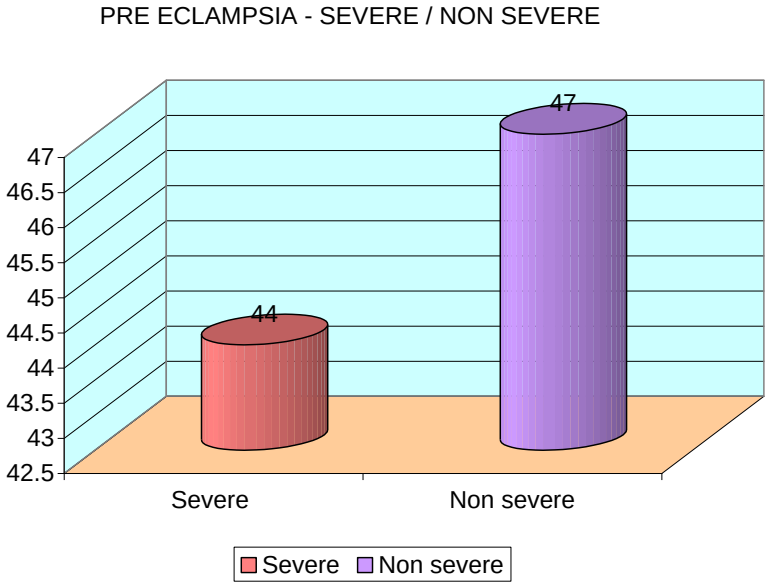
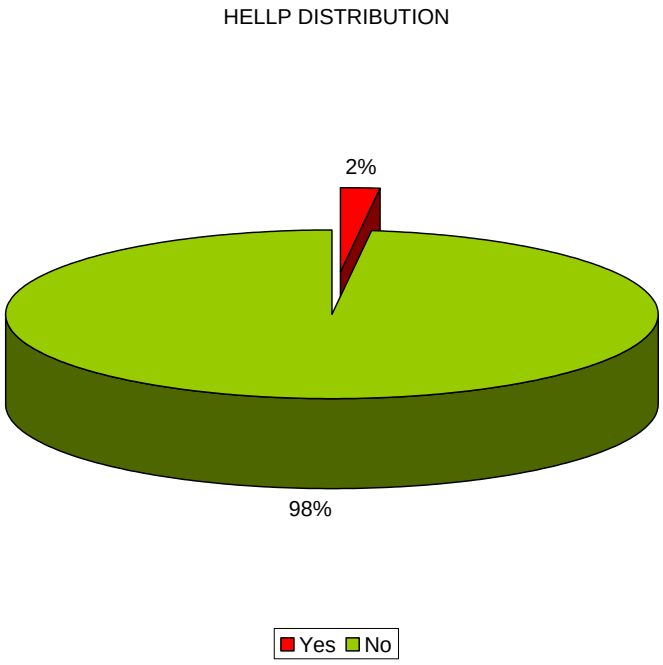


TABLE 6;HELLP SYNDROME

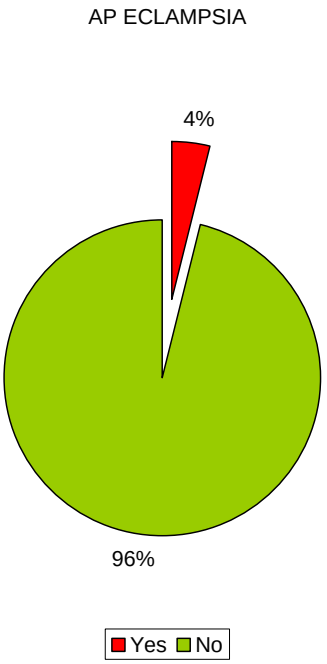
HELLP	No. of cases	%
Yes	4	2.00
No	196	98.00
Total	200	100.00



Among the study group,2% of preeclamptic patients have HELLP SYNDROME.

TABLE 7;APECLAMPSIA

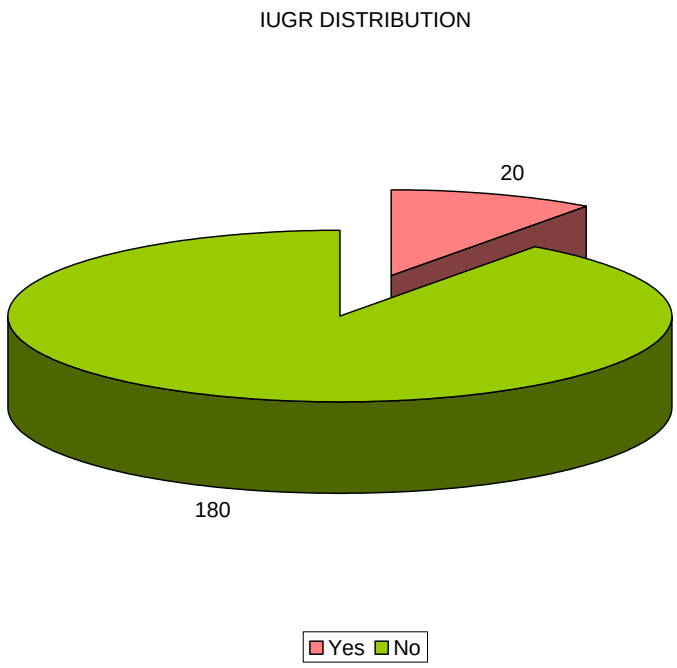
AP Eclampsia	No. of cases	%
Yes	8	4.00
No	192	96.00
Total	200	100.00



Among these study population,4% of preeclamptic patients are complicated with APECLAMPSIA.

TABLE 8;IUGR IN PREECLAMPSIA

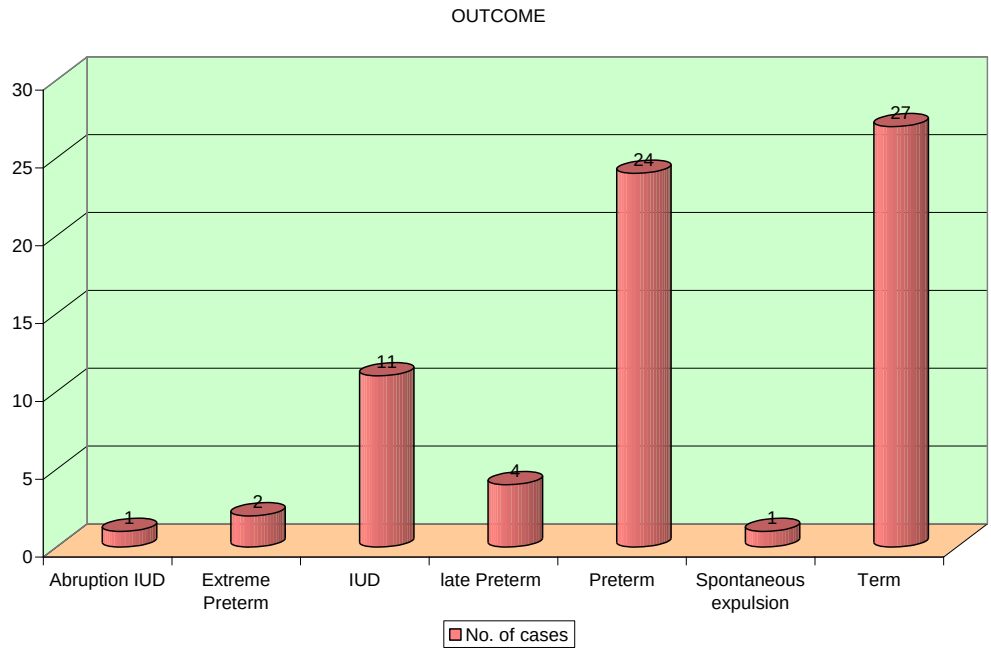
IUGR	No. of cases	%
Yes	20	10.00
No	180	90.00
Total	200	100.00



Among preeclamptic patients,10% of them have IUGR.

TABLE 9:OUTCOME AND ITS COMPLICATION

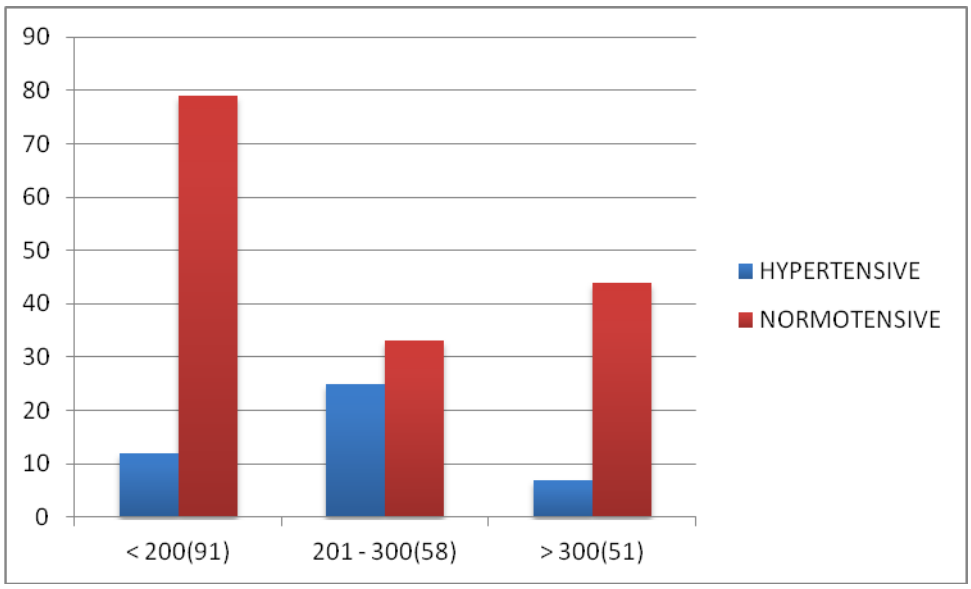
Outcome	No. of cases	%
Abruption IUD	1	0.50
Extreme Preterm	2	1.00
IUD	11	5.50
late Preterm	4	2.00
Preterm	24	12.00
Spontaneous expulsion	1	0.50
Term	27	13.50
Total	70	35.00



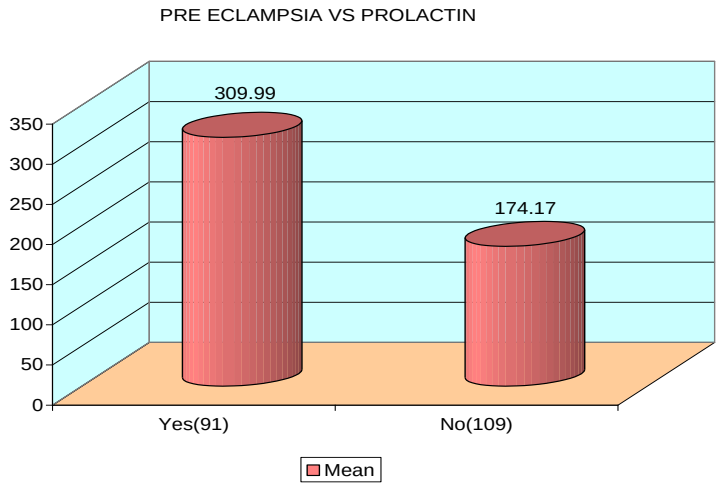
This table shows,preterm delivery has highest outcome of about 12%among the preeclamptic women,spontaneous expulsion and abruption placentae has least outcome of about 0.5%

TABLE10; Serum Prolactin Level in Study Population

Prolactin ng/ml vspreclampsia		
	Yes	No
< 200(91)	11	80
201 - 300(58)	29	29
> 300(51)	51	0



Preeclampsia vs Prolactin			
Preeclampsia	Mean	SD	p' value
Yes(91)	309.99	81.556	
No(109)	174.17	52.684	<0.001



The statistically significant difference between the mean serum prolactin level of the preeclamptic and normal patients denotes a significant association .

TABLE11; Prolactin Level in Nonsevere/Severe Preeclampsia

Prolactin ng/ml vs Severe		
	Yes	No
< 200(91)	0	91
201 - 300(58)	3	55
> 300(51)	42	9

This diagram shows ,mean value of prolactin level in nonsevere is about 245.66ng/ml and in severe is about 370.21ng/ml.

Preeclampsia Severity vs Prolactin			
Preeclampsia	Mean	SD	p' value
Non Severe(44)	245.66	69	
Severe(47)	370.21	29.978	<0.001

This table shows statistically significant association between prolactin level with nonsevere/ severe

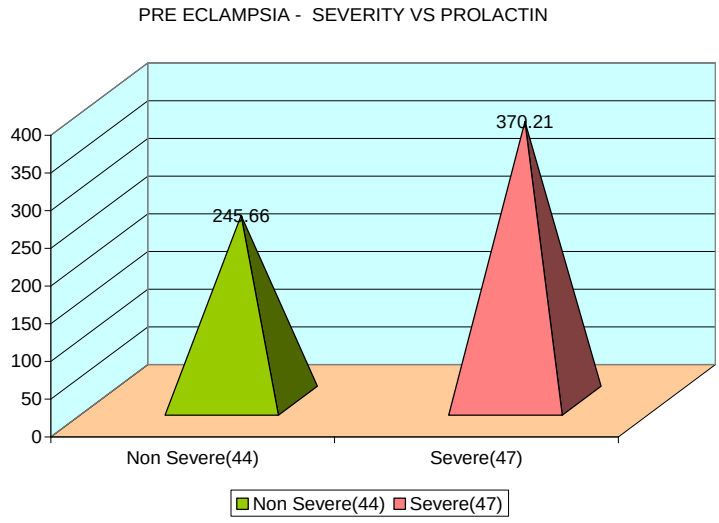
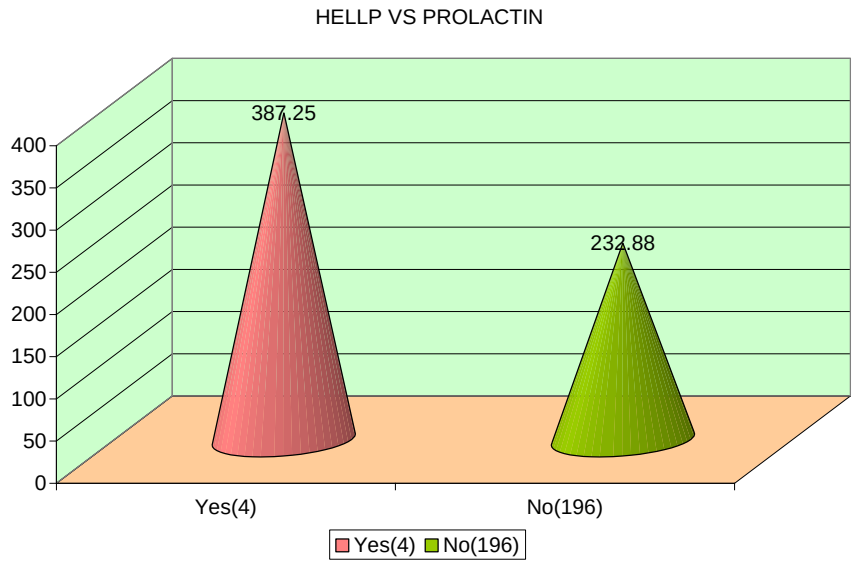


TABLE12; Prolactin in HELLP Syndrome

Prolactin ng/ml vs HELLP			
	Yes	Partial	No
< 200(91)	0	0	91
201 - 300(58)	0	0	58
> 300(51)	3	1	47



Prolactin vs HELLP			
HELLP	Mean	SD	p' value
Yes(4)	387.25	23.768	
No(196)	232.88	93.865	0.001

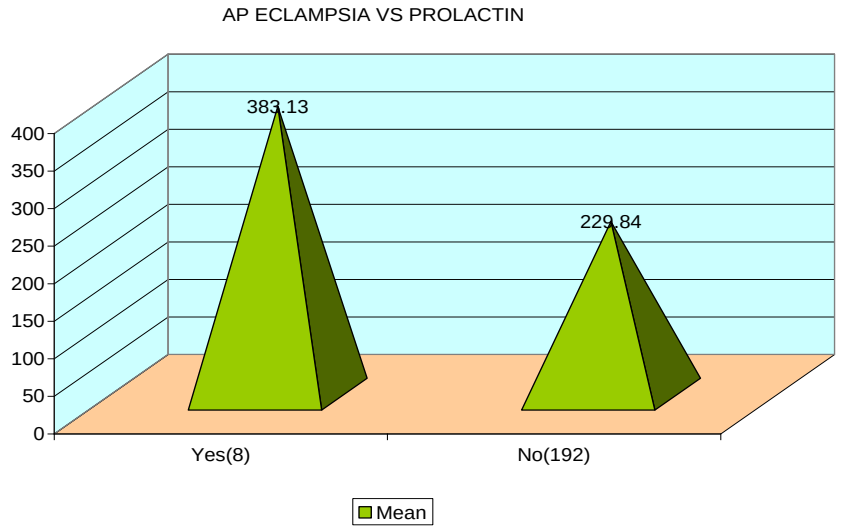
This shows significant association of serum prolactin level with HELLP syndrome.

This table shows that , among 4 patients of HELLP ,the mean level of prolactin is more than 380ng/ml.

TABLE13; Prolactin Level in ApEclampsia

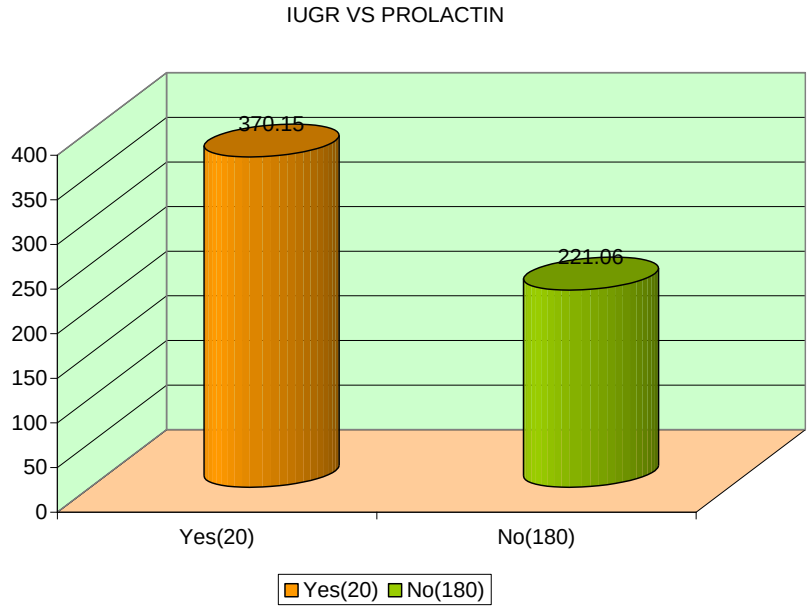
Prolactin ng/ml vs AP Eclampsia		
	Yes	No
< 200(91)	0	91
201 - 300(58)	0	58
> 300(51)	8	43

Prolactin vs AP Eclampsia			
AP Eclampsia	Mean	SD	p' value
Yes(8)	383.13	15.923	
No(192)	229.84	92.407	<0.001



This table shows that, 8 AP Eclamptic patients have serum prolactin level more than 300ng/ml,cut off value of about 383ng/ml.This denotes statistically difference between mean serum prolactin level and APEclampsia.

TABLE 14; Serum Prolactin in IUGR



Prolactin ng/ml vs IUGR		
	Yes	No
< 200(91)	0	91
201 - 300(58)	3	55
> 300(51)	17	34

Prolactin vs IUGR			
IUGR	Mean	SD	p' value
Yes(20)	370.15	47.068	
No(180)	221.06	87.517	<0.001

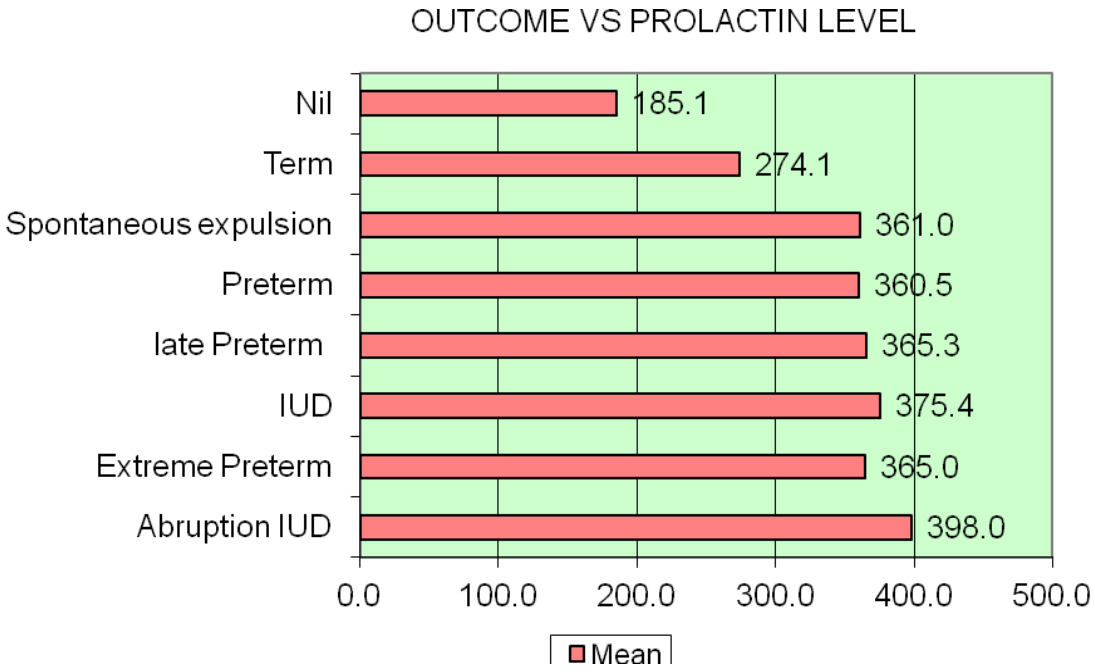
This table shows that ,the level of prolactin in IUGR patients cut off value about 370 ng/ml.

TABLE 15; Prolactin vs Outcome

Prolactin ng/ml vs Outcome

	Term	Late Preterm	Preterm	Abruption	Extreme Preterm	IUD	Spon taneous expulsion	No
< 200(91)	7	0	0	0	0	0	0	84
201 - 300(58)	10	1	3	0	0	0	0	44
> 300(51)	10	3	21	1	2	11	1	2

This shows, prolactin level was high in preterm delivery which is more than 300ng/ml



Outcome vs Prolactin			
Outcome	Mean	SD	p' value
Abruption IUD	398.0	0.00	<0.001
Extreme Preterm	365.0	21.21	
IUD	375.4	23.93	
late Preterm	365.3	43.71	
Preterm	360.5	45.73	
Spontaneous expulsion	361.0	0.00	
Term	274.1	94.43	
Nil	185.1	56.90	

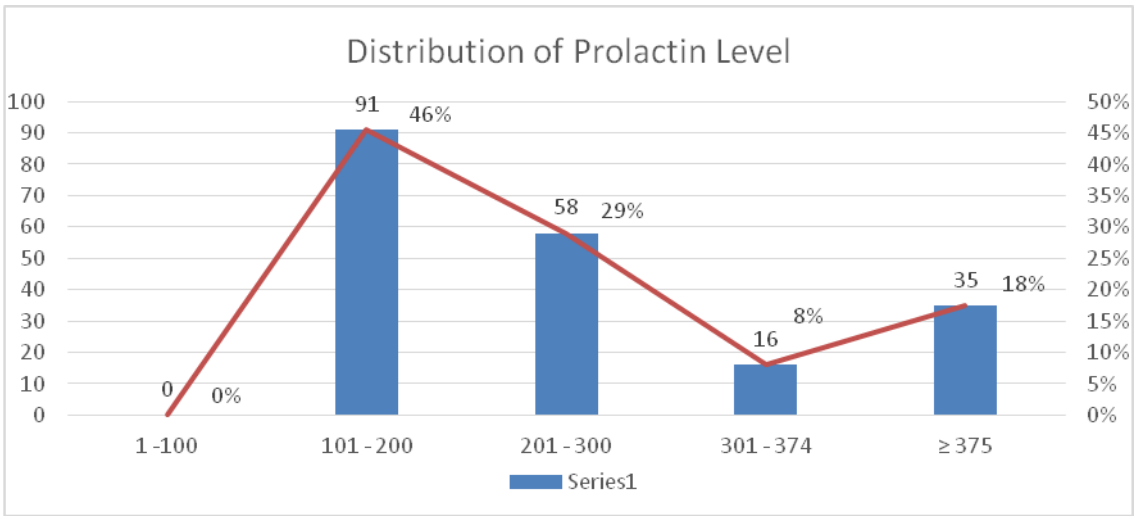


TABLE 16

Prolactin level	Hypertensive	Normotensive	Total
Prolactin>300ng/ ml	51(a)	0(b)	51(a+b)
Prolactin<300ng/ ml	40(c)	109(d)	149(c+d)
Total	91(a+c)	109(b+d)	200

Sensitivity : a / a+c x 100

51/91 x 100

56.04%

specificity : d/ c+d x 100

109/109 X 100

100%

positive predictive value : a/ a+b x 100

51/51 x100

100%

Negative predictive value : c/ c+d x 100

40/149 x 100

26.9%

RESULTS

In this study, majority of the women about 37.5% was in the age group between 21 and 25 years.51% were multigravida,49% were primigravida.45.5% of women are preeclampsia out of which 22%were developed nonsevere preeclampsia and 23.5% were developed severe preeclampsia. The complications like HELLP were about 4%,AP Eclampsia about 8% and IUGR 10%.The most common outcome of pregnancy was preterm delivery about 12%.It is found that mean prolactin level in preeclamptic women was 309.9 and non-preeclamptic women was 174.12 taken during mean gestational age between 31-35weeks.In which mean concentration of prolactin level in non-severe preeclampsia was 245.66and in severe preeclampsia was 309.9.The complication of preeclampsia like HELLP,AP Eclampsia occurred at mean level of prolactin was 383.13.Based upon the statistical analysis sensitivity of the test is 56.04% and specificity is 100%,positive predictive value is 100% and negative predictive value is 26.9%. Hence p value is <o.oo1 ,which is statistically significant.

SUMMARY

This prospective observational study was done at Theni Medical College and Hospital. After getting consent from the patients serum prolactin was taken from 200 women out of which 100 woman are normal,100 woman are preeclamptic women after 20 week of gestation.100 preeclamptic women came for follow up till delivery.

Proper history taking, clinical examination was done, BP and urine albumin was checked in every visit.

In my study, out of 91 preeclamptic women,51 patients show mean prolactin level more than 300ng/ml. There is a significant association between mean prolactin level and complications of preeclampsia like HELLP, APeclampsia, IUGR and adverse perinatal outcome(preterm).It is found that raised mean concentration of serum prolactin level associated with hypertension in pregnancy and its complications.

CONCLUSION

This study revealed increased level of prolactin was associated with preeclampsia when compared to healthy women and more with complications. Still large number of study is needed to conclude. Thus prolactin can be used as a reliable marker for preeclampsia.

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ABBREVIATIONS

PRL	-	Prolactin
UPRL	-	Urinary Prolactin
SPE	-	Severe Pre Eclampsia
MPE	-	Mild Pre Eclampsia
VEGF	-	Vascular Endothelial Growth Factor
PLGF	-	Placental Like Growth Factor
CO	-	Cardiac Output
PVR	-	Pulmonary Vascular Resistance
GA	-	Gestational Age
BP	-	Blood pressure

PROFORMA

NAME AGE IP NO

PHONE NUMBER

ADDRESS

HUSBANDS NAME

OCCUPATION

QUALIFICATION

SOCIOECONOMIC STATUS

OBSTETRIC HISTORY

PARITY

LMP EDD

GA BY LMP

GA BY USG

MENSTRUAL HISTORY

MARITAL HISTORY

PAST HISTORY

1.Diabetes

2.Hypertension

3.Heart disease

4.Thyroid disorders

5.Bronchial asthma

6.Liver/renal disease

7.Drug intake.

8.Epilepsy.

GENERAL EXAMINATION

HEIGHT

WEIGHT

PALLOR

PEDAL EDEMA

PULSE

BP

CVS

RS

CNS

PER ABDOMEN

THYROID

BLOOD INVESTIGATIONS

RFT LFT TSH

URINE ALBUMIN

SERUM PROLACTIN.

OUTCOME.

Sl.No.	Name	Age	Parity	GA at Which Prolactin taken	Prolactin ng/ml	Preeclampsia		Non severe	Severe	HE LLP	AP Eclampsia	IUGR	Outcome
						Yes	No						
1	Thavamani	23	G_2 A_1	30 + 2	220	✓	-	✓	-	-	-	-	Term
2	Gayathri	21	G_2 P_1 L_1	28 + 4	115	✓	-	✓	-	-	-	-	Term
3	Sarikala	20	Primi	33 + 2	215	-	-	-	-	-	-	-	-
4	Kokila	22	Primi	28 + 5	122	-	-	-	-	-	-	-	Term
5	Kamatchi	19	G_3 A_2	31 + 2	382	✓	-	-	✓	-	-	✓	Preterm
6	Mariyammal	19	G_2 P_1 L_1	29 + 1	218	-	-	-	-	-	-	-	-
7	Devi	35	G_2 P_1 L_0	35 + 1	390	✓	-	-	✓	-	✓	✓	Late Preterm
8	Archana	24	Primi	32 + 1	220	✓	-	✓	-	-	-	-	Term
9	Benazibegum	28	G_2 P_1 L_1	28 + 1	340	✓	-	-	✓	-	-	-	IUD
10	Revathy	20	G_3 P_2 L_2	32 + 4	118	-	-	-	-	-	-	-	-
11	Anitha	21	Primi	27 + 2	240	✓	-	✓	-	-	-	-	Term
12	Malathy	22	G_2 P_1 L_0	33	189	✓	-	✓	-	-	-	-	-
13	Maheswari	19	Primi	34 + 2	220	-	-	-	-	-	-	-	-
14	Savithri	32	Primi	32 + 6	300	✓	-	-	✓	-	-	✓	Late Preterm
15	Saraswathy	25	G_2 P_1 L_1	27 + 2	118	-	-	-	-	-	-	-	-

16	Akila	27	G_2 P_1 L_1 A_1	32 + 1	198	✓	-	✓	-	-	-	-	-
17	Kamatchiammal	21	G_2 P_1 L_1 A_2	34 + 3	390	✓	-	-	✓	Partial	-	✓	Late Preterm
18	Pandiyammal	20	G_2 A_1	30 + 2	180	-	-	-	-	-	-	-	-
19	Sasi	23	Primi	33 + 1	218	-	-	-	-	-	-	-	-
20	Kokila	26	G_3 P_2 L_2	36 + 1	300	-	-	-	-	-	-	-	-
21	Vimala	22	Primi	34 + 2	313	✓	-	✓	-	-	-	-	Term
22	Maheswari	25	Primi	32 + 3	390	✓	-	-	✓	-	-	-	Preterm
23	Zareena Begum	19	Primi	33 + 2	380	✓	-	-	✓	-	-	✓	Term
24	Venkateshwari	23	G_2 A_1	27 + 1	118	-	-	-	-	-	-	-	-
25	Vijayalakshmi	28	Primi	36 + 1	300	-	-	-	-	-	-	-	-
26	Vimala	18	Primi	32 + 4	220	✓	-	✓	-	-	-	✓	Preterm
27	Autrika	19	Primi	29 + 3	118	-	-	-	-	-	-	-	-
28	Chandra	19	Primi	30 + 1	184	-	-	✓	-	-	-	-	-
29	Devika	28	G_3 P_2 L_2	34 + 2	299	-	-	-	-	-	-	-	-
30	Roselin	19	Primi	29 + 2	153	-	✓	-	-	-	-	-	-
31	Devi	30	G_5 P_2 L_2 A_2	33 + 5	384	✓	-	-	✓	-	-	-	Preterm
32	Aushiya	18	Primi	27 + 3	118	-	-	-	-	-	-	-	-

33	Vidhya	21	G_3 A_2	31 + 4	221	✓	-	✓	-	-	-	-	-
34	Pandeeshwari	26	G_2 P_1 L_1	36 + 2	380	✓	-	-	✓	-	-	✓	Term
35	Velammal	24	Primi	33 + 1	284	✓	-	✓	-	-	-	-	-
36	Mudiyammal	21	Primi	30 + 2	210	-	✓	-	-	-	-	-	-
37	Ramya	22	G_2 P_1 4	28 + 3	190	-	✓	-	-	-	-	-	-
38	Munieshwari	19	Primi	27 + 2	118	-	✓	-	-	-	-	-	-
39	Vani	18	G_2 A_1	34 + 3	270	✓	-	✓	-	-	-	-	Term
40	Sridevi	31	G_4 P_1 L_1 A_2	28 + 5	380	✓	-	-	✓	-	✓	-	IUD
41	Vanaja	35	G_2 P_1 L_0	34 + 2	398	✓	-	-	-	-	✓	-	Abruption IUD
42	Visalatchi	23	Primi	26 + 1	170	-	✓	-	-	-	-	-	-
43	Vanitha	18	Primi	31	115	✓		✓	-	-	-	-	-
44	Selvi	24	G_2 P_1 L_1	34 + 2	250	-	✓	-	-	-	-	-	-
45	Pandriselvi	26	Primi	30 + 2	118	-	✓	-	-	-	-	-	-
46	Vijaya	28	G_3 P_1 L_1 A_2	32 + 1	254	-	✓	-	-	-	-	-	-
47	Vedamani	30	G_5 P_2 L_2 A_2	35 + 2	284	✓	-	✓	-	-	-	-	Term
48	Muthumani	18	Primi	28 + 2	112	-	✓	-	-	-	-	-	-
49	Kowsalya	19	Primi	32 + 4	375	✓	-	-	✓	-	-	✓	Term

50	Amutha	21	Primi	31 + 5	210	✓	-	✓	-	-	-	-	-
51	Rajina Beevi	20	G_3 A_2	28 + 3	184	-	✓	-	-	-	-	-	-
52	Vigneshwari	21	Primi	29 + 1	115	-	✓	-	-	-	-	-	-
53	Soundarya	25	G_4 P_1 L_1 A_2	23 + 2	130	-	✓	-	-	-	-	-	-
54	Sabeena begam	26	G_3 P_1 L_1 A_4	31 + 3	284	✓	-	-	✓	-	-	-	Preterm
55	Pandiyammal	34	G_6 P_2 L_1 A_4	34 + 2	380	✓	-	-	-	✓	-	-	IUD
56	Kokila	18	Primi	31 + 2	118	-	✓	-	-	-	-	-	-
57	Kavitha	19	Primi	33 + 1	121	✓	-	✓	-	-	-	-	-
58	Rukmani	25	G_2 P_1 L_1	29 + 2	186	-	✓	-	-	-	-	-	-
59	Mala	26	G_3 P_1 L_1 A_1	35 + 5	218	✓	-	✓	-	-	-	-	-
60	Manibharathi	29	G_3 P_1 L_1 A_1	36 + 3	284	✓	-	-	-	-	-	-	-
61	Andal	18	Primi	28 + 4	382	✓	-	-	✓	-	✓	-	IUD
62	Chitra	20	Primi	31 + 3	184	-	✓	-	-	-	-	-	-
63	Pandimeena	20	Primi	22 + 3	282	-	✓	-	-	-	-	-	-
64	Vishwa	22	G_2 P_1 L_1	24 + 4	382	✓	-	-	✓	-	-	✓	Preterm
65	Ashwini	23	G_3 A_2	26 + 5	184	-	✓	-	-	-	-	-	-
66	Devika	34	G_6 P_1 L_1	31 + 2	218	-	✓	-	-	-	-	-	-

			A_5										
67	Eswari	31	G_2 P_1 L_1	34 + 3	320ng	✓	-	✓	-	-	-	-	-
68	Mariyammal	18	Primi	36 + 1	219ng	✓	-	✓	-	-	-	-	Term
69	Munieshwari	22	G_3 A_2	27 + 2	117ng	-	✓	-	-	-	-	-	-
70	Pandiyammal	25	Primi	32 + 3	240ng	✓	-	✓	-	-	-	-	-
71	Anitha	26	G_3 P_1 L_1 A_1	28 + 1	340ng	✓	-	-	✓	-	-	-	Preterm
72	Bhoomeshwari	27	G_5 P_1 L_1 A_3	30 + 2	280ng	✓	-	✓	-	-	-	-	Term
73	Vijaya	20	Primi	31 + 3	118ng	-	✓	-	-	-	-	-	Term
74	Lakshmi	22	Primi	35 + 2	381ng	✓	-	-	✓	-	-	✓	late Preterm
75	Lavanya	25	G_2 A_1	29 + 3	121ng	-	✓	-	-	-	-	-	-
76	Meenakshi	26	G_3 P_1 L_1 A_1	33 + 2	300ng	✓	-	✓	-	-	-	-	Term
77	Nirmala	28	G_2 P_1 L_1	31 + 2	180	-	✓	-	-	-	-	-	-
78	Kokila	29	G_4 P_3 L_3	32 + 3	284	-	✓	-	-	-	-	-	-
79	Gomathy	31	G_3 P_1 L_1 A_1	36 + 7	389	✓	-	✓	-	-	-	-	Term
80	Vasanthi	32	G_4 P_1 L_1 A_2	33 + 1	298	-	✓	-	-	-	-	-	-
81	Nandhini	30	Primi	22 + 3	390	✓	-	-	✓	-	-	✓	Preterm
82	Chandralekha	28	G_2 A_1	31 + 2	284	✓	-	✓	-	-	-	-	-

83	Malini	27	$G_3 P_1 L_1 A_1$	37 + 1	210	-	✓	-	-	-	-	-	-
84	Kavitha	26	Primi	30 + 3	184	✓	-	✓	-	-	-	-	Term
85	Banumathy	25	Primi	28 + 4	375	✓	-	-	✓	-	-	-	IUD
86	Sonia	22	$G_2 A_1$	21 + 3	220	-	✓	-	-	-	-	-	-
87	Sivapriya	23	Primi	24 + 2	182	-	✓	-	-	-	-	-	-
88	Indumathy	29	$G_2 P_1 L_1$	30 + 3	198	✓	-	✓	-	-	-	-	-
89	Indhra	32	Primi	31 + 4	272	✓	-	✓	-	-	-	-	-
90	Pandiyammal	31	$G_3 P_1 L_1 A_1$	34 + 3	118	-	✓	-	-	-	-	-	-
91	Saranya	28	$G_2 P_1 L_1$	27 + 3	184	-	✓	-	-	-	-	-	-
92	Rekha	26	Primi	26 + 4	210	✓	-	✓	-	-	-	-	-
93	Yamuna	25	$G_3 A_2$	21 + 5	300	✓	-	-	✓	-	-	✓	Preterm
94	Ambika	23	$G_2 A_4$	25 + 4	312	✓	-	-	✓	-	-	-	Preterm
95	Devika	24	$G_2 P_1 L_1$	31 + 2	292	✓	-	✓	-	-	-	-	-
96	Banumathy	18	Primi	22 + 2	340	✓	-	-	✓	-	-	-	IUD
97	Selvi	21	Primi	28 + 3	118	-	✓	-	-	-	-	-	-
98	Lakshmipriya	22	$G_2 A_1$	33 + 1	240	-	✓	-	-	-	-	-	-
99	Mahalakshmi	35	$G_6 P_2 L_1 A_3$	34 + 1	400	✓	-	-	✓	-	✓	✓	Preterm

100	Saranya	34	G_2 P_1 L_1	31 + 2	312	✓	-	✓	-	-	-	-	-
101	Devipriya	25	Primi	30 + 1	184	-	✓	-	-	-	-	-	-
102	Sridevi	26	G_2 A_1	21 + 5	215	✓	-	✓	-	-	-	-	-
103	Pandipriya	21	G_3 P_1 L_1 A_1	31 + 2	350	✓	-	-	✓	-	-	-	Preterm
104	Inbarathi	22	Primi	30 + 1	118	-	✓	-	-	-	-	-	-
105	Revathy	18	Primi	29 + 1	210	-	✓	-	-	-	-	-	-
106	Priyadharshini	19	Primi	32 + 1	300	✓	-	✓	-	-	-	-	Term
107	Ashwini	20	Primi	31 + 5	188	-	✓	-	-	-	-	-	-
108	Pandimurugeshwari	22	G_2 A_1	22 + 3	398	✓	-	-	✓	-	-	✓	IUD
109	Muthumeena	22	Primi	24 + 3	118	-	✓	-	-	-	-	-	-
110	Leelavathy	23	Primi	31 + 5	125	-	✓	-	-	-	-	-	-
111	Skathipriya	25	G_2 A_1	35 + 3	218	-	✓	-	-	-	-	-	-
112	Maheshwari	26	G_2 P_1 L_1	32 + 1	380	✓	-	✓	-	-	-	-	Term
113	Subha	27	G_2 P_1 L_1	33 + 2	382	✓	-	-	✓	-	-	-	Preterm
114	Sathya	28	G_3 P_1 L_1 A_1	35 + 3	270	✓	-	✓	-	-	-	-	-
115	Chinnapoonu	29	G_4 P_2 L_1 A_1	37 + 2	255	-	✓	-	-	-	-	-	-
116	Sundrammal	31	Primi	21 + 3	174	-	✓	-	-	-	-	-	-

117	Suganya	32	G_2 P_1 L_1	24 + 4	184	-	✓	-	-	-	-	-	-
118	Vijayapriya	28	G_2 P_1 L_1	27 + 3	115	-	✓	-	-	-	-	-	-
119	Komathy	25	Primi	31 + 4	180	-	✓	-	-	-	-	-	-
120	Nirmaladevi	18	Primi	32 + 5	172	-	✓	-	-	-	-	-	-
121	Marieshwari	31	G_3 P_2 L_2	36 + 1	374	✓	-	-	✓	-	-	-	Term
122	Elakiya	19	Primi	32 + 3	184	-	✓	-	-	-	-	-	-
123	Priya	23	Primi	33 + 4	187	-	✓	-	-	-	-	-	-
124	Sangeetha	24	Primi	26 + 1	167	-	✓	-	-	-	-	-	-
125	Nandhini	26	Primi	27 + 2	350	✓	-	-	✓	-	✓	-	Extreme Preterm
126	Fathima	27	G_2 A_1	31 + 3	415	✓	-	-	✓	-	-	✓	Preterm
127	Thangamani	19	Primi	34 + 1	128	-	✓	-	-	-	-	-	-
128	Kamatchi	20	Primi	35 + 2	134	-	✓	-	-	-	-	-	-
129	Komala	38	G_4 P_2 L_1 A_1	28 + 2	212	✓	-	✓	-	-	-	-	-
130	Alandhinipriya	19	Primi	30 + 2	118	-	✓	-	-	-	-	-	-
131	Punitha	18	Primi	32 + 3	151	-	✓	-	-	-	-	-	-
132	Radha	22	Primi	27 + 2	167	-	✓	-	-	-	-	-	-
133	Subathra	24	G_2 P_1 L_1	31 + 3	415	✓	-	-	✓	-	-	✓	Preterm

134	Hemalatha	24	Primi	28 + 2	188	-	✓	-	-	-	-	-	-
135	Yasmin	25	Primi	33 + 5	218	✓	-	✓	-	-	-	-	-
136	Aryamal	38	G_3 P_1 L_1 A_2	35 + 2	124	-	✓	-	-	-	-	-	-
137	Sudha	19	Primi	22 + 3	343	✓	-	-	✓	-	-	-	Preterm
138	Kannagi	18	G_2 A_1	24 + 6	210	-	✓	-	-	-	-	-	-
139	Seetha	20	G_2 A_1	31 + 4	118	-	✓	-	-	-	-	-	-
140	Dharani	21	Primi	32 + 4	175	-	✓	-	-	-	-	-	-
141	Rupa	22	Primi	33 + 2	184	-	✓	-	-	-	-	-	-
142	Vaishnavi	23	Primi	21 + 1	115	-	✓	-	-	-	-	-	-
143	Jayanthi	24	G_3 A_2	31 + 3	110	-	✓	-	-	-	-	-	-
144	Usha	24	G_2 P_1 L_1	34 + 2	117	-	✓	-	-	-	-	-	-
145	Ruthra	19	Primi	23 + 5	182	-	✓	-	-	-	-	-	-
146	Sharmila	18	Primi	24 + 2	190	-	✓	-	-	-	-	-	-
147	Alphone	26	G_3 P_1 L_1 A_1	28 + 1	342	✓	-	-	✓	-	-	-	Preterm
148	Geetha	27	G_2 P_1 L_1	30 + 2	184	-	✓	-	-	-	-	-	-
149	Karpagam	28	G_2 A_1	31 + 3	186	-	✓	-	-	-	-	-	-
150	Dhivya	30	G_2 A_1	35 + 2	147	-	✓	-	-	-	-	-	-

151	Alamelu	31	G_3 P_1 L_1 A_1	36 + 1	247	-	✓	-	-	-	-	-	-
152	Alayammal	32	G_2 P_1 L_1	32 + 1	284	-	✓	-	-	-	-	-	-
153	Janaki	28	G_2 P_1 L_1	31 + 5	380	✓	-	-	✓	-	-	-	Extreme Preterm
154	Pavithra	25	Primi	30	171	-	✓	-	-	-	-	-	-
155	Krishnaveni	26	Primi	31 + 1	180	✓	-	✓	-	-	-	-	-
156	Bhuvaneshwari	24	Primi	21 + 4	174	-	✓	-	-	-	-	-	-
157	Rajalakshmi	21	Primi	25 + 2	181	-	✓	-	-	-	-	-	-
158	Shanthi	24	G_2 P_1 L_1	27 + 8	134	-	✓	-	-	-	-	-	-
159	Mohana	22	Primi	31 + 1	212	-	✓	-	-	-	-	-	-
160	Saiyani	18	Primi	32 + 3	230	-	✓	-	-	-	-	-	-
161	Selvapriya	20	Primi	33 + 4	254	✓	-	✓	-	-	-	-	-
162	Aruna	18	Primi	21 + 3	184	-	✓	-	-	-	-	-	-
163	Preethi	24	Primi	31 + 1	418	✓	-	-	✓	✓	-	-	IUD
164	Kayalvizhi	26	G_2 A_1	32 + 3	220	-	✓	-	-	-	-	-	-
165	Jyothi	27	G_3 P_1 L_1 A_1	33 + 1	184	-	✓	-	-	-	-	-	-
166	Kanimozhi	30	G_5 P_2 L_1 A_2	34 + 5	380	✓	-	-	✓	-	-	-	Preterm
167	Narmadha	28	G_2 P_1 L_1	28 + 3	115	-	✓	-	-	-	-	-	-

168	Poogulai	27	Primi	22 + 4	125	-	✓	-	-	-	-	-	-
169	Vishnupriya	19	Primi	21 + 3	130	-	✓	-	-	-	-	-	-
170	Akila	20	Primi	31 + 1	140	-	✓	-	-	-	-	-	-
171	Radha	23	Primi	30 + 1	272	-	✓	-	-	-	-	-	-
172	Stella	20	Primi	26 + 2	350	✓	-	-	✓	-	-	-	Preterm
173	Chellammal	21	Primi	33 + 3	380	✓	-	✓	-	-	-	-	Term
174	Manimozhi	25	G_2 P_1 L_1	21 + 6	118	-	-	-	-	-	-	-	-
175	Karthikeyani	26	Primi	23 + 6	375	✓	-	-	✓	-	✓	✓	IUD
176	Haripriya	27	G_3 P_1 L_1 A_1	31 + 2	118	-	✓	-	-	-	-	-	-
177	Sindhu	28	G_4 P_1 L_1 A_2	32 + 1	131	-	✓	-	-	-	-	-	-
178	Swetha	30	G_3 P_1 L_1 A_1	33 + 1	141	-	✓	-	-	-	-	-	-
179	Vasumathi	32	G_2 P_1 L_1	28 + 2	181	-	✓	-	-	-	-	-	-
180	Gnanamathi	19	Primi	30 + 1	200	-	✓	-	-	-	-	-	-
181	Poornima	18	Primi	21 + 5	211	-	✓	-	-	-	-	-	-
182	Punithamani	22	Primi	22 + 8	118	-	✓	-	-	-	-	-	-
183	Jayalakshmi	23	Primi	24 + 5	361	✓	-	-	✓	✓	-	-	Spontaneous expulsion
184	Hema	25	Primi	26 + 1	390	✓	-	-	✓	-	✓ (PRES)	-	IUD

185	Mariya	26	Primi	28 + 3	115	-	✓	-	-	-	-	-	-
186	Kalpana	30	G_2 P_1 L_1	30 + 2	131	-	✓	-	-	-	-	-	-
187	Ruby	18	Primi	33 + 1	148	✓	-	✓	-	-	-	-	Term
188	Deepa	25	Primi	34 + 2	184	✓	-	✓	-	-	-	-	Term
189	Jennija	22	G_2 A_1	35 + 1	391	✓	-	✓	-	-	-	-	Term
190	Vinodhini	23	G_3 A_2	31 + 4	171	✓	-	✓	-	-	-	-	Term
191	Pushpa	24	G_2 P_1 L_1	37 + 1	118	-	✓	-	-	-	-	-	-
192	Saiyamitha	27	G_3 P_2 L_2	32 + 1	400	✓	-	-	✓	-	-	✓	Preterm
193	Shymala	28	Primi	33 + 1	380	✓	-	-	✓	-	-	-	Preterm
194	Manimozhi	29	G_2 A_1	25 + 6	340	✓	-	-	✓	-	-	✓	Preterm
195	Nabeesha	18	Primi	25 + 6	351	✓	-	-	✓	-	-	-	IUD
196	Gayathri devi	20	Primi	27 + 1	381	✓	-	-	✓	-	-	-	Preterm
197	Raka Sri	21	Primi	28 + 1	284	✓	-	✓	-	-	-	-	Term
198	Reena	22	G_2 A_1	30 + 1	380	✓	-	-	✓	-	-	-	Term
199	Kavitha	21	G_2 P_1 L_1	34 + 2	281	-	✓	-	-	-	-	-	-
200	Vanisri	22	G_3 A_1	31 + 3	390	✓	-	-	✓	-	-	✓	Preterm

URKUND

Urkund Analysis Result

Analysed Document:	ANITHA THESIS LP.docx (D42581972)
Submitted:	10/15/2018 5:54:00 PM
Submitted By:	priyaalakshmi49@gmail.com
Significance:	2 %

Sources included in the report:

A prospective study for the prediction of preeclampsia with serum prolactin level.docx (D27818210)

Instances where selected sources appear:

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