PREDICTION OF PREECLAMPSIA IN EARLY PREGNANCY BY SPOT URINE PROTEIN CREATININE RATIO – A PROSPECTIVE CROSS SECTIONAL STUDY CONDUCTED OVER A ELEVEN MONTHS PERIOD AT A TERTIARY CARE INSTITUTION

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BONAFIDE CERTIFICATE

This is to certify that the Dissertation entitled, "**PROSPECTIVE CROSS SECTIONAL STUDY ON PREDICTION OF PREECLAMPSIA IN EARLY PREGNANCY BY SPOT URINE PROTEIN CREATININE RATIO"**, is the Bonafide original work of **Dr.S.NITHIYA** under the guidance of **Prof.Dr.V.SUMATHI**, Department of Obstetrics and Gynecology, Kilpauk Medical College & Hospital, Chennai in partial fulfillment of the requirement for M.S (Obstetrics and Gynaecology), Branch – II, of the Tamil Nadu Dr.M.G.R. Medical University to be held in April 2014.The Period of Postgraduate Study and Training was from May 2012 to April 2014.

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DECLARATION

I **Dr.S.NITHIYA** solemnly declare that this Dissertation, "**PROSPECTIVE CROSS SECTIONAL STUDY ON PREDICTION OF PREECLAMPSIA IN EARLY PREGNANCY BY SPOT URINE PROTEIN CREATININE RATIO"** was prepared by me at Government Kilpauk Medical College and Hospital, Chennai, under the guidance and supervision of **Prof.Dr.V.SUMATHY M.D.,D.G.O.,** Professor, Department of Obstetrics and Gynaecology, Government Kilpauk Medical College, Chennai.

This Dissertation is submitted to the Tamilnadu Dr.M.G.R.Medical University, Chennai, in partial fulfillment of the University regularities for the award to the degree of M.S.OBSTETRICS and GYNAECOLOGY, Branch - II.

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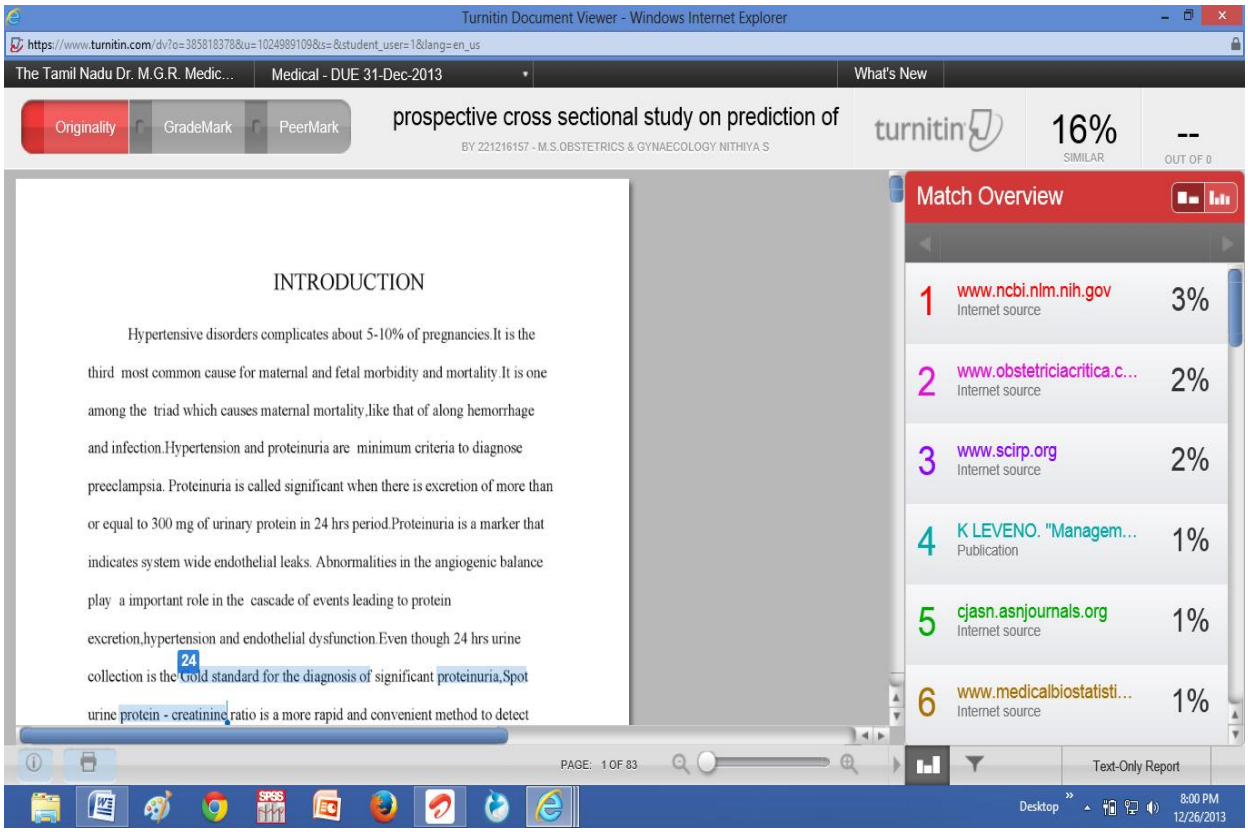

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LIST OF ABBREVIATIONS

BMI	-	Body mass index
CSE	-	Combined spinal and Epidural
MgSO4	-	Magnesium sulphate
PCR	-	Protein creatinine ratio
SE Class	-	Socioeconomic Class

INTRODUCTION

Hypertensive disorders complicates about 5-10% of pregnancies. It is the third most common cause for maternal and fetal morbidity and mortality. It is one among the triad which causes maternal mortality, like that of along hemorrhage and infection. Hypertension and proteinuria are minimum criteria to diagnose preeclampsia. Proteinuria is called significant when there is excretion of more than or equal to 300 mg of urinary protein in 24 hrs period.

Proteinuria is a marker that indicates system wide endothelial leaks. Abnormalities in the angiogenic balance play a important role in the cascade of events leading to protein excretion, hypertension and endothelial dysfunction.

Even though 24 hrs urine collection is the Gold standard for the diagnosis of significant proteinuria, Spot urine protein - creatinine ratio is a more rapid and convenient method to detect protein excretion. It avoids the influence of variations in urinary solute concentration. Therefore it is an accurate test and provides efficient in-patient and out-patient monitoring.

Berg and Colleagues (2003) reported that about16% of maternal deaths are due to complications related to preeclampsia and more than half of it are preventable.

Therefore prediction of preeclampsia in early gestation is of utmost importance to detect and to intervene in the management of high risk pregnancies much earlier to reduce the maternal death and fetal mortality and neonatal morbidity.

REVIEW OF LITERATURE

Hypertension is one of the most common medical disorders complicating pregnancy. In India it is the second most common condition that complicates pregnancy, next to anemia. Preeclampsia is a multisystem disorder which occurs after 20 weeks' of gestation that results in widespread vascular endothelial malfunction and vasospasm. The normal physiological changes in pregnancy causes reduced vascular tone and low periperal vascular resistance which reduces the maternal blood pressure as early as 7 wks of gestation .It reaches a nadir at 16 to 20 wks of gestation, and increases after 28 wks to reach the pre-pregnancy level before term.

Hypertension is defined by the International Society for the study of Hypertension in pregnancy (ISSHP) as, a blood pressure more than or equal to 140/90 mm Hg, recorded 4-6 hrs apart.

Classification:

The Working group classification of Hypertensive disorders, classifies hypertensive disease as,

a) Gestational hypertension

b) Preeclampsia and Eclampsia syndromes

c) Preeclampsia superimposed on chronic hyprtension

d) Chronic hyprtension

- Gestational hypertension is defined as blood pressure 140/90mm Hg and above, diagnosed for the first time after 20 wks of gestation, without proteinuria and the blood pressure recording comes to normal within 12 weeks duration of postpartum period . It is a diagnosis of exclusion. About half of these patients develop preeclampsia syndrome later.
- Preeclampsia syndrome is specific to pregnancy that affects almost every organs. Its adverse outcome is reflected by the severity of the hypertension and proteinuria.
- Eclampsia is onset of seizures that occur in a case of preeclampsia that cannot be attributed to any other cause.
- Preeclampsia superimposed on chronic hyprtension:
- This term is defined as new onset proteinuria or when the blood pressure suddenly increases or poteinuria occurs in chronic hypertensive women.

❖ **Chronic hypertension:**

Chronic hypertension can be defined as presence of hypertension prior to pregnancy or hypertension which was diagnosed prior 20 weeks of pregnancy, but not due to gestational trophoblastic disease. Hypertension which was first detected after 20 weeks & persisting even after 12 weeks postpartum is also considered as chronic Hypertension.

* **Epidemiology**

Pre-eclampsia which is a multisystem disorder complicates about 3%–8% of pregnancies in Western countries. About 10%–15% of maternal mortality are directly related with pre-eclampsia syndrome and eclampsia. There is 2-fold to 5-fold risk of pre-eclampsia in pregnant women with a maternal history. The incidence of pre-eclampsia occirs in about 3% to 7% of nulliparas women and 1% to 3% of multiparas women. Nulliparity and exposure to a new partner are the important risk factors.

- The risk factors of Preeclampsia includes
  - African American ethnicity
  - Nulliparity
  - Extremes of age with more risk in teenege pregnancy
  - With history of preeclampsia in previous pregnancy
  - Family history suggestive of preeclampsia

- Obesity
- mutiple pregnancy,hydrops fetalis,hydatiform mole
- Preexisting medical disorders like diabetes, kidney disease, lupus, or rheumatoid arthritis,thrombophilias
- Environmental factors

- **Etio Pathogenesis**

* Preeclampsia occurs due to culmination of maternal, placental and fetal factors which includes,

* Incomplete invasion of the uterine vessels by the trophoblastic cells.

* Maladaptive immunological tolerance appearing between maternal, placental and fetal component.

* Maladaptation to normal physiological changes in the cardiovascular system and inflammatory changes that occurs in pregnancy.

* Genetic predisposition

* The exact etiology is not known.There are various theories proposed but the two major ones are:

a) Abnormal trophoblastic invasion

b) Endothelial cell dysfunction

a) Abnormal Trophoblastic Invasion:

Placenta is the inciting factor responsible for preeclampsia-eclampsia syndrome. In normal pregnancy, the villous cytotrophoblastic cells invades upto the inner third portion of the myometrium, and in the spiral arteries, there is loss of endothelial layer and their muscle fibers are replaced by cytotrophoblast. These modifications makes the spiral arteries as low-resistance vessels, and thus render them less sensitive, or even insensitive, to vasoconstrictive substances.

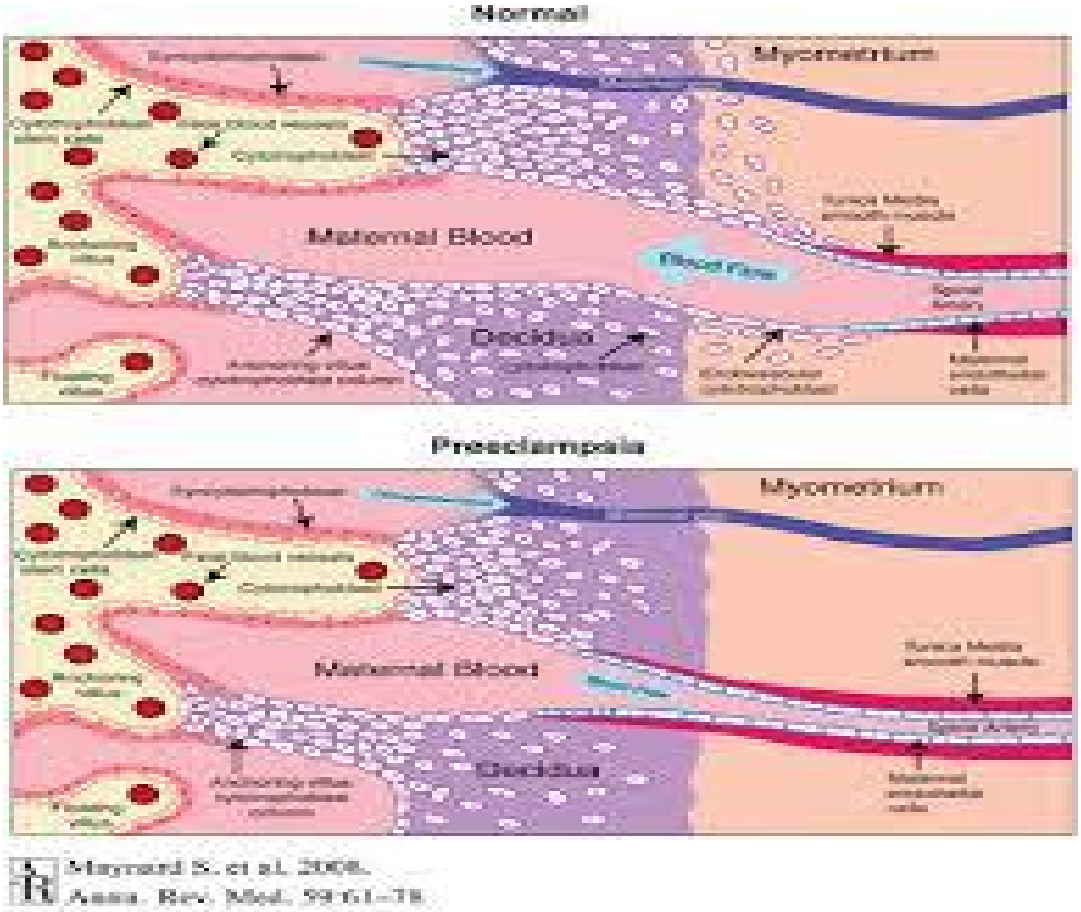
This process begins around 10-12 wks of gestation and completed by 18 -20 wks of gestation.

In preeclampsia, due to incomplete trophoblastic invasion, the deeper myometrial arterioles does not lose their musculoelastic tissue and endothelial lining. Therefore the external diameter of the vessels is only half that of vessels when compared to the vessels in normalplacenta.

FIGURE - 1

TROPHOBLASTIC INVASION OF IN NORMAL PLACENTA

AND IN PREECLAMPSIA

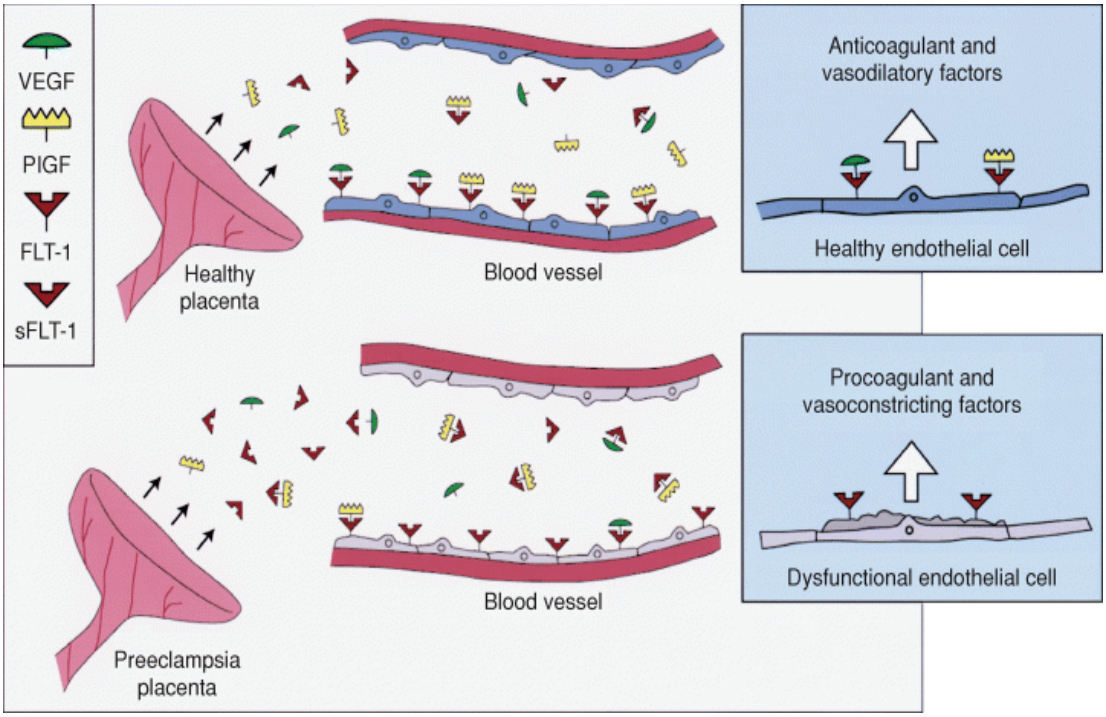


Maynard S. et al. 2008.
Annu. Rev. Med. 59:61–78

The impaired placental blood flow through the narrow spiral arterioles leads to diminished perfusion and hypoxic environment which in turn releases cytokines and vasoactive substances leading to systemic inflammatory response that leads to cascade of events to provoke endothelial cell injury.

FIGURE - 2

EFFECT OF VASOACTIVE SUBSTANCES IN PREECLAMPSIA



- **Endothelial cell activation**

* Defective placentation causes release of cytokines such as tumour necrosis factor (TNF-alpha), and interleukins (IL) leads to the formation of reactive oxygen species and free radicals which injures the endothelial cells and modifies its nitric oxide production and prostsglandin balance. It also leads to the production of lipid laden macrophages and formation of atherosis and initiates microvascular coagulation cascade and it is manifested as thrombocytopenia. Increased capillary permeability resuts in edema and proteinuria.

* Pre-eclampsia may results in impairment of the immune system of the mother which prevents it to recognise the fetoplacental unit, high production of immune mediated cells causes the production of tumor necrosis factor alpha, which may induce apoptotic death of the extravillous cytotrophoblast.

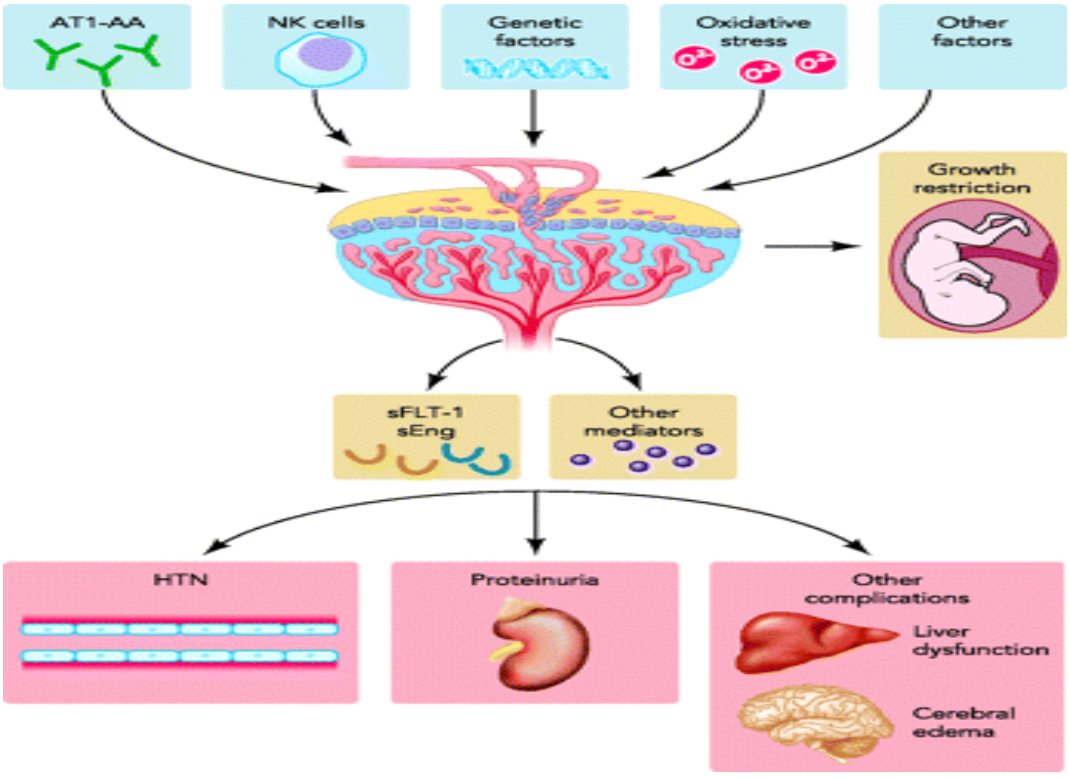
* The human leukocyte antigen (HLA) system also plays an important a role in the incomplete invasion of spiral arteries, in the women affected by pre-eclampsia, and they show decreased levels of HLA-E and HLA-G.

* In normal pregnancies, the interaction between these cells and the trophoblast is due to secretion of vascular endothelial growth factor and the placental growth factor, by natural killer cells.

* Increased secretion of soluble fms-like tyrosine kinase 1 (sFlt-1) an antagonist of vascular endothelial growth factor and placental growth factor, have been found in women with pre-eclampsia. Assays of sFlt-1, placental growth factor, endoglin, and vascular endothelial growth factors increases about 4–8 weeks before the onset of the disease. These factors may be used as predictors of pre-eclampsia.

FIGURE - 3

PATHOGENESIS OF PREECLAMPSIA



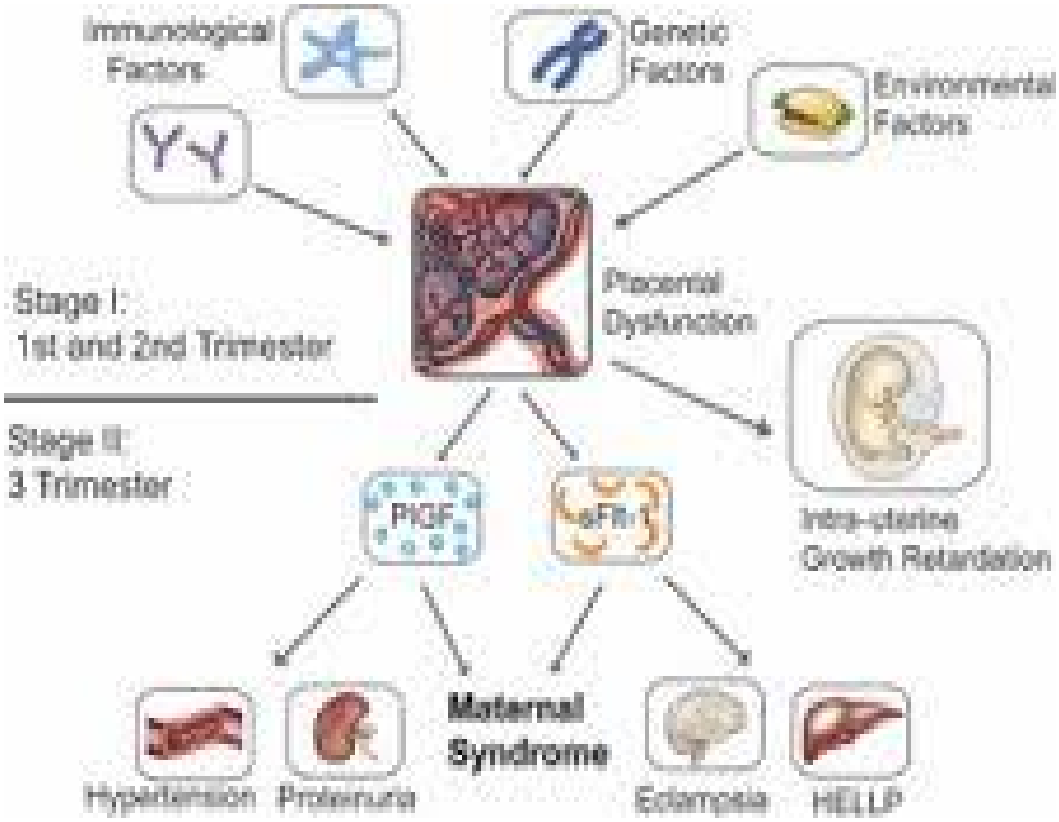
* Latest data show the protective effect of heme oxygenase 1 and its byproduct the carbon monoxide, and its positive effect in pregnancy, and identified these products as a potential target in the treatment of patients with pre-eclampsia.

* **Pathophysiology**

* As a consequence of vasospasm, endothelial dysfunction and ischemia, preeclampsia affects multiorgan systems.

FIGURE – 4

ETIOLOGY AND EFFECTS OF PREECLAMPSIA



▪ **Cardiovascular system:**

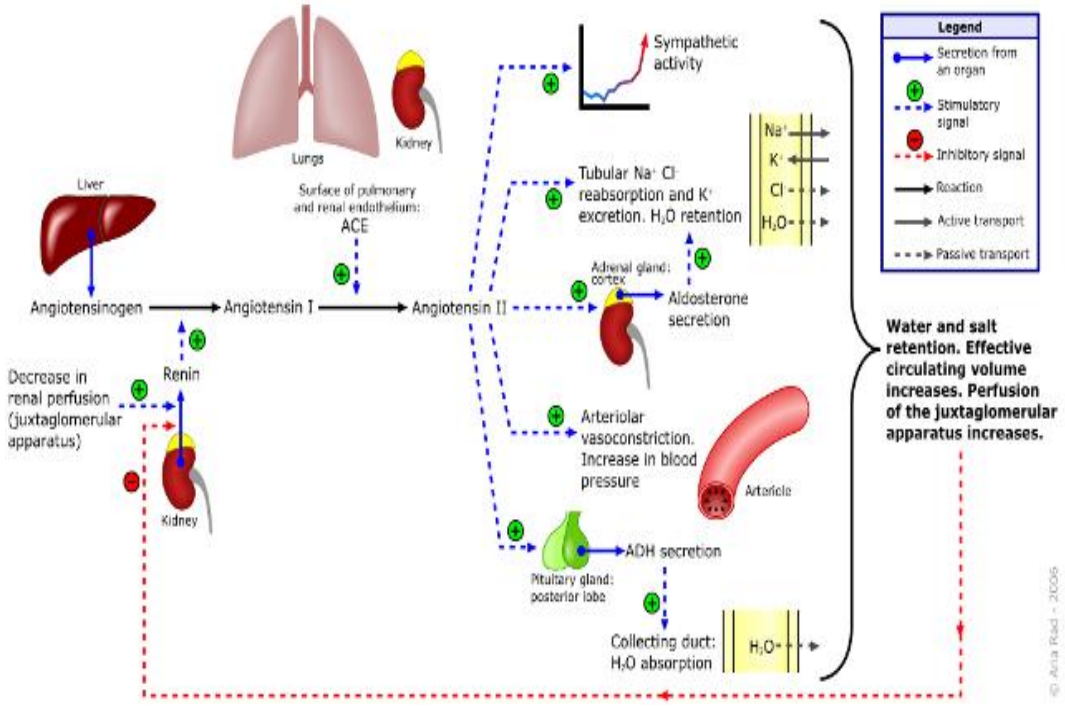
✓ Hypertension increases preload and afterload. Endothelial activation leads to extravasation of intravascular fluid to extracellular space.

- **Endocrine System:**

✓ Elevated blood pressure and increase in vascular resistance seen in preeclampsia is due to interference in the sensitivity of the vessels to endogenous hormones like angiotensin II, vasopressin and catecholamines. There is refractoriness to the pressor effect of angiotensin II in normal pregnancy.

FIGURE – 5

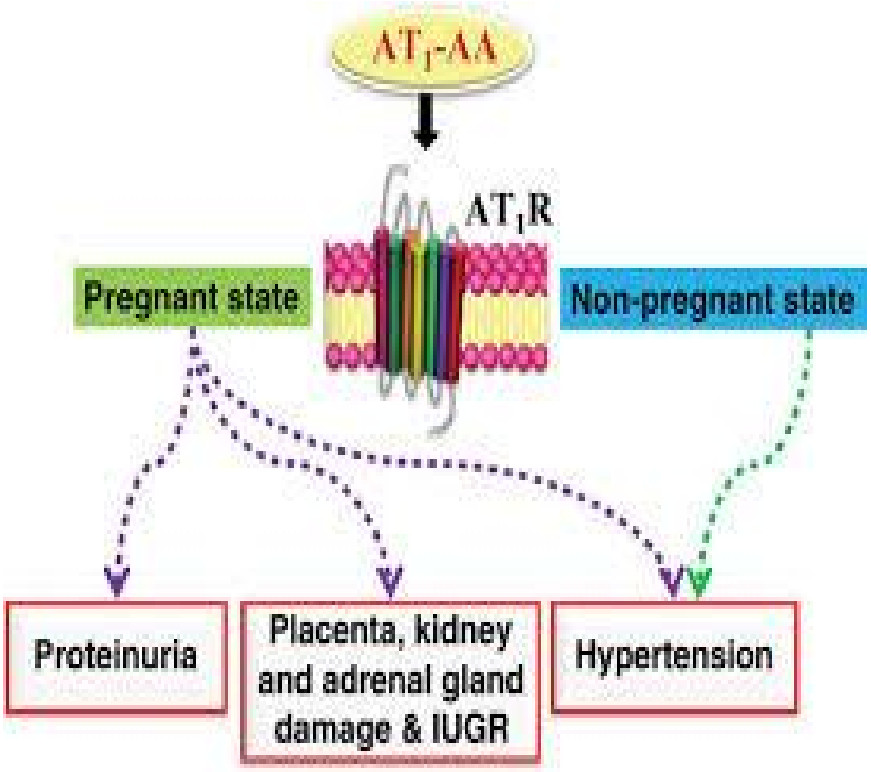
RENIN – ANGIOTENSIN – ALDOSTERONE SYSTEM



In preeclampsia there is increased vascular reactivity to these pressor hormones.

FIGURE – 6

EFFECT OF GENETIC FACTORS ON PREGNANCY



- The abnormal sensitivity occurs between 17 weeks and the clinical onset of gestational hypertension.

- Gant and colleagues reported that loss of refractoriness to angiotensin II occurs 8 to 12 weeks before the onset of the clinical manifestations of gestational hypertension.

- ✓ Platelets and trophoblasts produces Thromboxane A2, which is a potent vasoconstrictor and platelet aggregator.

- ✓ In preeclampsia, the ratio between thromboxane A2 and prostacyclin increases thus decreaseing placental production of prostacycline.

- ✓ In gestational hypertension, the prostacyclin metabolite, 6-keto-prostaglandin F1α decreases in maternal, placental, and umbilical vessels.

- **Hematological System:**

- ✓ The hemoconcentration seen in gestational hypertension leads to decreased regional perfusion.

- ✓ Due to increase in the vascular tone and vasospasm in preeclampsia, in the absence of hemorrhage, the intravascular compartment is not underfilled.

- ✓ Hematocrit increases with increased severity of gestational hypertension.

- ✓ Vascular spasm and hemoconcentration results in the reduction in the intravascular space in patients with preeclampsia.

- ✓ The vasospasm, result in endothelial injury. Dadak and associates detected marked damage to the endothelium of the umbilical

arteries of mothers with gestational hypertension which could be the cause of the microangiopathic hemolysis.

✓ Gestational hypertension is found to be associated with high levels of fibronectin, low levels of antithrombin III and α2-antiplasmin.

✓ Changes in the levels of these factors helps to diagnose preeclampsia and to differentiate it from chronic hypertension.

- **Placenta**

o Placenta shows features of infarcts, hematomas, proliferative endarteritis and degeneration.

o Preeclampsia causes atherosis, fibrinoid necrosis, mononuclear and macrophage cell infiltration.

- **Kidney**

Glomerular capillary endotheliosis, is the characteristic renal lesion seen in preeclampsia.

- Light microscopy Examination of the preeclamptic kidney shows prominence of endocapillary (mesangial and endothelial) cells.
- There was also infiltration of macrophages, lymphocytes and polymorphonuclear leukocytes within capillary lumens. The hypertrophy of endothelial cells, results in loss of capillary patency.

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- There was variable thickening of glomerular capillary walls, related to mesangial interposition, and prominent subendothelial hyaline deposits.
- Transmission electron microscopy showed features of endothelial cell hyperplasia, and exudation of foamy macrophages, lymphocytes, and polymorphonuclear leukocytes within the capillary lumina and mesangium.
- The lesions resolves completely after delivery.

- **Liver**

o The changes that occurs in preeclampsia are periportal haemorrhages, fibrin deposition and ischemic lesion.

o Liver damage ranges from mild hepatocellular necrosis to very severe liver injury which increases liver enzymes.

o It also causes subcapsular rupture.

Brain –Cerebral blood flow and oxygen metabolism in brain are usually unaltered. There is an increase in the cerebrovascular accidents in preeclampsia when compared with normal pregnancy. CT Brainshows multiple petichial haemorrhages, in the cortex, pons and midbrain. Eventhough 60 % of women developing eclampsia,is complicated with intracerebral bleeding, it causes only 50% of maternal mortality.

❖ **Clinical presentation:**

Preeclampsia syndrome shows severe neurological manifestations every complication needs immediate attension.

1. *Headache / scotomata* : occurs due to hyperperfusion of the cerebral vessels, more commonly involving the occipital lobes. Headaches is seen in 50 % to 75% of women with preeclampsia and 20 to 30 percent have changes in the vision eclamptic seizures occurs. The headaches present as mild to severe. The headache may be intermittent, or present constantly. magnesium sulfate. administration usually reduces headache and visual disturbances.

2. Convulsions which is the diagnostic feature of eclampsia.

3. *Blindness* is present in about 15 percent of women with eclampsia and is rarely present in preeclampsia. Blindnesscan occur even one week after delivery.

4. *Generalized cerebral edema* –present as changes in the mental status. Clinically it presents as confusion to the stage of coma. This is dangerous, because it may lead to supratentorial herniation and death.

- **Eyes**

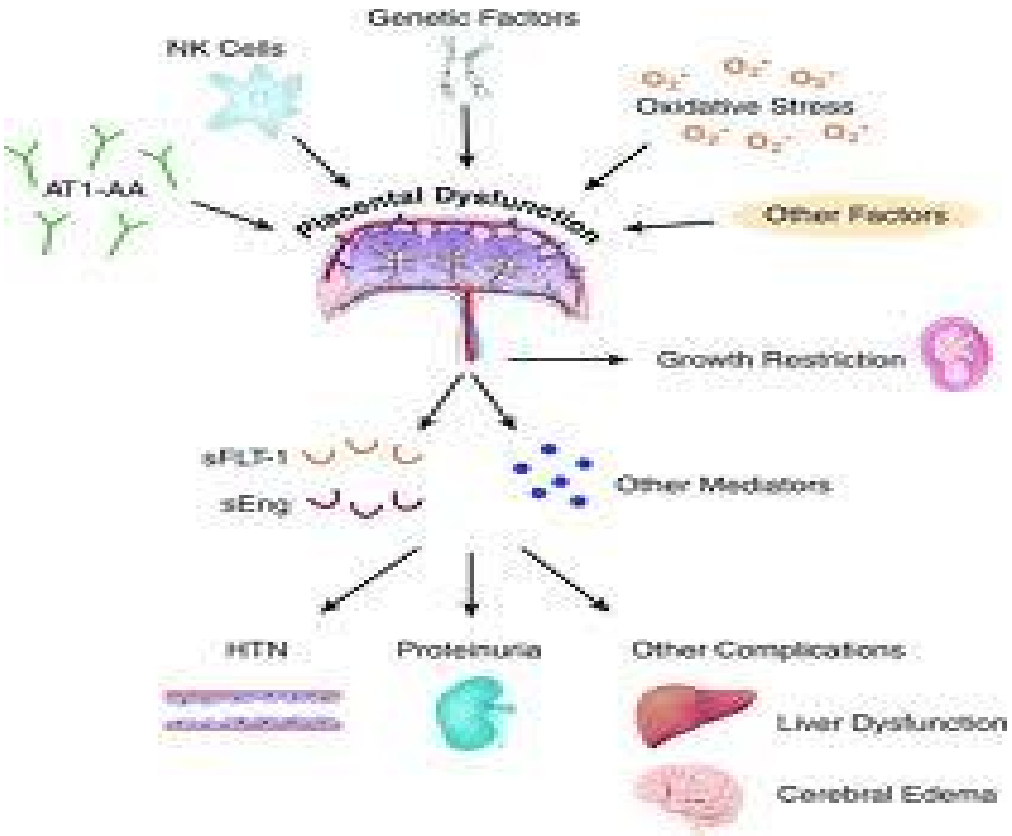
  The commonest finding is localised retinal vasospasm. Retinal Haemorrhages and papilloedema may be seen in severe cases. Retinal artery ischemia or infarction, are the causes of blindness in preeclampsia.

- **Heart**

  Subendocardial petichial haemorrhages and acute left ventricular failure due to left ventricular dilatation.

FIGURE – 7

PATHOPHYSIOLOGY OF PREECLAMPSIA



- **Criteria to Diagnose Severe Preeclampsia:**

- Systolic blood pressure more than or equal to 160 mmHg or more than or equal to 110 mm Hg of diastolic pressure.

- Protein excretion > 5 g in 24 hours or ≥2+ dipstick

- Severe, Persistent cerebral or visual disturbances (headache, scotoma, blurred vision)

- Persistent and severe right upper quadrant pain or epigastric pain

- Increased LDH-due to microangiopathic hemolysis

- Platelet count <1,00,000 lakh/ml

- Elevated serum AST, ALT levels.

- **Complications:**

- Severe maternal complications that occurs in preeclampsia includes.
- Eclampsia – the seizures that occurs due to increased intracranial blood pressure resulting in cerebral hemorrhage as a consequence of rupture of cerebral blood vessels which is the major cause of maternal death.

- Blindness due to retinal detachment

- Abruptio placentae -. The bleeding may endanger the life of both the mother and the fetus. Abruptio placentae may result in renal failure.

- HELLP syndrome : HELLP Syndrome: _indicates **H**emolysis, **E**levated **L**iver Enzymes, **L**ow **P**latelets. *Hemolysis* due to destruction of red blood cells. Elevated liver enzymes indicates inflamed or overactive liver. Low Platelets causes hemorrhage, especially in the brain.

Differential Diagnosis are.

- Hepatitis, cholecystitis, acute fatty liver of pregnancy, thrombocytopenic purpura (TTP)
- 20% of HELLP syndrome occurs in the postpartum period
- Peak time of occurence is 24-48 hrs after delivery.
- 50% of the affected women have nausea and vomiting.
- When it occurs in the postpartum period, HELLP syndrome is more fatal and leads to pulmonary edema and renal failure.

- Left ventricular failure.
- Disseminated intravascular coagulation
- Acute pulmonary edema

- Fetal complications:
  - Intrauterine fetal growth restrictions
  - Intrauterine asphyxia
  - Premature delivery
  - Intrauterine fetal death
  - Neonatal asphyxia
  - Mental retardation

- **Predictors of Preeclampsia:**

There are various clinical, biophysical and biochemical markers for prediction and early detection of preeclampsia.

- **Isometric exercises:**

During the handgrip test, increase in systolic pressure by 15 mm Hg predicts development of gestational hypertension with sensitivity of 81.8% and specificity of 68.4%

- **Roll over test:**

Gant et al reported that, at 18-22 wks of gestation, when the diastolic blood pressure rises by 20 mm Hg or more within 5 minutes after changing to supine position from left lateral position.

- **Uterine artery Doppler study:**

Persistence of diastolic notching after 24 wks of gestation predicts development of preeclampsia.

- **Angiotensin Sensitivity test**

- It is based on the theory that loss of refractoriness to angiotensin II, between 28-32 weeks of gestation, develop pre-eclampsia later.

- In normal pregnancy, the patient requires mean angiotensin II doses of 13.5 to 14.9 ng/kg/minute to raise the diastolic pressure by 20 mm Hg.

- About Ninety-one percent of women remained normotensive throughout pregnancy and they required more than 8 ng/kg/minute to achieve this blood pressure elevation.

- **Serum Uric Acid estimation:**

- Increased serum uric acid level is one of the earliest laboratory manifestations of preeclampsia (Powers and associates, 2006).

- Due to reduced glomerular filtration, increased tubular reabsorption, and decreased secretion uric acid clearance reduces (Lindheimer and colleagues, 2008a).

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- Cnossen and associates (2006) reported its sensitivity of about 0 to 55 percent and specificity of about 77 to 95 percent.

- **Microalbuminuria**

Conde-Agudelo and associates (2009), reported sensitivity of about 7 to 90 percent and specificity of about 29% and 97 % and it indicated a poor clinical predictive value.

- **Free Fetal DNA:**

- Free fetal DNA in maternal plasma was detected by polymerase chain reaction. It was reported by, Lo and colleagues in 1997and Holzgreve and associates in 1998, that fetal-maternal cell trafficking is increased in preeclampsia.

- It is reported that free DNA is released by accelerated apoptosis of cytotrophoblasts.

- Conde-Agudelo and associates (2009) reported that free fetal DNA quantification is not useful to predict preeclampsia.

- **Other biophysical and biochemical markers are,**

✓ Elevated levels of inhibin A, activin A, serum alpha-fetoprotein, humanchorionic gonadotropin.

✓ Decreased level of placental growth factor in the second trimester.

- ✓ Increased solublefms-like tyrosine kinase-1insecondtrimester.
- ✓ Elevated levels of soluble endoglin in second trimester.
- ✓ Rise in asymmetric dimethyl arginine in second trimester.
- ✓ Decreased serum placentalprotein-13 in the first trimester.
- ✓ Reduced pregnancy associated plasma protein A in first trimester.

❖ **Normal Renal Adaptation in Pregnancy**

- o In order to accommodate the demands of the fetoplacental unit, normal pregnancy is characterized by changes in almost every organs.
- o Pregnancy affects both the kidney and the urinary tract.
- o There is increase in size of both the kidneys by about 1 to 1.5 cm length during pregnancy. The volume of the kidney increases by about 30 %, as a result of increase in vascular and interstitial cell volume of the kidney.
- o The glomerular filtration rate is also increased by 40%-60%, leading to increase in creatinine clearance to about 150 to 200 mg / min, which decreases creatinine level in serum from 0.8 mg/dl to 0.5 mg to 0.6 mg/dl. Therefore non pregnant level of 1.0 mg/dl, reflects renal impairment in pregnancy.
- o Hyperfiltration results primarily from decreased plasma hydrostatic pressure in the capillaries of the glomerulus.

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- The reduction in oncotic pressure is due to two mechanism in pregnancy.
- The first is due to hemodilution, which is due to hypervolemia, that lowers the concentration of the protein in the plasma that flows through the glomerular microcirculation.
- The second one, due to raise in Renal plasma flow. Hyperperfusion of the glomerular capillaries reduces the extent to which the hydrostatic pressure can increase along the glomerulus in the process of filtrate formation.
- The renal pelvises and calyces are dilated due to the effect of progesterone and compression of the ureters in the region of pelvic brim.
- **Ureters** — on the right side, Hydroureter and hydronephrosis is more prominent than the left and is present in about 80 percent of pregnant women. These changes are visualized on ultrasound examination from the second trimester, and does not reverse to normal until after 6 to 12 weeks postpartum.
- There are no changes in number of nephrons or histological changes do not occur.

- In preeclampsia, there are variable degrees of insufficiency of the renal system associated with “glomerular endotheliosis”, characteristic lesion of the glomerulus, in preeclampsia

- In patients with preeclampsia, decrease in the density and the size of the endothelial fenestrae and there is subendothelial deposition of fibrinoid material decreases glomerular hydraulic permeability. Mesangial cell interposition also reduces the available surface area for filtration, leading to reduction in GFR.

- The basis for the hypofiltration in patients with preeclampsia is due to structural changes in the glomerulus as opposed to vasoconstriction of the renal vessels and a redution in renal plasma flow.

- **Proteinuria:**

- In 1843, it was, John Lever of Guy's Hospital from London, first discovered the presence of albumin in the urine of the pregnant women with puerperal convulsions.

- Proteinuria differentiates preeclampsia from gestational hypertension.

- The amount of protein excretion in the urine varies widely. Significant proteinuria is defined as ≥300 mg in a 24-h urine

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collection or 1+ or more on testing the two random urine samples by dipstick method. Two samples should be collected at least 4 hrs apart but not more than 7 days.

- According to ACOG Guidelines, the diagnosis of Preeclampsia is excretion of >300 mg protein in 24 hrs urine collection.

- Excretion of intermediate size Glomerular proteins, like that of albumin, either identified alone or in combination with tubular proteins, like B_2-microglobulin, reflects the tubular destruction that can occur in severe preeclampsia.

- Protein excretion in preeclampsia range from minimum to nephrotic range.

- Eventhough 24 hrs urine protein is the gold standard method, the urine protein to creatinine ratio is considered as preferred method for quantification of proteinuria, due to inconvenience to the patient to collect 24 hrs urine collection, and due to under collection and delayed result.

- When the GFR is stable, the excretion of protein and creatinine is almost constant throughout the day.

- Variation in the protein and albumin excretion in urine samples collected throughout the day are lesser when their concentrations are expressed as a ratio to creatinine or specific gravity.

- The primary cause of defect in the glomerular filtration barrier in patients with preeclampsia, is loss of charge selectivity.

- Borderline proteinuria (250 to 400mg / day) leads to misclassification. Therefore it is advisable to use the P/C RATIO to predict the occurrence of preeclampsia.

- A Study conducted in 2008 found that sensitivity of P/C Ratio is 66% when compared to Dipstick method which is 41%.

- P/C Ratio also predicted presence or absence of proteinuria which is 64% when compared to Dipstick method which predicted only 19%.

- Therefore P/C Ratio is a better screening tool as well as excellent alternative to cumbersome 24 hour urine collection.

❖ **Management:**

The main goals of treatment are:

- To prevent convulsions
- To protect the patients from complications, such as cerebrovascular hemorrhage, pulmonary edema, renal failure, abruptio placentae, and fetal death,
- To deliver a healthy baby with minimal trauma to the mother.

❖ **Mild preeclampsia :**

- Hospitalization is usually advisable for patients with preeclampsia who are diagnosed for the first time.
- Monitoring of maternal condition and fetal condition is essential, even in patients with mild preeclampsia, who can be treated on an outpatient basis .
- When the patient is compliant, and with immature fetus, she can be treated as out patient with careful maternal and fetal monitoring.
- She should be adviced to visit every fortnightly. She should be explained about the severity of preeclampsia and about the imminent symptoms.
- At each visit, her blood pressure, urine for protein and fetal wellbeing should be monitored.
- When the patient is non-complaint, she should be hospitalized.

➢ **Maternal monitoring:**

- Regular diet without salt restriction
- Blood pressure monitoring-4 times daily
- Urine protein daily
- Daily monitoring of weight
- Watch for imminent symptoms
- Check twice weekly- peripheral smear, platelet count, renal and liver function tests, uric acid, coagulation profile.

➢ **Fetal surveillance:**

- The frequency of monitoring depends upon the severity of the disease and presence of IUGR
- Daily fetal kick count monitoring
- NST and amniotic fluid volume assessment
- Ultrasound assessment of fetal growth and well being
- Doppler velocimetry in IUGR

❖ **Antihypertensives:**

- Careful monitoring and control of hypertension is necessary, to protect the patients from complications, such as maternal cerebrovascular accidents and abruption placenta.

- Antihypertensive treatment is usually started when systolic blood pressure exceeds 160 mm Hg or diastolic blood pressure is equal to or more than 110 mm Hg.

- The commonly used antihypertensives are alpha methyl dopa, nifedipine and labetolol.

- Labetalol, which is a combined α- and β-adrenoreceptor antagonist, is used to induce a controlled and rapid decrease in blood pressure by reducing systemic vascular resistance in patients with severe hypertension.

- There are favorable studies, on the efficacy and safety of labetalol to treat hypertension complicating pregnancy.

- Mabie and colleagues, studied comparison between bolus dose of intravenous administration of labetalol with intravenous hydralazine, in the emergency management of severe hypertension.

- The results of the study showed that the drug labetalol had a more rapid onset of action and there was no reflex tachycardia.

- Other effects of Labetalol are ,it has a positive effect on early fetal lung maturation.

- Lunell and associate reported increased uteroplacental perfusion and decreased uterine vascular resistance after the use of labetalol.

- Labetalol is administered parenterally as intravenous injection or slow continuous infusion.

- In intravenous injection, an initial dose of 20 mg is administered and additional doses of 40 to 80 mg at intervals of 10-minutes, until the desired effect is achieved can be given if required. A total of 220 mg can be administered.

- If continuous infusion is used, labetalol is started at a dose of 2 mg/minute. Maximum effect is achieved about 5 minutes after intravenous administration.

- Oral dosage of labetalol can be given as 100 mg twice daily. Maximum dose of 2400 mg/day can be given.

o Nifedipine is started as a oral dose of 10 mg. It can be given orally again after 30 minutes, for the acute emergency management of severe hypertension; after that 10 to 20 mg may be administered orally every 6 to 8 hours, if needed.

* **Role of MGSO4:**

* Magnesium Sulfate is the dug of choice to Control Convulsions.

* It Acts as a vasodilator in cerebral vessels and menbrane stabilizer

* Loading dose of 4 grams diluted in 12 ml distilled water or with normal saline is given slow iv over 20 min and maintenance dose is continued every 4 hrs, till 24 hrs postpartum or from last fit whichever is later.

* Over dose of MgSO4 lead to depression of respiratory system and cardiac arrest.

* Deep tendon reflexes, respiratory rate and urine output should be monitored to continue the next dose.

* Antidote-10 ml of 10% solution of calcium. Gluconate should be given in over dosage. Therapeutic dose should be maintained between 4-7 mq/l.

❖ **Mode of delivery:**

- The only cure for patients with preeclampsia is termination of pregnancy.

- When the fetus is immature, well-being of the fetus and placental function should be assessed, to prolong the pregnancy for a few

weeks more in utero which reduces the risk of morbidity and mortality of the premature neonates.

- In case of severe preeclampsia without control of blood pressure after admission, termination of pregnancy is advisable for the sake of both mother and baby. Labor induced with preinduction cervical ripening with a prostaglandin or osmotic dilator. In case of failed induction, cesarean delivery is indicated.

- In patients with preeclampsia in term gestation, with controlled blood pressure, should have a trial of vaginal delivery.

- For the patient near term with soft, partially effaced cervix, even in milder degrees of preeclampsia the risk to the mother and her fetus is high.

- Barton and colleagues (2009) reported that there is excessive neonatal morbidity in women delivered before 38 weeks of gestation even when the patient is with mild nonproteinuric gestational hypertension.

❖ **Expectant management:**

- In severe preeclampsia remote from term, "conservative" or "expectant" management is adviced to improve neonatal outcome without compromising maternal safety.

- Expectant management includes, careful daily monitoring of the woman and fetus, with or without antihypertensive drugs.

- Expectant management is not followed in women with HELLP syndrome or fetus with growth restriction.

❖ **Expectant Management of Severe Preeclampsia in Midtrimester:**

- There are various studies about expectant management of patients with severe preeclampsia syndrome before 28 weeks.

- There were no live infants delivered before 23 weeks.

- Neonates delivered at 23 weeks, the perinatal survival rate was 18 percent, but long-term perinatal morbidity is not yet known.

- When terminated at 24 to 26 weeks, perinatal survival rate was 60 percent, and the survival rate for women delivered at26 weeks is almost 90 percent.

❖ **Glucocorticoids for Lung Maturation:**

- Glucocorticoids are given to women with severe hypertension who are remote from term to enhance fetal lung maturation.

- It also reduces the incidence of respiratory distress, intraventricular hemorrhage, and death. (Bloom and Leveno, 2003; Leveno and Cunningham, 2009).

o **Indications for immediate termination of pregnancy:**

o **Maternal indications**

✓ imminent symptoms, such as severe headache or blindness

✓ Patients with Shortness of breath, pulmonary edema

✓ Uncontrollable severe hypertension inspite of management with antihypertensives

✓ Serum creatinine level $\geq$ 1.5 mg/dL

✓ Decreased urine output < 500 mL/24 hr

✓ Persistent thrombocytopenia < 100,000/l

✓ Suspected case of abruption

✓ Abnormal renal function or liver function tests or coagulation disorder.

Fetal indications

Severe intrauterine growth restriction—< 5th percentile for EGA

Persistent reduced liquor—AFI < 5 cm

Biophysical profile score <=4 ,assessed 6 hrs apart

Reversed end-diastolic umbilical artery flow in Doppler study

Anesthesia in Preeclampsia:

* Epidural in labour – there is gradual onset of sympathetic blockade → it provides cardiovascular stability and therefore it avoids neonatal depression.

* Epidural anesthesia may reduce the vasospasm and HTN – may improve uteroplacental blood flow

* Regional anesthesia reduces the risk of complications in the airway and it avoids hemodynamic instability which is associated with intubation.

* Some studies suggest neuraxial anesthesia

* Use of single shot spinal anesthesia is also controversial.

* In general anesthesia ,there is risk of difficult intubation due to airway edema.

* Neuraxial techniques is the preferred method, but contraindicated, when coaguloapthy is present.

* When general anesthesia is given to patients who gets $MgSO_4$,it potentiates the action of succinyl choline.

* Sensitivity to agents like non-depolarizing muscle relaxants is increased.

* $MgSO_4$ blunts the response to vasconstrictors and also inhibits the release of catecholamine after sympathetic stimulation.

* Prevention:various strategies are used in the prevention and modificaton of preeclampsia severity.

Dietary manipulation includes low-salt in diet, supplementation of calcium, supplementation with fish oil .

Salt restriction is found to be ineffective in preventing preeclampsia.

Calcium supplementation : various studies shows that, low intake of calcium has an increased risk of developing gestational hypertension. Various trials shows that calcium supplementation

Is helpful only in women who is deficient in calcium.

It was believed that fatty acids of fish oil would prevent atherogenesis caused by inflammation, but randomized trials shows no such effects.

Antioxidants like vitamin c and vitamin E, helps to reduce oxidative stress, but randamised trials shows, that there is no reduction in the risk of preeclampsia, when antioxidants were supplemented, when compared to placebo.

Low dose aspirin : clinical trials shows only limited effects in the prevention of preeclampsia. aspirin inhibits thromboxane A2 production and its effects is only minimal on production of prostacyclin.

Clinical trials shows that the relative risk is reduced by 10 percent, to develop preeclampsia, preeclampsia superimposed on chronic hypertension, preterm labour. Administration of low dose aspirin must be individualized, to prevent recurrence of preeclampsia.

* Sethuram R, Kiran TS, Weerakkody AN assessed, spot protein/creatinine ratio as the diagnostic test for pre-eclampsia and correlated it to the 24h urine protein. Patients were selected from District General Hospital >24 weeks' gestation with hypertension and >1+ proteinuria (n=32). The results of the test were correlated

to 24hrs urine protein results using Pearson's correlation coefficient. They found that Correlation was significant (r(2)=0.82).The results were Sensitivity, 83%; specificity, 92%; positive likelihood ratio, 10.3; negative likelihood ratio, 0.18. They concluded that, spot PCR correlates well to the 24h urine protein examination

* Laleh Eslamian1, Fariba Behnam1, Zahra Foroohesh Tehrani2, Ashraf Jamal1 and Vajiheh Marsoosi1.

(26 Apr. 2009;) studied the reliability of random urinary protein–creatinine ratio by using receiver operator characteristic (ROC) curve to detect significant proteinuria (300mg/day) using 24hrs Urine protein as a gold standard).

The study concluded that Random urinary protein creatinine ratio is a simple inexpensive and excellent alternative to 24h urine collection.

Therefore spot urine protein creatinine ratio is helpful in diagnosis of preeclampsia and suggested to use it as a pre admission test in PIH cases.

* Amita Sharma1, Pandey Kiran2, Bhagoliwal Ajai3 (3 August 2013); Spot urine P/C ratio and the 24- hour urine protein was measured

The comparison between the spot P/C ratio and 24-hour urine protein measurement was done. ROC curve analysis wasused to analyse data.

They found that there was a strong correlation between the spot P/C ratio and 24-hour urine protein excretion (pearson's correlation coefficient $r = 0.71$; $P < 0.0001$).

The optimal cut off point of spot P/C ratio was 0.25, for 300 mg/24 h of protein excretion, with sensitivity and specificity of 69% and 75% respectively.

The study concluded that Spot urine P/C ratio is a quick and reliable test which can be used as an alternative method for evaluation of proteinuria for diagnosis of pre-eclampsia.

* Nahid Shahbazian, Farzaneh Hosseini-Asl (July 2008) prospectively studied 81 pregnant women with preeclampsia for proteinuria and observed the correlation between the spot P/C ratio and 24-hour urine protein

The optimal cutoff point for spot P/C ratio was found to be 0.20 for 300 mg/24 h.

The sensitivity, specificity, positive predictive value, and negative predictive value was found to be 91.2%, 87.8%, 94.4%, and 96.8%, respectively.

The spot P/C ratios less than 0.19 indicates a sensitivity of 100% for exclusion of preeclampsia.

They concluded that Urine P/C ratio could be used for exclusion of preeclampsia.

* Shahrzad, Mohammad Reza,(14 NOV 2006) compared random urine protein to creatinine ratio (p:c ratio) and 24-h urine protein excretion rate in pregnant women suspicious of pre-eclampsia.

The study was conducted on 100 pregnant women ≥ 20 weeks gestation, of which 50 patients were suspected of having pre-eclampsia and 50 were selected as healthy pregnant women.

A random urine p:c ratio and a 24-h urine sample for protein measurement were obtained. Results showed that all women suspected of having pre-eclampsia had significant proteinuria.

With the cut-off ≥ 0.2 mg/mg the sensitivity was 94% and the specificity of 96% . Using the same cut-off value in the normal pregnant

women who were not thought to have pre-eclampsia, the sensitivity of the test (p:c ratio) was 29% and the specificity was 87%.

Pearson's correlation coefficient was found to be 26 ($P < 0.06$). Negative predictive value and positive predictive value were found to be 34% and 83%, respectively.

* Thomas L. Wheeler (5 July 2006) , studied the correlation between spot urine protein to creatinine (P:C) ratios with 24 hour urine collections for protein in women who was evaluated for preeclampsia.

The study population was 126 patients admitted to evaluate for preeclampsia. Correlation between the spot protein :creatinine ratio with the 24 hour urine protein collections was calculated.

The result showed that there was strong correlation between random spot P:C ratios and 24 hour urine protein levels (Pearson r = 0.88).

The optimal P:C cut-offs value was 0.21 (300 mg per 24 hours) and 3.0 (5000 mg per 24 hours). The study reported that P:C ratio of less than 0.21 (300 mg per 24 hours) had a negative predictive value (NPV) of 83.3% and a P:C ratio value < 3.0 (5000 mg per 24 hours) had 100% NPV.

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AIM OF THE STUDY

Primary objective:

Prediction of Preeclampsia by spot urinary Protein : Creatinine ratio in early pregnancy [before 20 weeks of pregnancy].

Secondary objective:

To find the Maternal outcome in developing Preeclampsia and Eclampsia.

MATERIALS AND METHODS

STUDY DESIGN:

Prospective cross sectional study

STUDY PERIOD:

January 2013 to November 2013

INCLUSION CRITERIA :

Women with 16 to 20 wks of gestation with singleton pregnancy both Primi and Multigravida.

EXCLUSION CRITERIA:

* Patients with chronic hypertension
* Known case of renal disease
* Diabetes mellitus complicating pregnancy
* Heart disease complicating pregnancy
* Jaundice complicating pregnancy
* Gestational age >20 wks
* Patients with urinary tract infection
* Previous history of preeclampsia

SAMPLE SIZE FOR FREQUENCY IN A POPULATION :

Population size (for finite population correction factor or fpc) (N) : 600

Hypothesized % frequency of outcome factor in the population (p):25%+/-5

Confidence limits as % of 100 (absolute +/-%) (d) : 5%

Design effect (for cluster surveys – DEFF) : 1

SAMPLE SIZE :

- $N=(Z)^2\ [P]\ [1-P]/\ d^2$
- Proportion of Preeclampsia=0.25[25%]
- $(1.96)^2\ [0.25]\ [0.75]/[0.05]^2$ =288[300]
- Total no of samples=300

METHODOLOGY :

My study population included a total number of 300 antenatal women who attented the antenatal clinic in the department of Obstetrics and Gynaecology at kilpauk medical college. They were selected according to inclusion and exclusion criteria.

Informed consent was obtained from each patient after explaining about my study. A detailed history was obtained regarding her name, age, height, prepregnancy weight, obstetric score, place of residence, socio

economic class, past history of preeclampsia, family history suggestive of preeclampsia, associated comorbid conditions.

Her vitals were checked and basic investigations was taken.

Patients urine sample was collected and protein creatinine ratio was estimated. protein estimation was done using pyrogalloll method, creatinine estimation was done by modified jaffeys method and the ratio was obtained between the two.

Patients were adviced to attend the antenatal clinic every two weeks. In her follow up visit she was examined thoroughly, especially her blood pressure, urine albumin was checked. Fetal well being was assessed in each visit.

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RESULTS OF THE STUDY

The study group was grouped into two, depending upon the development of preeclampsia, as normal cohort and preeclamptic cohort.

The variables taken into consideration in this study are, age group, obstetric score, socio economic class, prepregnancy weight, body mass index, urine spot protein creatinine ratio value. For each variable Mean $\pm$ SD of all variables of interest were determined for preeclampsia cohort and for normal cohort separately and difference was tested by chi-square test.

The predictive values of urine protein creatinine ratio was analysed using pearson's ROC curve.

Analysis was done by SPSS version 15.

Comparison of variables was done using chi-square test.

TABLE - 1

RISK FACTORS ASSOCIATED WITH OCCURRENCE OF PREECLAMPSIA

	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
AGE GROUP * OCCURRENCE OF PREECLAMPSIA	300	100.0%	0	.0%	300	100.0%
OBSTETRIC SCORE * OCCURRENCE OF PREECLAMPSIA	300	100.0%	0	.0%	300	100.0%
COMORBID CONDITIONS * OCCURRENCE OF PREECLAMPSIA	300	100.0%	0	.0%	300	100.0%
SE CLASS * OCCURRENCE OF PREECLAMPSIA	300	100.0%	0	.0%	300	100.0%

TABLE - 2

AGE GROUP - OCCURRENCE OF PREECLAMPSIA

			OCCURRENCE OF PREECLAMPSIA		
			0	**1**	**Total**
AGE GROUP	1	Count	14	9	23
		% within OCCURRENCE OF PREECLAMPSIA	5.0%	42.9%	7.7%
	2	Count	176	4	180
		% within OCCURRENCE OF PREECLAMPSIA	63.1%	19.0%	60.0%
	3	Count	67	0	67
		% within OCCURRENCE OF PREECLAMPSIA	24.0%	.0%	22.3%
	4	Count	22	8	30
		% within OCCURRENCE OF PREECLAMPSIA	7.9%	38.1%	10.0%
Total		Count	279	21	300
		% within OCCURRENCE OF PREECLAMPSIA	100.0%	100.0%	100.0%

TABLE – 3

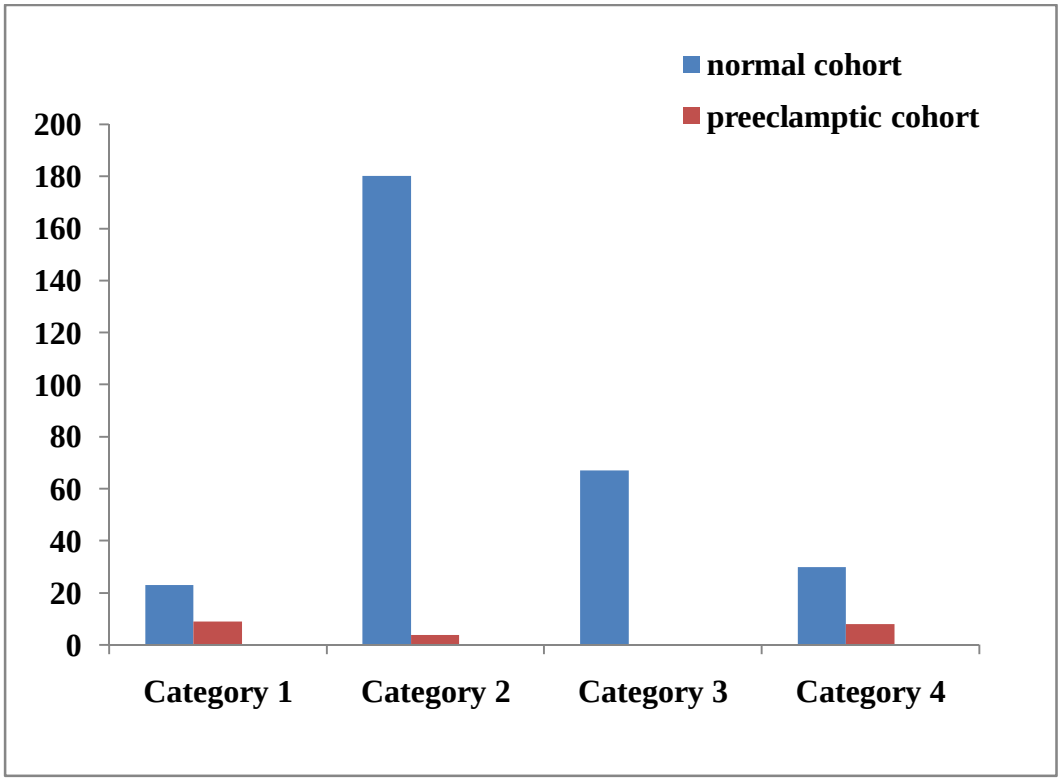
OCCURRENCE OF PREECLAMPSIA AMONG VARIOUS AGE GROUP

AGE GROUP(YRS)	PREECLAMPTIC COHORT		NORMAL COHORT	
	NO OF CASES	%	NO OF CASES	%
<20	9	42.9%	14	5%
21-25	4	19.0%	176	63.1%
26-30	0	0.0%	67	24.0%
31 AND ABOVE	8	38.1%	22	7.9%

- Chi-square=65.652 p=0.000
- Age group distribution showed,42.9% of preeclamptic cohort and 5% of normal cohort belonged to age group less than 20 years.
- In the age group 31 and above ,38.1% developed preeclampsia
- It indicates that, preeclampsia is distributed and more common among teenage pregnancy and elderly gravid

FIGURE – 8

AGE GROUP – DISTRIBUTION AMONG STUDY POPULATION



INFERENCE:

As ‘p’ value is 0.000,there is statistically significant between preeclamptic cohort and normal cohort with regard to age group

TABLE - 4

OBSTETRIC SCORE - OCCURRENCE OF PREECLAMPSIA

			OCCURRENCE OF PREECLAMPSIA		
			0	**1**	**Total**
OBSTETRIC SCORE	1	Count	146	17	163
		% within OCCURRENCE OF PREECLAMPSIA	52.3%	81.0%	54.3%
	2	Count	93	1	94
		% within OCCURRENCE OF PREECLAMPSIA	33.3%	4.8%	31.3%
	3	Count	32	1	33
		% within OCCURRENCE OF PREECLAMPSIA	11.5%	4.8%	11.0%
	4	Count	6	2	8
		% within OCCURRENCE OF PREECLAMPSIA	2.2%	9.5%	2.7%
	5	Count	2	0	2
		% within OCCURRENCE OF PREECLAMPSIA	.7%	.0%	.7%
Total		Count	279	21	300
		% within OCCURRENCE OF PREECLAMPSIA	100.0%	100.0%	100.0%

- Chi-square=12.964 p=0.011

TABLE – 5

PERCENTAGE DISTRIBUTION OF PREECLAMPSIA AMONG PRIMI GRAVIDA AND MULTI GRAVIDA

PARITY	PREECLAMPTIC COHORT		NORMAL COHORT	
	NO OF CASES	%	NO OF CASES	%
PRIMI	17	81%	146	52.3%
GRAVIDA 2	1	4.8%	93	33.3%
GRAVIDA 3	1	4.8%	32	11.5%
GRAVIDA 4	2	9.5%	6	2.2%
GRAVIDA 5	0	0.0%	2	0.7%

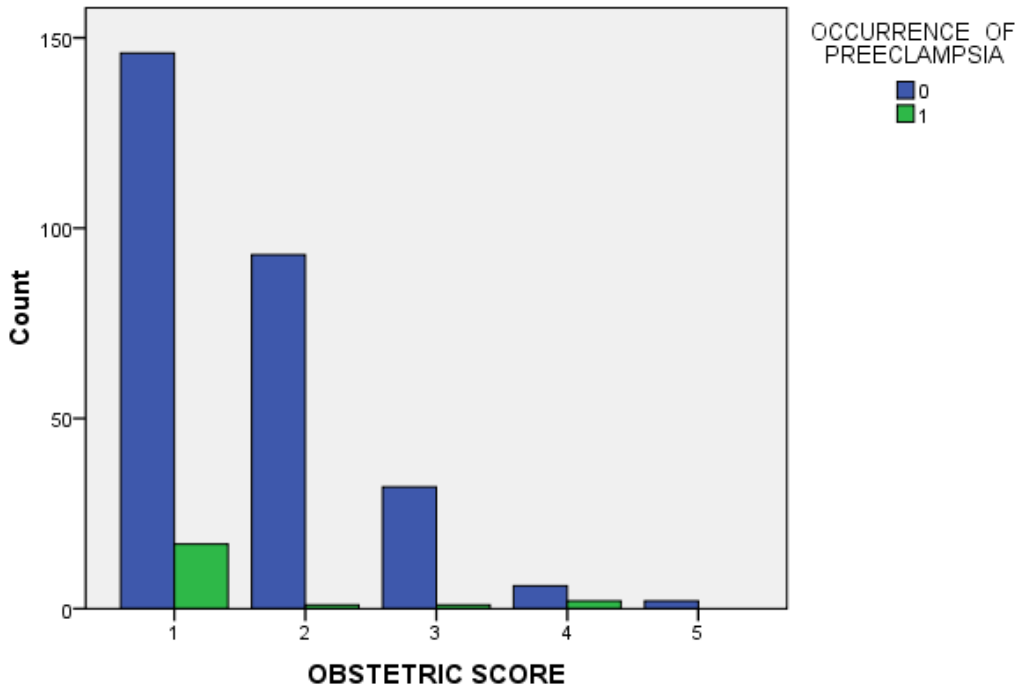
This study indicates statistical significance between normal cohort and preeclamptic cohort.

Regarding parity,81% of preeclampsia occurred in primigravida.

About 9.5% of preeclampsia occurred in fourth gravid, but it affected only 4.8% of gravid 2 and gravid 3.

FIGURE - 9

OBSTETRIC SCORE – DISTRIBUTION OF PREECLAMPSIA AMONG STUDY GROUP



- 0=normal cohort 1=preeclamptic cohort
- INFERENCE:

TABLE - 6

COMORBID CONDITIONS - OCCURRENCE OF PREECLAMPSIA

			Total
COMORBID CONDITIONS	0	Count	300
		% within OCCURRENCE OF PREECLAMPSIA	100.0%
	Total	Count	300
		% within OCCURRENCE OF PREECLAMPSIA	100.0%

Patients in the study group were selected without any comorbid conditions, like chronic hypertension, renal disease, heart disease etc.

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TABLE - 7

SE CLASS - OCCURRENCE OF PREECLAMPSIA

	OCCURRENCE OF PREECLAMPSIA		
	0	**1**	**Total**
SE CLASS 2 Count	1	0	1
% within OCCURRENCE OF PREECLAMPSIA	.4%	.0%	.3%
SE CLASS 4 Count	91	5	96
% within OCCURRENCE OF PREECLAMPSIA	32.6%	23.8%	32.0%
SE CLASS 5 Count	187	16	203
% within OCCURRENCE OF PREECLAMPSIA	67.0%	76.2%	67.7%
Count	279	21	300

About 67.7% of the pregnant women belonged to socioeconomic class 5.Out of which,76.2% developed preeclampsia and 67% belonged to normal cohort

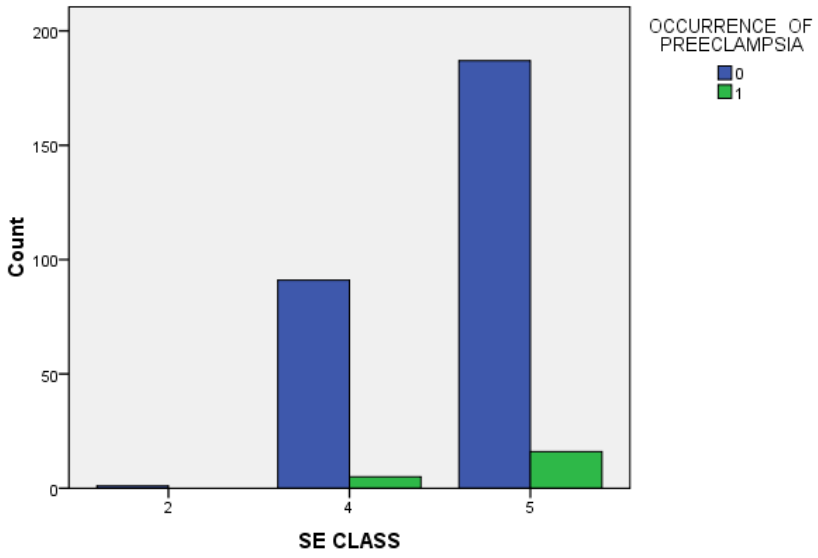
TABLE – 8

SE CLASS – PERCENTAGE DISTRIBUTION OF PREECLAMPSIA

SE CLASS	PREECLAMPTIC COHORT		NORMAL COHORT	
	NO OF CASES	%	NO OF CASES	%
2	0	0.0%	1	0.4%
4	5	23.8%	91	32.6%
5	16	76.2%	187	67.0%

FIGURE - 10

SE CLASS – DISTRIBUTION OF PREECLAMPSIA



0=normal cohort 1=preeclamptic cohort

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When SE class was taken into consideration,67% of normal cohort and 76.2% of preeclamptic cohort occurred in the class 5,whereas,32.6% of normal cohort and 23.8% of preeclamptic cohort belonged to class 4 SE class.

INFERENCE:

Since, the p- valve is 0.673, there is no statistical significance between preeclamptic cohort and normal cohort with regard to socioeconomic class.

TABLE - 9

BMI GROUP - OCCURRENCE OF PREECLAMPSIA

			Occurrence of Preeclampsia		
			0	**1**	**Total**
BMI GROUP	1	Count	34	0	34
		% within OCCURRENCE OF PREECLAMPSIA	12.2%	.0%	11.3%
	2	Count	128	2	130
		% within OCCURRENCE OF PREECLAMPSIA	45.9%	9.5%	43.3%
	3	Count	96	7	103
		% within OCCURRENCE OF PREECLAMPSIA	34.4%	33.3%	34.3%
	4	Count	16	10	26
		% within OCCURRENCE OF PREECLAMPSIA	5.7%	47.6%	8.7%
	5	Count	5	2	7
		% within OCCURRENCE OF PREECLAMPSIA	1.8%	9.5%	2.3%
Total		Count	279	21	300
		% within OCCURRENCE OF PREECLAMPSIA	100.0%	100.0%	100.0%

- Chi-square=53.058 p=0.000

TABLE - 10

BMI - OCCURRENCE OF PREECLAMPSIA

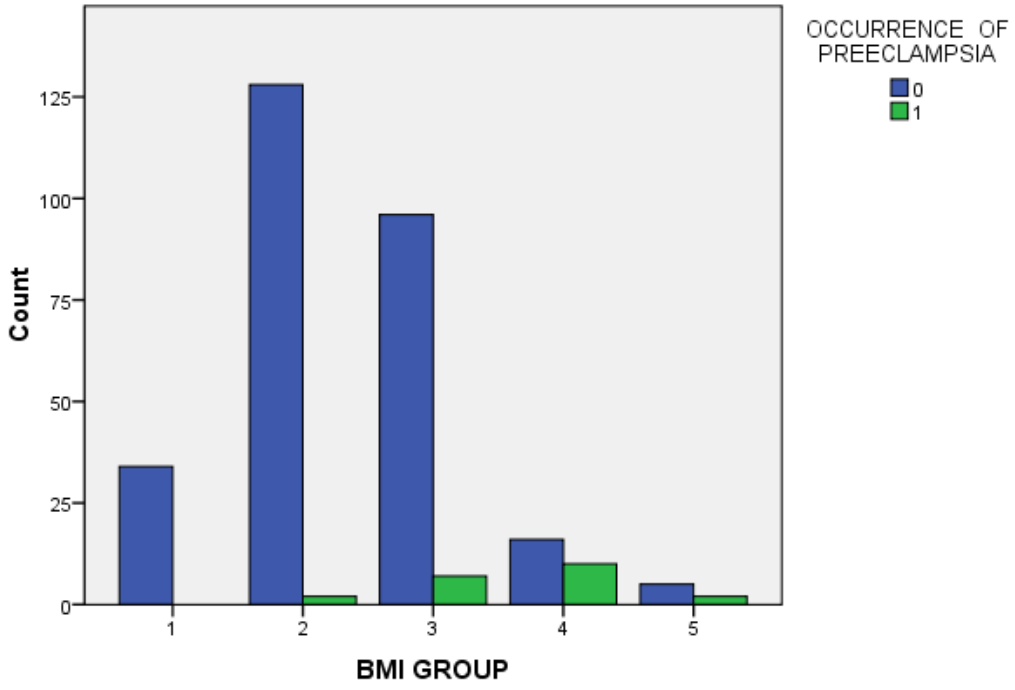
BMI	PREECLAMPTIC COHORT		NORMAL COHORT	
	NO OF CASES	%	NO OF CASES	%
<18.5	0	0.0%	34	12.2%
18.5-24.9	2	9.5%	128	45.9%
25-29.9	7	33.3%	96	34.4%
30-35	10	47.6%	16	5.7%
35-40	2	9.5%	5	1.8%

- BMI of the study population was calculated according to her prepregnant weight.
- Quetelet index was used to calculate the BMI.
- From the above table it is clear that, about 47.6% of preeclampsia occurred in the moderately obese group.
- 33.3% of preeclamptic cohort and 34.4% of normal cohort, were present in overweight group.
- In women with normal BMI ,preeclampsia occurred in 9.5% and 45.9% comes under normal cohort.

- My study population also included severely obese women and about 9.5% developed preeclampsia and 1.8% comes under normal cohort.

FIGURE - 11

BMI - DISTRIBUTION OF PREECLAMPSIA AMONG STUDY GROUP



INFERENCE:

- As p=0.000,there is statistical significance between, preeclamptic cohort and normal cohort, with regard to BMI.

FIGURE - 12

ROC CURVE - URINE SPOT PROTEIN CREATININE RATIO

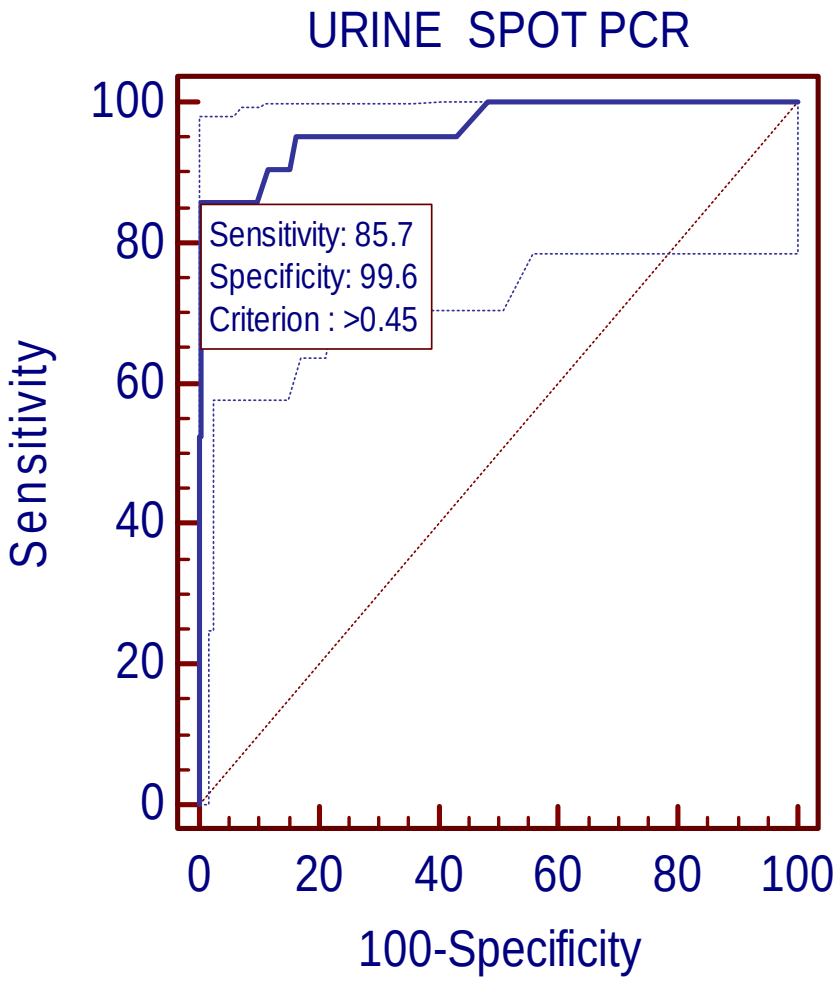


TABLE – 11

URINE SPOT PCR – OCCURRENCE OF PREECLAMPSIA

URINE SPOT PCR	TOTAL	PREECLAMPTIC COHORT	NORMAL COHORT
>0.3	21	18	3
0.2-0.29	54	2	52
<0.2	225	1	224

Area under the ROC curve (AUC)	0.964543
Standard Error[a]	0.0230
95% confidence interval[b]	0.936806 to 0.982438
z statistic	20.192
Significance level P (Area = 0.5)	<0.0001

The above table & ROC, infer that there is a Good Fit in the prediction for the cut off value >0.45 and the Area Under the ROC curve(AUC) is 0.964543.Sensitivity is 87.5 and specificity is 99.6.It indicates Spot pcr is the good indicator for prediction of Pre eclampsia.

Area Under a Receiver Operating Characteristic Curve (ROC):

Total area under ROC curve is used as a single index for measuring the performance a test. when the AUC is larger, the better is overall performance of the medical test to correctly identify diseased and non-diseased subjects. When the AUCs of two tests are equal, it represents similar overall performance of tests but this does not necessarily mean that both the curves are identical. It indicates that they may cross each other.

- Regarding urine spot PCR values, when the cut off value is >0.45, the sensitivity is 85.71%., specificity is 99.64%.
- When the cut off value is >0.5, the sensitivity of urine spot pcr is 76.19% and the specificity is the same 99.64%.
- If the cut off value is reduced to 0.2, the sensitivity of the test increases to 95.24%.

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TABLE – 12

MEAN DISTRIBUTION OF PREECLAMPSIA AMONG VARIOUS VARIABLES

	OCCURRENCE OF PREECLAMPSIA	N	Mean
AGE(YRS)	1	21	24.71
	0	279	24.77
HT(CM)	1	21	152.48
	0	279	152.18
WT(KG)	1	21	69.14
	0	279	55.55
BMI	1	21	29.8481
	0	279	88.5271
SAMPLE TAKEN GA(WKS)	1	21	18.00
	0	279	18.01
URINE SPOT PCR	1	21	.73
	0	278	.12

TABLE – 13

OCCURRENCE OF PREECLAMPSIA – STANDARD DEVIATION AMONG VARIOUS FACTORS

	OCCURRENCE OF PREECLAMPSIA	Std. Deviation	Std. Error Mean
AGE(YRS)	1	5.596	1.221
	0	3.412	.204
HT(CM)	1	5.810	1.268
	0	6.175	.370
WT(KG)	1	8.873	1.936
	0	11.422	.684
BMI	1	4.11899	.89884
	0	1078.18279	64.54912
SAMPLE TAKEN GA(WKS)	1	1.549	.338
	0	1.373	.082
URINE SPOT PCR	1	.482	.105

From this study, it was found that the following variables are statistically significant.

- Age of the patient
- Obstetric score
- Socioeconomic class
- Prepregnancy weight of the patient and BMI
- Urine spot Protein creatinine ratio

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TABLE – 14

THE FINAL OUTCOME OF THE STUDY

VARIABLE	CHI-SQUARE VALUE	P
AGE GROUP	65.652	0.000
PARITY	12.964	0.011
SE CLASS	0.791	0.673
BMI	53.058	0.000

URINE SPOT PCR WITH SIGNIFICANT P'=<0.0001

SUMMARY

From this study it is found that, there is statistical significance between preeclamptic cohort and normal cohort with regard to following variables :

- Age group
- Obstetric score
- Socioeconomic class
- BMI
- Urine PCR

* When age group was taken into consideration, about 42.9% developed.

* Preeclampsia and 5% did not develop preeclampsia in the age group <20 years.

* In the age group >30 years,38.1% developed preeclampsia and 7.9% did not develop preeclampsia. There was statistical significance between normal cohort and preeclamptic cohort.

* In my study about 81% preeclampsia occurred in primigravida and only 4.8% occurred in gravid 2 and gravid 3.

* About 9.5% of preeclamptic cohort and 2.2% of normal cohort were present among gravid 4.

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* Among the people belonging to SE class 5,about 76.2% developed

* Preeclampsia and 23.8% belonged to preeclamptic cohort in women belonging to SE class 4.

* There is no statistical significance with regard to SE class.

* About 47.6% of preeclamptic cohort, were moderately obese patients. In my study group, preeclampsia did not occur in underweight persons.

* Only 9.5% of preeclampsia occurred in women with normal BMI and 33.3% in overweight individual. The variable BMI is also statistically significant.

* The cut off value for urine PCR was taken as >0.45,to predict preeclampsia with 85.71% sensitivity and 99.64% specificity. When the cut off value is reduced the sensitivity increases.

* The Area under the ROC curve ,for urine PCR is 0.964.

DISCUSSION

- Our study population included 300 antenatal women who attended antenatal out- patient department. Among them ,urine spot PCR predicted preeclampsia in 21 patients.

- Out of 21 patients,18 women had urine spot PCR cut off value >0.45.

- Only 2 patients developed preeclampsia ,in the cut off value between 0.2 to 0.29.

- In the cut off value <0.2 , only one patient developed preeclampsia.

- It was also found that, preeclampsia is more common among women with increased prepregnant weight and BMI > 25.

- Our study also reported that, primigravida and age group less than 20 years were more prone to develop preeclampsia.

- Our study is supported by the analysis done by Laleh Eslamian1, Fariba Behnam1, Zahra Foroohesh Tehrani2, Ashraf Jamal1, and Vajiheh Marsoosi1 (26 Apr. 2009;). The study showed a cut off value of 0.22mg/mg for protein creatinine ratio and it best

predicted significant proteinuria with sensitivity, specificity, positive and negative predictive values of 87%, 92.6%, 90.6% and 89.3% respectively.

- Amita Sharma1, Pandey Kiran2, Bhagoliwal Ajai3 (3 August 2013); Spot urine P/C ratio and the 24- hour urine protein was measured.

- They found that there was a strong correlation between the spot P/C ratio and 24-hour urine protein excretion (pearson's correlation coefficient $r = 0.71$; $P < 0.0001$).

- The optimal cut off point of spot P/C ratio was 0.25, for 300 mg/24 h of protein excretion, with sensitivity and specificity of 69% and 75% respectively.

CONCLUSION

After investigating and analysing the study, it was found that,

- Urine spot PCR is a simple method and rapid test to predict preeclampsia. when cut of value is more, the specificity increases.

- From this study it is concluded that when the cut off value for urine spot PCR is >0.45, the sensitivity is 85.71% and specificity is 99.64%.

- Urine spot PCR can be used to predict preeclampsia in early gestation itself, so that the patient can be kept under proper surveillance, with more frequent antenatal check up,and to detect the complications earlier to prevent maternal and fetal morbidity and mortality.

- Urine spot PCR can be used at the level of primary health centre, to detect the high risk pregnancies and refer them to the tertiary care centre at the earliest.

- It was also found that, more number of preeclampsia occurred in women with increased prepregnancy weight, with raised BMI. overweight and obese women developed preeclampsia more than

the normal individual therefore, proper weight reduction will reduce the risk of developing preeclampsia.

- Urine spot PCR can be used to predict preeclampsia with a single random midstream urine sample when compared to 24 hrs urine protein estimation and routine dipstick method.

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KEY TO MASTER CHART

BMI	-	Body mass index
Ht	-	Height
PCR	-	Protein creatinine ratio
SE Class	-	Socioeconomic Class
s.no	-	Serial number
wt	-	Weight

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PROFORMA

NAME: AGE: OPNO:

ADDRESS: PHONE NO:

OBSTETRIC SCORE: LMP: EDD:

COMPLAINTS:

PREVIOUS H/O PREECLAMPSIA:

FAMILY H/O PREECLAMPSIA:

ASST COMORBID FACTORS:

HEIGHT: WEIGHT: BMI:

GENERAL EXAMINATION:

PALLOR:YES/NO ICTERUS:YES/NO PEDAL EDEMA:YES/NO

BLOOD PRESSURE:

SYSTEMIC EXAMINATION:

CARDIOVASCULAR SYSTEM:

RESPIRATORY SYSTEM:

GESTATIONAL AGE BY,

PER ABDOMEN EXAMINATION:

USG:

INVESTIGATIONS:

HB%: TC: PLATELET COUNT:

URINE R/E: ALBUMIN: SUGAR: DEPOSITS:

RFT: SUGAR: UREA: CREATININE:

LFT:

S.BILIRUBIIN:

SGOT:

SGPT:

S.ALP:

S.URIC ACID:

TOTAL PROTEIN:

ALBUMIN:

GLOBULIN:

URINE PCR:

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