A Dissertation on

SPOT URINE PROTEIN-CREATININE RATIO AND 24 HOUR URINE PROTEIN EXCRETION IN WOMEN WITH PREECLAMPSIA – A COMPARATIVE STUDY

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This is to certify that this dissertation entitled " **SPOT URINE PROTEIN-CREATININE RATIO AND 24 HOUR URINE PROTEIN EXCRETION IN WOMEN WITH PREECLAMPSIA – A COMPARATIVE STUDY** submitted by Dr.T.K.MADHUMITHA, appearing for Part II MS, Branch II Obstetrics and Gynecology Degree Examination in April 2017, is a Bonafide record of work done by her, under my direct guidance and supervision as per the rules and regulations of the Tamil Nadu Dr. MGR Medical university, Chennai, Tamil Nadu, India. I forward this dissertation to the Tamil Nadu Dr. MGR Medical University Chennai, India.

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DECLARATION

I Dr.T.K. MADHUMITHA, solemnly declare that the dissertation titled, **"SPOT URINE PROTEIN-CREATININE RATIO AND 24 HOUR URINE PROTEIN EXCRETION IN WOMEN WITH PREECLAMPSIA – A COMPARATIVE STUDY"** is a bonafide work done by me at R.S.R.M. Lying in Hospital. Stanley Medical College, Chennai – during December 2015–to September 2016 under the guidance and supervision of Prof.Dr.K. Kalaivani M.D., D.G.O.,DNB., Professor and Head of the department , Obstetrics and Gynaecology. The dissertation is submitted to the Tamilnadu Dr. M.G.R. Medical University, in partial fulfillment of University rules and regulations for the award of M.S. Degree in obstetrics and Gynaecology.

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Dr.T.K.MADHUMITHA

INTRODUCTION

Hypertensive disorders , the commonest medical disorder during pregnancy affects 7-15% of all gestations and account for approximately a quarter of all admissions in antenatal ward.

According to World Health Organization's systemic review on maternal mortality worldwide,hypertensive disease remains a leading cause of direct maternal mortality. Together with haemorrhage and infection , hypertension forms the deadly triad that contributes to morbidity and mortality during pregnancy and childbirth.

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Preeclampsia contributes a greater risk, complicating approximately 5 – 8 % of all pregnancies

Preeclampsia is a disease process involving multiorgans of unknown aetiology characterized by de novo onset of hypertension and proteinuria after 20 weeks of gestation, sometimes progressing into a multiorgan cluster of varying clinical features. It is a syndrome specific to pregnancy that can affect every organ system

Appearance of proteinuria in association with hypertension is an important diagnostic criterion. Preeclampsia syndrome is characterized by systemwide endothelial leak where proteinuria remains the surrogate objective marker.

Obstetricians currently rely on the 24 hour urine collection to determine proteinuria. However, 24 hour urine collection is inconvenient, both for the patient and the health provider handling collection of urine . This will be subject to error because of incompleteness or inaccurate timing in collection. Further, there is a delay in diagnosis of 24 hours till the time of collection .

A reliable rapid test which will accurately predict the results of a 24 hour urine collection would be useful. Measurement of protein to creatinine ratio in a spot urine sample is an alternative method for the quantitative evaluation of proteinuria. In patients with preeclampsia, implementing urine protein to creatinine ratio as a alternative for 24 hour urine protein excretion for significant proteinuria still remains unclear.

AIM OF THE STUDY

1. To study the correlation between the spot protein to creatinine ratio of a single random sample and 24 hour urine protein excretion in women admitted for evaluation of preeclampsia.

2. To know if spot protein to creatinine ratio would provide quantification of proteinuria in preeclampsia accurately.

MATERIALS AND METHODS

Study period : October 2015 to September 2016

Sample size : 150

Study design : Prospective comparative observational study

Source of data :

One hundred and fifty antenatal women who were admitted for evaluation of preeclampsia were studied prospectively after getting written informed consent. The study was conducted at the Department of Obstetrics & Gynaecology at Govt. R.S.R.M. Lying-in Hospital attached to Stanley Medical College, after getting approval from the Hospital Ethical Committee.

Selection criteria

Inclusion criterion

Pregnant women with preeclampsia, being defined as systolic blood pressure of $\geq$ 140 mm Hg or diastolic blood pressure of $\geq$ 90 mm Hg on at least two occasions 6 hours apart , accompanied by a proteinuria of $\geq$ + 1 as detected by dipstick test, after 20 weeks of gestation.

Exclusion criteria

- Pre-existing renal disorder
- Urinary tract infections
- Chronic hypertension
- Gestational diabetes
- In addition, woman who got delivered during the day of urine collection were excluded

Procedure

One hundred and fifty patients who satisfied the above criteria were recruited for the study. Informed written consent was obtained from all the patients.

1. History was taken in detail.
2. General and systemic examination was done.
3. The blood pressure was measured with an appropriate size cuff with the patient sitting in an upright position after at least 10 minutes rest. Diastolic BP was determined as the disappearance of sound (Korotkoff Phase V).

4. Complete obstetric examination was done. Per speculum examination was done to rule out vaginal infection clinically.

5. Urine microscopy was done to rule out the presence of infection.

6. Proteinuria was assessed in a random sample of urine by the dipstick method. Grading of Proteinuria by dipstick as follows:

Trace	0.1g/l
1+	0.3g/l
2+	1g/l
3+	3g/l
4+	10g/l

If the dipstick test showed proteinuria of 1+ or more, tests for quantifying proteins were carried out.

7. Spot urine protein – creatinine ratio

A spot midstream sample of urine was collected from all the patients, immediately prior to the beginning of the collection for 24 hour urine protein estimation. In the Biochemistry laboratory, samples were processed where

a) Measurement of urine protein was done by the sulphosalicylic acid method

b) Urine creatinine was estimated by Modified Jaffe's method

c) The urine protein and creatinine ratio was obtained by dividing the urine protein concentration (in mg/dl) by the urine creatinine concentration (in mg/dl)

8. Urine samples were collected for 24 hours (after collecting the specimen for spot test) and the urinary protein excretion in 24 hours was estimated.

9. Normal values for protein excretion

24 hours urinary protein (in mg/24 hours)

Not significant	< 300
Clinically significant	>300
Severe proteinuria	>5000

Spot Protein creatinine ratio

Not significant	<0.3
Clinically significant	≥ 0.3

10. Hemoglobin (g/dl), Platelet count, Blood urea, serum creatinine and liver function test (Sr. bilirubin, Sr. proteins (total and albumin), SGOT & SGPT, LDH) were done for all patients.

11. Fundus examination was done for all patients.

12. USG and Doppler study was done wherever indicated (suspicion of IUGR)

13. Analysis of the collected data were made by appropriate statistical methods. Demographic data uses descriptive statistics and are summarized as mean, ±S.D., median and percentage, wherever appropriate.

14. The relationship between the urine protein creatinine ratio and 24 hour protein excretion was estimated with Pearson's correlation test and correlation coefficient was calculated which is expressed as "r".

REVIEW OF LITERATURE

Hypertension , the most common medical complication during pregnancy, complicate 5 to 10 percent of all pregnancies which is a leading cause of maternal and perinatal mortality and morbidity rates. The incidence of preeclampsia has risen which might be related to increased prevalence of risk factors such as chronic hypertension, diabetes & obesity.

TERMINOLOGY AND CLASSIFICATION

The National High Blood Pressure Education Program Working Group (NHBPEP 2000) classifies hypertension in pregnancy as follows:

1. Gestational Hypertension
2. Preeclampsia and eclampsia syndrome
3. Preeclampsia syndrome superimposed on chronic hypertension
4. Chronic hypertension

HYPERTENSION

Hypertension during pregnancy is diagnosed when the systolic pressure is 140mmHg or more and or diastolic pressure of 90 mmHg or more(korotkoff V) ,measured on two occasions at least 6 hours apart. Increase in systolic blood pressure of > 30 mmHg or diastolic blood pressure of > 15 mmHg above the patients baseline has been abandoned from the diagnostic criteria of hypertension which did not prove to be a good prognostic indicator.

PROTEINURIA

Significant proteinuria is defined as the urinary excretion of 300 mg/l or more of proteinuria in a 24 hour urine collection or persistent 30 mg/dl (1+) on dipstick testing for proteinuria in random urine samples .

GESTATIONAL HYPERTENSION

New onset hypertension developing after 20 weeks of gestation, during labour,or in the first 24 hour postpartum, without proteinuria, in a previously normotensive nonproteinuric woman and the blood pressure resolves within 3 months postpartum.

PREECLAMPSIA

Hypertension associated with proteinuria of > 0.3g/L in a 24 hour urine collection or 1+ by dipstick(qualitative urine examination) , after 20 weeks of gestation on a previously normotensive and non proteinuric pregnant women.

ECLAMPSIA

Eclampsia is termed as the onset of convulsions in women with preeclampsia that is not due to other causes .

SUPERIMPOSED PREECLAMPSIA ON CHRONIC HYPERTENSION

It is defined by the new onset proteinuria in a hypertensive woman, but no proteinuria before 20 weeks of gestation or a sudden increase in proteinuria or blood pressure or platelet count of less than 100,000/µl in a woman with hypertension and proteinuria before twenty weeks of gestation.

CHRONIC HYPERTENSION

A diagnosis of chronic hypertension complicating pregnancy is made when there is a pre-pregnancy hypertension or hypertension

diagnosed before 20 weeks of gestation not attributable to hypertension or gestational trophoblastic disease, which persists after 12 weeks postpartum.

INCIDENCE AND PREDISPOSING FACTORS

The incidence of hypertensive disorders in pregnancy varies between 5-10%, and it is rising ,as women are postponing their first pregnancy to a later age and increased pre-pregnancy weight. 70% of them are gestational hypertension ,preeclampsia or eclampsia and 30% being chronic hypertension complicating pregnancy.

Factors like age, family and genetic factors influence the incidence. Young primigravida has increased incidence of preeclampsia. Approximately 15-25% of women initially diagnosed with gestational hypertension will develop preeclampsia, more in patients who present earlier or in patients with a prior miscarriage

Preeclampsia is more likely to occur at both extremes of reproductive age, but is greater in women younger than 20 years of age. The increased incidence in patients older than 35 years is probably due to chronic hypertension which is undiagnosed with superimposed preeclampsia.

The incidence was also increased in patients with twin gestation (13%) and the incidence was unrelated to zygosity .

The incidence is also increased in patients who had preeclampsia in previous pregnancy, the probability of recurrence being approximately 30% and this increases in an inverse relationship to the gestational age when patient developed the disease.

Smoking has been associated with reduced risk of hypertension during pregnancy consistently though it causes many adverse outcomes

PREECLAMPSIA

Preeclampsia is a disease process affecting multiorgans characterized by denovo onset of hypertension and proteinuria occuring after 20 weeks of gestation. Classically ,it is defined as a triad of hypertension, oedema and proteinuria. The clinical findings of preeclampsia can manifest as either maternal syndrome alone (hypertension and proteinuria > 0.3g/24 hour urine with or without other multisystem dysfunction) or in association with fetal syndrome (fetal growth restriction , oligohydramnios). Important objective criteria is the appearance of proteinuria which remains to differentiate from gestational hypertension.

The following are the indicators of the severe preeclampsia :

1. Systolic blood pressure of $\geq$160 mm Hg or diastolic blood pressure of $\geq$110 mm of Hg
2. Proteinuria of 5 g or higher in a 24 hour urine specimen or 3+ or greater on dipstick testing of two random urine samples collected at least four hours apart.
3. Oliguria of < 500 ml in 24 hours
4. Cerebral and visual disturbances
5. Pulmonary edema
6. Right upper quadrant or epigastric pain
7. Impaired liver function
8. Fetal growth restriction
9. Thrombocytopenia

ETIOPATHOGENESIS

The exact nature of the primary event causing preeclampsia is not known . However, abnormal trophoblastic invasion of spiral arteries, inappropriate activation of endothelial cell , exaggerated inflammatory response are main features in the pathogenesis of preeclampsia .

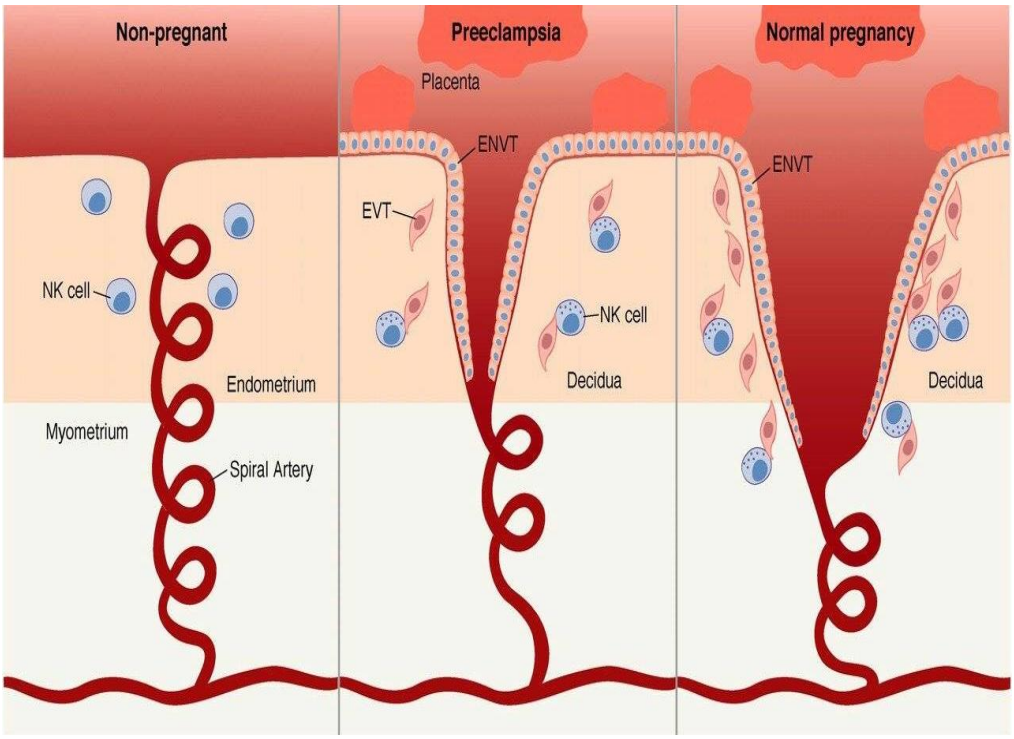
The preeclamptic syndrome has been hypothesized as a two stage disorder

1. Primary stage involves abnormal placentation. In preeclampsia, there is an incomplete trophoblastic invasion of the spiral arterioles of the uterus which results in a smaller vessel caliber with a high resistance to flow. It is likely that the abnormally narrow arterioles impair the placental blood flow.

2. The second stage of preeclampsia involves the conversion of the uteroplacental maladaptation to the maternal systemic syndrome of preeclampsia. These inflammatory response stimulates the synthesis of inflammatory cytokines, products that affect angiogenesis and abnormal lipid perioxidation.

Abnormal placentation & Diminished Placental perfusion

in preeclampsia



Several other factors have been considered in the causation of preeclampsia like:

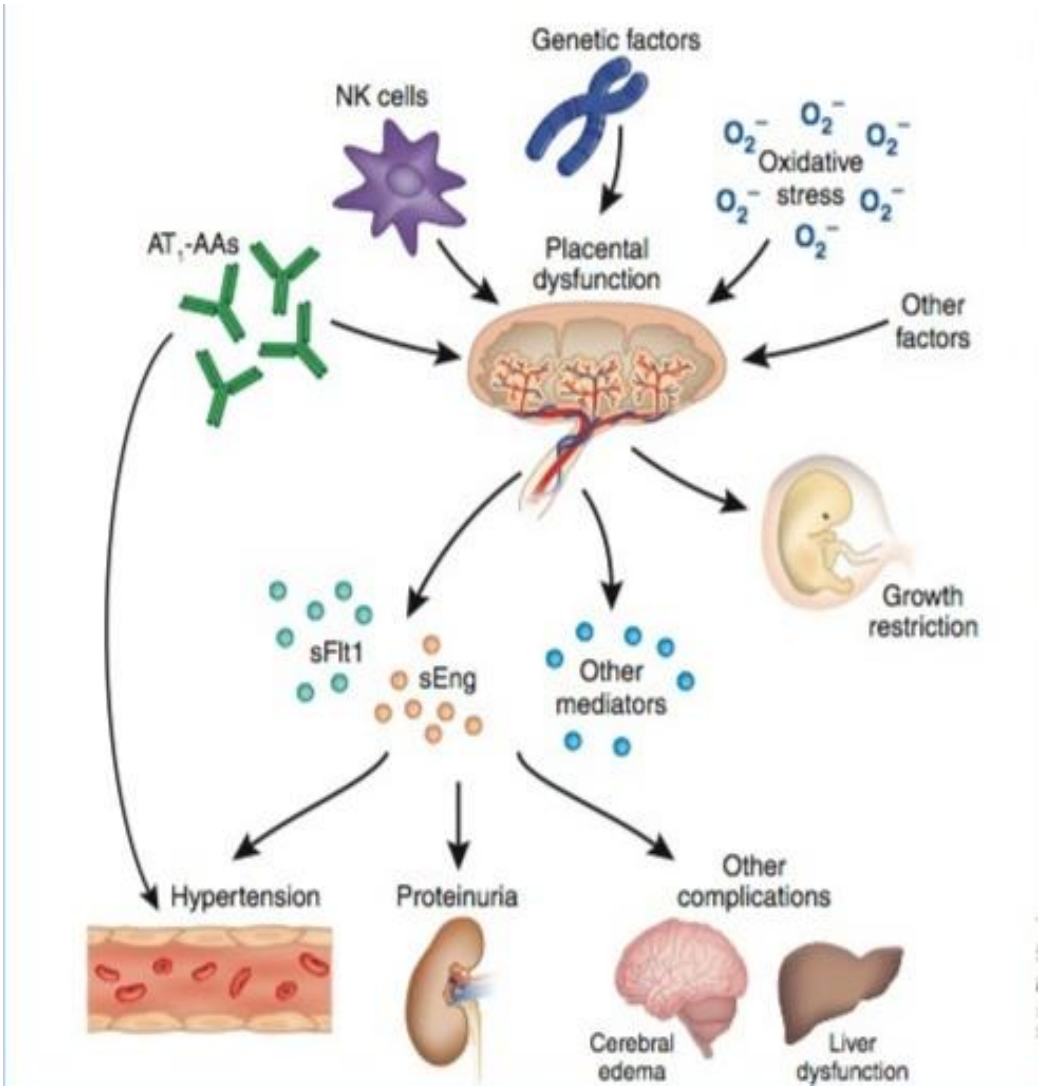
VASCULAR ENDOTHELIAL DYSFUNCTION

In response to placental factors released by ishaemia ,a cascade of events set into motion provoking endothelial cell injury. Cytokines like tumour necrosis factor α and interleukins (IL)contribute to the oxidative stress by formation of free radicals and self propagating lipid peroxides production and interfere with prostaglandin balance. This oxidative stress presents as atherosis by production of lipid laden macrophages ,as microvascular coagulation manifested as thrombocytopenia , and increased permeability manifest as proteinuria and oedema.

ANGIOGENIC IMBALANCE

Worsening hypoxia at uteroplacental interphase stimulates the production of excessive amounts of antiangiogenic factors by the trophoblastic tissue . Soluble Fms-like tyrosine kinase1(sFlt-1) ,a placental protein , binds to the receptor binding domains of placental like growth factor (PLGF) and vascular endothelial growth factor (VEGF) Increased maternal levels of sFlt-1 levels inactivate and decrease circulating free PLGF and VEGF concentration resulting in dysfunction of endothelial cell . The increase in sFlt-1 levels correlate with severity of the disease.

Factors involved in causation of preeclampsia



GENETIC FACTORS

A variety of genetic associations to preeclampsia have been recognized. The incident risk of preeclampsia is 20 - 40 % for daughters of women with preeclampsia & 11 – 17 % for sisters . The hereditary predisposition is due to interactions of multiple inherited genes – both maternal and paternal. More than 70genes have been studied for their possible association with preeclampsia. Seven of these have been widely investigated and are listed below.

Genes Frequently Studied for their Association with Preeclampsia Syndrome

Gene (polymorphism)	Function affected	Chromosome	Biological Association
MTHFR (677T)	Methyl tetrahydro-folate reductase	1p 36 – 3	Vascular disease
F 5 (Leiden)	Factor V Leiden	1 q 2 3	Thrombophilia may coexist with other thrombophilic genes
AGT (M 235 T)	Angiotensinogen	1 q 42 – q 43	Blood pressure regulation, linked to essential hypertension
HLA (various)	Human leukocyte antigen	6 p 21. 3	Immunity
NOS3(Glu 298 Asp)	Endothelial nitric oxide	7q3 6	Vascular endothelial function
F 2 (G20210 A)	Prothrombin (Factor II)	11 p 11 q-12	Coagulation-weakly associated. Studied with other thrombophilic genes
ACE	Angiotensin converting enzyme	17 q 2 3	Blood pressure regulation

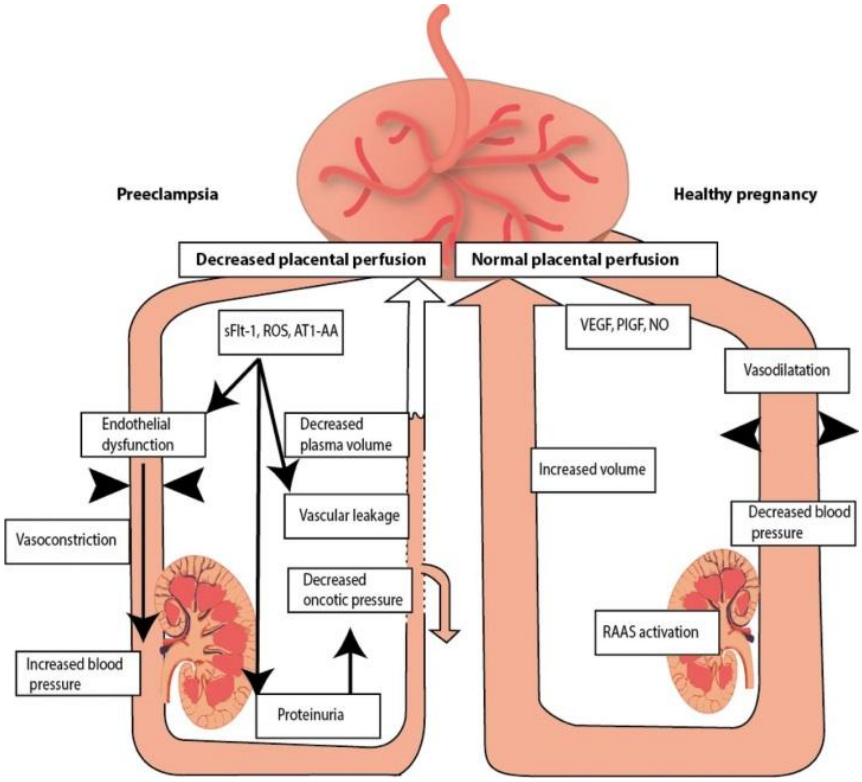
Adapted from Ward and Lindheimer, 2009

ROLE OF VASOACTIVE AGENTS

1. Renin-Angiotensin-Aldosterone System

In normal pregnancy, all the elements of this system, i.e. renin activity, plasma renin concentration, and angiotensin II levels increase. However the pregnant woman shows reduced responsiveness to the angiotensin II effects

In preeclampsia, plasma renin and angiotensin II levels are reduced than normal throughout the pregnancy. In addition, the refractoriness to angiotensin II will not be there as soon as mid trimester in women who are destined to develop preeclampsia



2. Prostaglandins

The blunted pressor response seen in normal pregnancy is due to increased production of endothelial prostacyclin.. In preeclampsia, there is decreased production of prostacyclin(PGI2) mediated by phospholipaseA_2. The secretion of thromboxane A_2 by the platelets is increased simultaneously. The prostacyclin:thromboxane A_2 ratio decreases leading to increased sensitivity to vasopressor response.

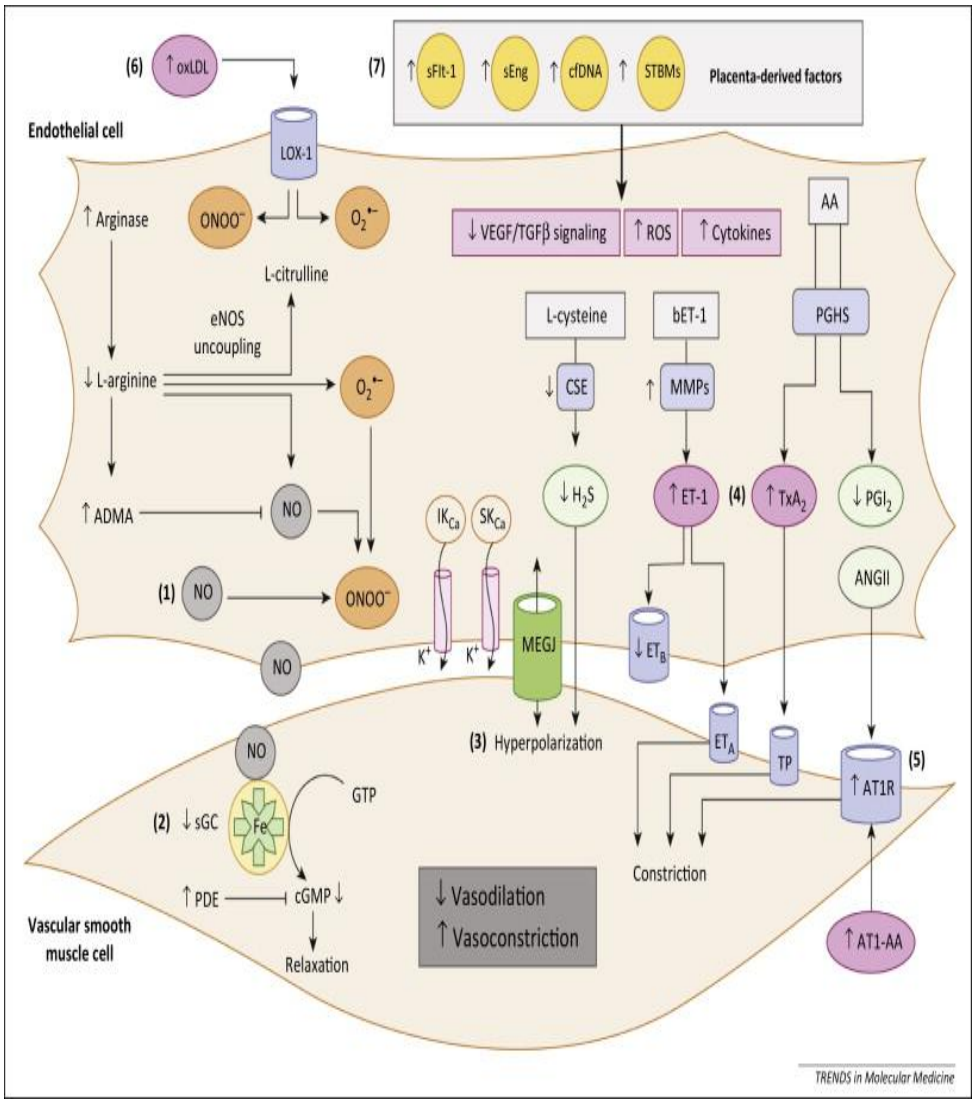
3. Nitric oxide

Nitric oxide is a potent vasodilator produced by the endothelial cells from L arginine. It appears that there is decreased endothelial nitric oxide synthase expression.

4. Endothelins

Endothelins are potent vasoconstrictors and Endothelin - I is the primary isoform produced by the human endothelium and its levels are increased in preeclampsia.

VASOACTIVE AGENTS IN PREECLAMPSIA



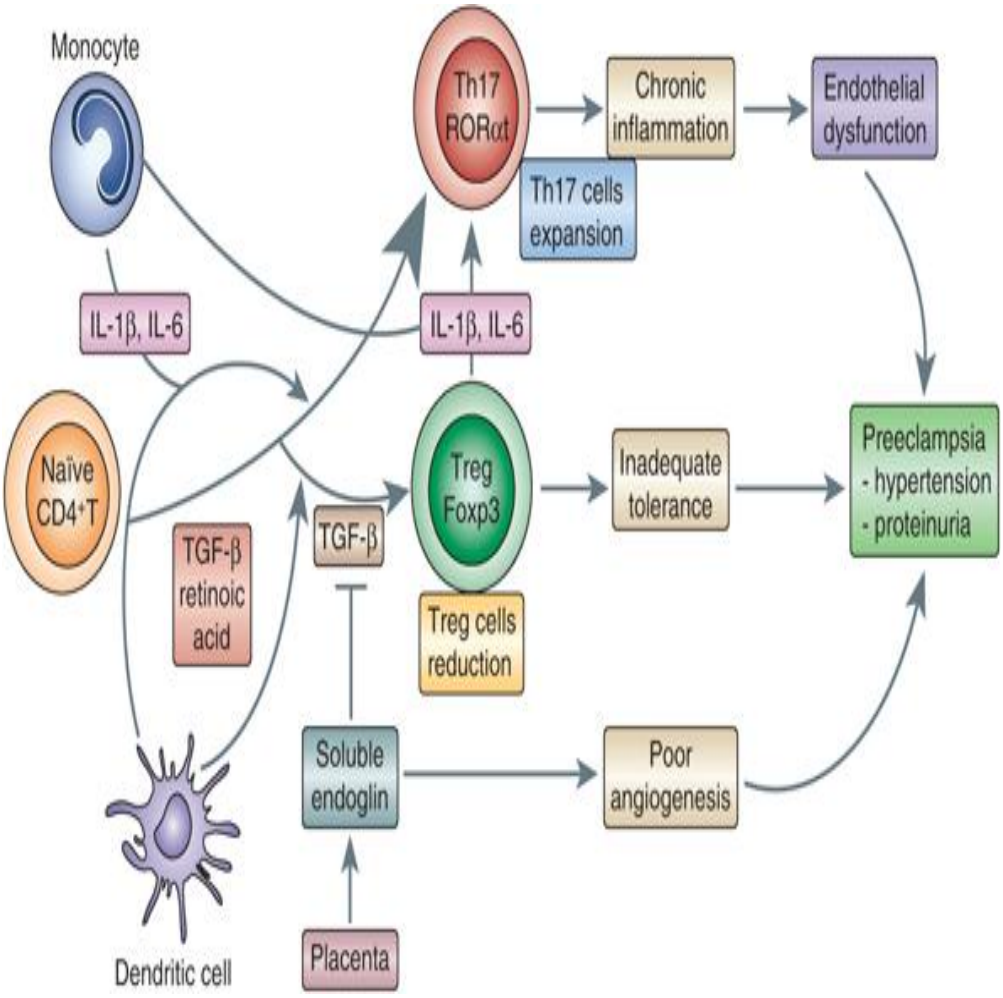
5. Immunological factors

Loss or dysregulation of maternal immune tolerance to paternally derived placental and fetal antigens is another theory cited to account for the preeclamptic syndrome. Inferential datas to suggest an immune mediated disorder include:

i. The risk of preeclampsia is enhanced in circumstances where the formation of blocking autoantibodies to placental antigenic sites might be impaired. In this scenario, the first pregnancy would carry a higher risk .

ii. Tolerance dysfunction might also explain an increased risk when the placental antigenic load is increased, ie., with 2 sets of paternal chromosomes – “a double dose”. For example, higher incidence of preeclampsia is seen in molar pregnancies

iii. Conversely, women previously exposed to paternal antigens, such as a prior pregnancy with the same but not different partner are immunized against preeclampsia.



Immunological Factors

PATHOPHYSIOLOGY

MATERNAL CHANGES IN PREECLAMPSIA

1. Cardiovascular system

a) Haemodynamic changes

i. Increase in maternal cardiac output than increased PVR is the most common haemodynamic feature in mild preeclampsia .However, once preeclampsia becomes severe ,there is a switch to normal or decreased cardiac output and elevated PVR as a manifestation of systemic vasoconstriction.

ii. Extravasation of intravascular fluid into extravascular space with endothelial activation

b. Blood volume

Hemoconcentration is the hallmark of preeclampsia. In patients with established preeclampsia,the average plasma volume is about 9% below expected values and falls by 30-40% in cases of severe preeclampsia. The reduced plasma volume results in haemo concentration as the disease progresses. Hypovolaemia in preeclampsia is particularly associated with growth restriction , oligohydramnios and preterm labour.

2. Hematological system

1. Thrombocytopenia – It is the most commonly identified hematological abnormality in preeclamptic women. Overt thrombocytopenia- platelet count of < 100,000/µl implies severe disease. After delivery it will usually reach normal level in 3 to 5 days.

2. Hemolysis – severe preeclampsia is frequently associated with hemolysis, which is semiquantified by increased serum lactate dehydrogenase levels.

3. HELLP syndrome - In addition to hemolysis and thrombocytopenia, it has also become appreciated that elevated serum hepatic transaminase levels were commonly found with severe preeclampsia and were indicators of hepatocellular necrosis. Weinstein (1992) stated these combination of events as 'HELLP syndrome'

4. Coagulation – Subtle changes consistent with intravascular coagulation are commonly found in preeclampsia and superimposed preeclampsia .

Some of these changes include:

i. Increased Factor VIII consumption

ii. Increased levels of fibrinopeptide and fibrin degradation products

iii. Decreased levels of regulatory proteins – Antithrombin III and protein C and S

iv. Plasma fibrinogen levels do not change much from levels seen in normal pregnancy, unless complicated by abruption.

5. Other clotting factors

i. Hypercoagulability can occur in thrombophilias which are clotting factor deficiencies which is associated with early onset preeclampsia

ii. In preeclamptic women, a glycoprotein called Fibronectin is raised which is associated with vascular endothelial cell basement membrane and so endothelial injury.

3. Volume Homeostasis

a. Endocrine changes

i. Plasma levels of angiotensin II ,rennin and aldosterone levels decrease substantially with preeclampsia despite decreased blood volume

ii. Vasopressin levels are similar to that in normal pregnant women

iii. In preeclamptic women , there is reduced secretion of atrial natriuretic peptide

b. Fluid & electrolyte changes

i. In women with severe preeclampsia, the volume of extracellular fluid, manifesting as edema, is usually greater than that of normal pregnant woman

ii. In preeclamptic women, electrolytes do not differ much with that of normal pregnancy.

4. Kidney

1. Reduced renal perfusion and hence a reduced glomerular filtration rate, probably as a result of increased renal afferent arteriolar resistance.

2. Serum creatinine may rise to values seen in non pregnant individuals, i.e. 1 mg/dl.

3. Plasma serum uric acid concentration is typically elevated in preeclampsia, probably as a result of reduction in glomerular filtration rate and due to enhanced tubular reabsorption.

4. Proteinuria which is non selective and is due to endothelial injury in the glomeruli.

5. Preeclampsia is associated with hypocalciuria as a result of increased tubular reabsorption .

6. Anatomical changes – Glomeruli are diffusely enlarged and are avascular termed as ‘Glomerular capillary endotheliosis’.

5. Liver

1. Anatomical changes – Subcapsular hemorrhages and rarely rupture can occur in preeclampsia. The characteristic lesions are periportal hemorrhages in the periphery of liver.

2. Elevated serum hepatic transaminase levels and LDH which along with hemolysis and thrombocytopenia constitute the HELLP syndrome

6. Brain

In response to severe hypertension , there is overregulation of cerebrovascular system causing vasospasm, ishaemia, cytotoxic edema and eventually tissue infarction. Hyperreflexia and clonus are hallmarks of severe preeclampsia and are due to neurological irritability. Brain may show multiple petechial hemorrhages or larger hemorrhages in the cortex, pons or midbrain. The classic findings are fibrinoid necrosis in the arterial wall and hemorrhages and perivascular microinfarcts microscopically.

7. Visual changes and blindness

Scotoma, blurred vision or diplopia are common with severe preeclampsia or eclampsia. Blindness usually reversible and may arise from three potential regions – visual cortex, lateral geniculate body or retina (ischaemia, infarction or retinal detachment).

PROTEINURIA

Urinary protein excretion in a normal women is approximately 20 – 80 mg/day (with an upper limit being 150mg/day). This is 40 % albumin, 15 – 20 % immunoglobulins and remaining is Tamm Horsfall glycoprotein which is from the tubules and the lower urinary tract

The movement of proteins across the capillary walls in the glomeruli is influenced by the protein size, configuration and charge.

Renal handling of proteins in normal pregnancy

In pregnancy, the renal hemodynamic changes mean that larger amounts of solute and colloids pass through the glomerular barrier. In addition, increased excretion of protein may occur due to changes in permeability of the glomerular membrane and alteration in tubular reabsorption of filtered proteins. The recently accepted upper limit of normal is 300 mg/24 hours for total protein excretion .

Low molecular weight proteins that have similar plasma concentration in pregnant and non pregnant women are measured to demonstrate alteration in tubular reabsorption. These proteins, along with ù-2 microglobuliin ,Retinal Binding Protein are filtered freely by glomerulus .They are compared with albumin whose excretion is

influenced by the size and charge selectivity of the glomerular barrier. Since there is decreased reabsorption in proximal tubule ,there is elevated excretion in uncomplicated pregnancy .

Renal handling of proteins in preeclampsia

Many classifications for the hypertensive disorders of pregnancy have emphasised the progression of proteinuria above a cutoff value of 300 mg/24 hours to differentiate gestational hypertension from preeclampsia which is the cutoff for significant proteinuria.

In preeclampsia, there is alteration in glomerular barrier causing elevated albumin excretion. When the total protein excretion exceeds 1.0 g/24 hours, there will be saturation of tubular reabsorption . When there is retainment of large protein molecules, they are called selective proteinuria and when the ability of the glomerular barrier is lost, they are called non selective proteinuria. In preeclampsia, there will be nonselective proteinuria .

The incidence of proteinuria in most populations is about 10 percent in pregnancy. Causes of Proteinuria includes pregnancy itself, or may be from prepregnancy. However, diagnosis of proteinuria may be done at the time of pregnancy which may be preexisting. Although

prevalency is less, primary renal disease or secondary disorders like essential hypertension or diabetes may present with proteinuria in pregnancy.

Proteinuria and clinical outcome

From a clinical perspective, over-estimating or over-diagnosing preeclampsia is preferable to under-estimating or under-diagnosing the condition, as the timing of delivery is among the most important components of management protocol. The prognosis of preeclampsia depends on the severity of the disease, period of gestation and response to treatment. Increased maternal mortality is mainly related to eclampsia, abruption ,renal failure, pulmonary edema, DIC and HELLP syndrome. Risk of placental abruption in preeclamptic women ranges from 5-20% and women with HELLP syndrome , the risk of preeclampsia in subsequent pregnancy is about 20%.Also there is increased risk of growth restriction in fetus and perinatal mortality of about 20%

Page et al., reported that in patients with significant proteinuria and hypertension there is increase in still births, growth restriction in fetus and perinatal morbidity, in a prospective study .

Ferrazzani et al. in a study containing 444 antenatal women with hypertension with proteinuria as 1+ by dipstick or 0.3g/l, found increased serum uric acid levels, low birth weights, and more pretem deliveries , if there is associated proteinuria .

It is the presence of proteinuria that has got an adverse maternal or fetal outcome and it is not the severity or the degree of proteinuria .

Waugh et al. studied among 197 antenatal women and found that the threshold of 500 mg/24 hours and not 300mg/day was predictive of the adverse outcome.

ASSESSMENT OF PROTEINURIA

All antenatal women are screened routinely for proteinuria at their first visit and then at regular intervals by dipstick test. Significant proteinuria is precluded clinically if there is negative result; but further investigation is necessary, if the test is positive.

Heat coagulation test

3 – 4 drops of acetic acid is added to the urine after heating. Results are subjective and grading is done which depends on the turbidity. And so, they have higher number of false positive and false negative results.

Dipstick test

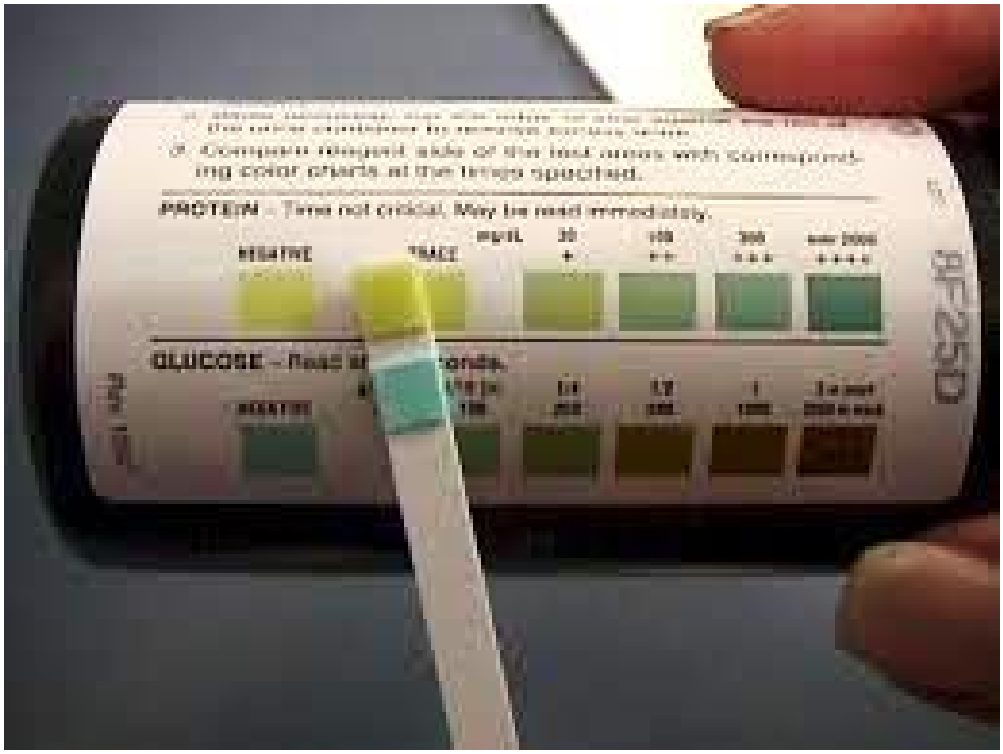
The most commonly used test to identify proteinuria is a urine dipstick.This test is done on the first morning urine specimen, as it will be more concentrated and usually doesnot get influenced by postural factors. They are albumin sensitive than other plasma proteins. A buffered indicator is coated on the reactive portion of the dipstick where colour changes occurs when there is proteinuria and a time of 60 seconds should be taken to read the test.

It is graded as follows :

Trace	0.1g/l
1+	0.3g/l
2+	1g/l
3+	3g/l
4+	10g/l

Testing in dipstick is, however, has increased false positive results that may be because of highly concentrated specimen (specific gravity of more than 1.030), alkaline urine, contamination with antiseptics like chlorhexidine or quaternary ammonium compounds or vaginal discharge. Also very dilute urine (specific gravity of less than 1.010) causes false negative results.

Urine Dipstick Analysis



PROTEINURIA- QUANTITATIVE ASSAY

Further evaluation is required for persistent proteinuria in dipstick. Quantitative assay of proteinuria is usually done on timed collections, usually a 24 hour urine specimen.

24 hour urine collection

The 24 hours of urine collection for estimation of proteinuria is the gold standard in diagnosis of proteinuria in preeclampsia. Eventhough it is a reliable quantifier of proteinuria, it is cumbersome and time consuming, which is subjective to collection error and also it requires good compliance from patients. Further, there is a delay in diagnosis till the time of collection.

Dipstick analysis and 24 hour urine protein excretion

The relative less cost and a simple, ease technique is the main reason for its dependence upon the dipstick test . It is believed that 1+ proteinuria by dipstick corresponds to 300 mg/day total protein excretion. There are many studies which analysed the relationship between semiquantitative dipstick urine analysis on random urine samples and subsequent collection of 24 hour urine sample.

In Meyer et al. study, false negative dipstick result was seen in 66% women among 300 hypertensive women, if significant proteinuria was considered as ≥ 300 mg/24 hours. In the same study,26% false positive rate was found at the 1+ level .

In a Brown et al.study, they found a 8-18% false negative result and a false positive rate of 67 % which is very high with 1+ score. They suggested that the dipstick is highly sensitive at the 1+ level and so it may be useful for the preeclampsia management as it minimizes the false negative results

Waugh et al.'s study on hypertensive women, inspite of significant proteinuria had a high false negative rate of 65 % in women with < 1+ proteinuria on dipstick analysis.

All these suggest that the correlation between 24 hour protein estimation and dipstick urinalysis is at its best imprecise. Over investigation and intervention may be due to false positive results whereas false negative result may be a potential threat to pregnant woman .

The review of literature thus shows there is poor accuracy of dipstick test by using a threshold to predict significant proteinuria. However, it is not possible to remove dipstick urinalysis from antenatal care and if so ,a viable alternative test is necessary to replace it.

Protein to creatinine ratio in spot urine samples

A good correlation was reported in the measurement of protein to creatinine ratio in random samples with subsequent 24 hour estimation of urine protein in non pregnant populations (kidney transplants, renal disease and diabetes). Also a strong correlation was found between spot protein creatinine ratio and 24 hour protein excretion collected subsequently in preeclamptic population.

A protein to creatinine ratio of < 0.3 is said to be within normal limits and a protein to creatinine ratio of > 3.5 represents nephrotic range of proteinuria in the presence of a normal renal function test. Studies

reasoned out that the ratio of two stable excretion rates (protein and creatinine) minimize the time consumed, thus it provides a faster estimate of 24 hour protein excretion .

Leanos-Miranda et al. from their cross-sectional study of 927 hospitalised pregnant women with suspected preeclampsia and 161 pregnant women in whom hypertensive disorders of pregnancy was ruled out for comparison, found that the protein to creatinine ratio and the 24 hour protein excretion had significant correlation ($p < 0.001$, $r = 0.98$). The protein to creatinine ratio as a threshold of protein excretion of $\geq$ 300 mg/24 hours was ≥ 0.3. They concluded that protein to creatinine ratio can be a good alternative to the 24 hour urine collection method

In a study by Shahbazian et al. among 81 pregnant women with preeclampsia, a good correlation between the spot protein to creatinine ratio and 24 hour urine protein excretion was seen.($r = 0.84$, $p < 0.001$). The optimal spot protein to creatinine ratio cut off point was 0.20 for 300 mg/24 hours of protein excretion, with a sensitivity and specificity of 91.2% and 87.8% respectively. Positive predictive value and negative predictive value were 94.4 % and 96.8 %, respectively.

In another study by Nisell et al., there was a excellent correlation between the albumin to creatinine ratio and twenty four hour albumin excretion values ($p < 0.001, r=0.95$) and they concluded that in most cases, the more convenient protein -creatinine ratio can be an alternative to 24 hour urine collection which is cumbersome.

Papanna and colleagues in a systematic review, concluded that the random urine protein to creatinine ratio are primarily helpful when they are below 130 – 150 mg/g, in that 300 mg or > proteinuria is unlikely below this threshold.

In Wheeler et al. study, though random spot urine protein to creatinine ratio was strongly correlated with the 24 hour urine protein levels ($r = 0.88$), it was concluded that the use of spot protein to creatinine ratio was not justified as a substitute for timed collection .

In a systematic review, Cote et al. concluded that the spot protein to creatinine ratio is a good "rule out'' test to detect proteinuria of 0.3 g/day or more in preeclampsia .

Durnwald and Mercer in their study among 220 women found a poor correlation between the spot urine protein to creatinine ratio and 24

hour urine protein (r2 = 0.41) and it cannot be a replacement for 24 hour total protein excretion .

Ray Rabindranath et al study concluded that spot urine P/C ratio can be used as a convenient, quick , accurate diagnostic test for significant proteinuria estimation in patients with preeclampsia.

So the clinical use of urine protein to creatinine ratio as a substitute of 24 hour urinary protein excretion for detecting significant proteinuria still remains unclear. Though some researchers have suggested the use of spot urine protein to creatinine ratio, there are also reports with controversial results.

In this study, the correlation between the spot urine protein to creatinine ratio and 24 hour urine protein excretion in patients being evaluated for preeclampsia has been studied

RESULTS AND ANALYSIS

Table 1: Age distribution of subjects

Age in years	Frequency	Percent
18-20	27	18.0
21-25	71	47.3
26-30	47	31.3
31-40	5	3.3
Total	150	100.0

In this study , it was noticed that majority (47.3% + 31.3%) of the 150 subjects were in the age group of 21-30 years (Fig .1)

Fig.1 Age distribution of subjects with preeclampsia

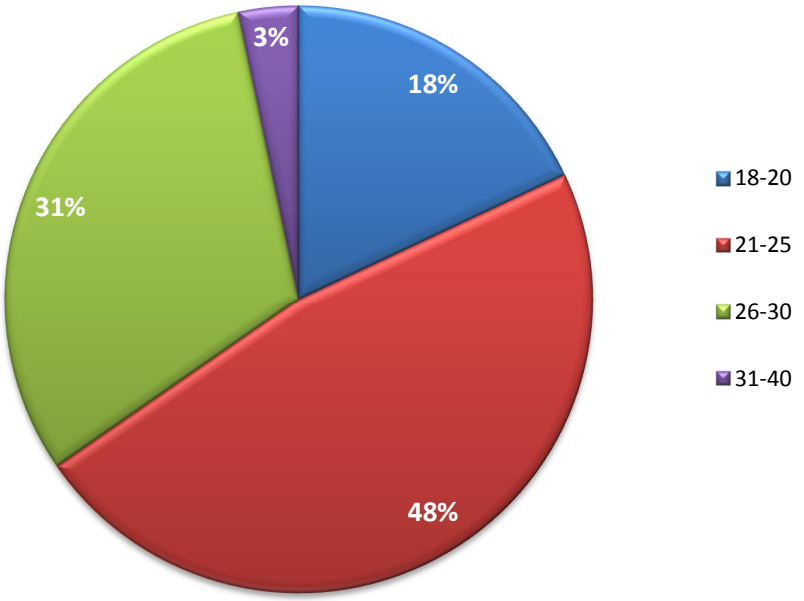


Table 2: Paritywise distribution of subjects

Parity	Frequency	Percent
Primi	100	66.7
Multi	50	33.3
Total	150	100.0

It is observed in this study that the incidence of preeclampsia in primigravida was 66.7 % and multigravida was 33.3%(Fig 2)

Figure 2 Paritywise distribution of subjects

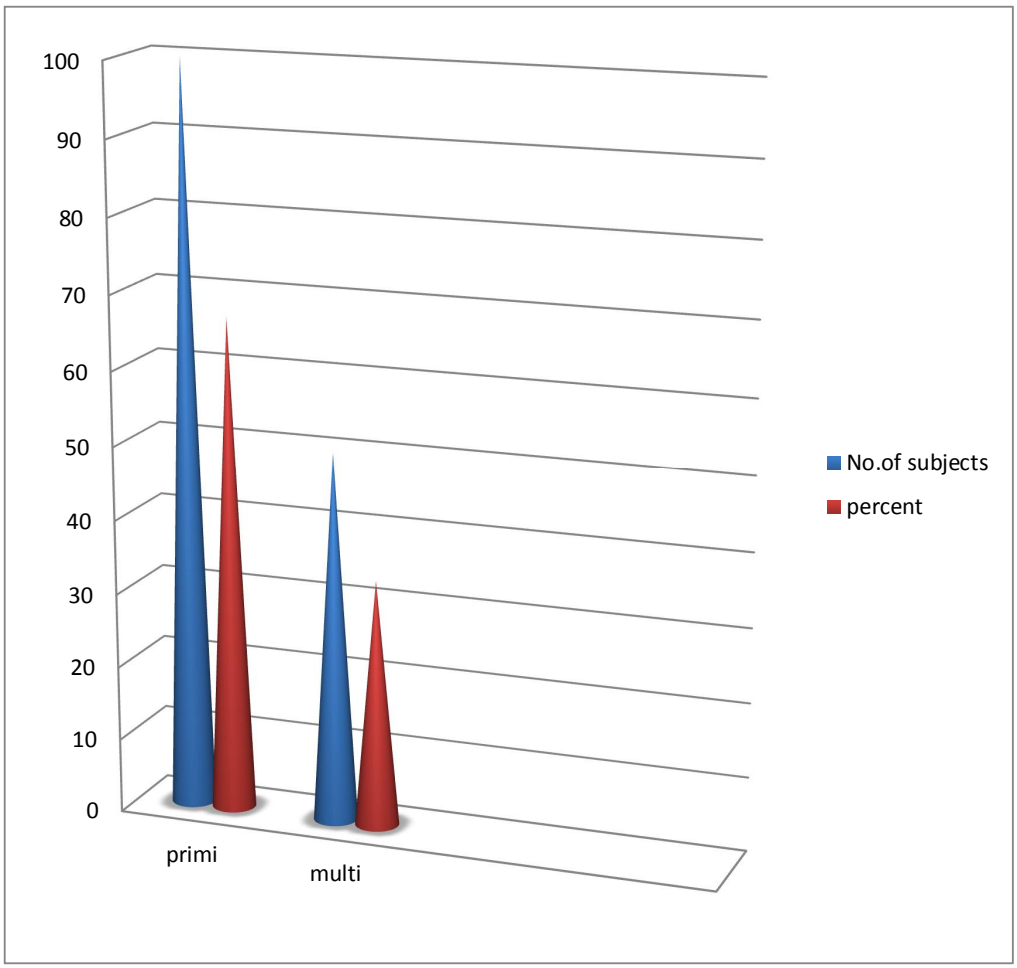


Table 3: Distribution of subjects as per gestational age

Gestational age(wks)	Frequency	Percent
<= 28	12	8.0
29-36	97	64.7
> 36	41	27.3
Total	150	100.0

It was observed that out of 150 subjects majority (64.7%) were between 28-36 weeks.(Fig 3)

Figure 3 : Distribution of subjects as per gestational age

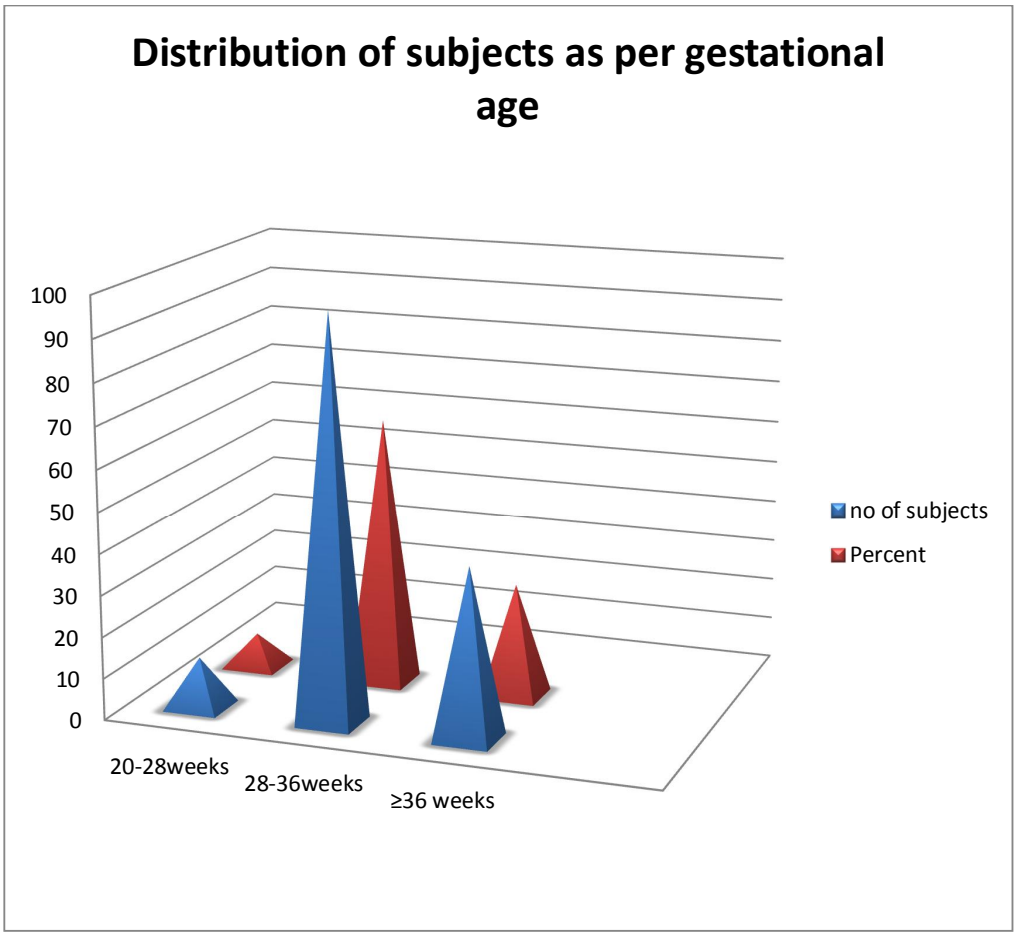


Table 4: Summary statistics of different parameters

	N	Minimum	Maximum	Mean	Std. Deviation
Age in years	150	18	38	24.30	3.727
Sys.BP in mm of Hg	150	130	160	143.01	8.250
Dia. BP in mm of Hg	150	80	110	92.68	5.879
Gestational Age in weeks	150	24	40	34.75	3.173
24 Hours urine protein in mg/day	150	58	3550	549.02	476.084
Protein creatinine ratio	150	.0	8.3	.815	.9535

N- Number of subjects

Table 5: comparison of urinary dipstick against 24 hours urine protein

DIPSTICK		24 HUP			Total	P value
		<= 300	301-2000	> 2000		
1+	Count	49	55	0	104	<0.001**
	% within DIP	47.1%	52.9%	.0%	100.0%	
	% within 24 HUP	90.7%	58.5%	.0%	69.3%	
2+	Count	5	38	2	45	
	% within DIP	11.1%	84.4%	4.4%	100.0%	
	% within 24 HUP	9.3%	40.4%	100.0%	30.0%	
3+	Count	0	1	0	1	
	% within DIP	.0%	100.0%	.0%	100.0%	
	% within 24 HUP	.0%	1.1%	.0%	.7%	
Total	Count	54	94	2	150	
	% within DIP	36.0%	62.7%	1.3%	100.0%	
	% within 24 HUP	100.0%	100.0%	100.0%	100.0%	

The box plot analysis of 24 hour urine protein extraction at different dipstick readings(Fig 4) showed that at dipstick reading of 1+, the median line is almost in the centre of the box, indicating more or less normal distribution of these values. However at the dipstick value of 2+, there is a skewed distribution.

Figure 4 : Box plot analysis of 24 hour urine protein excretion at different dipstick values

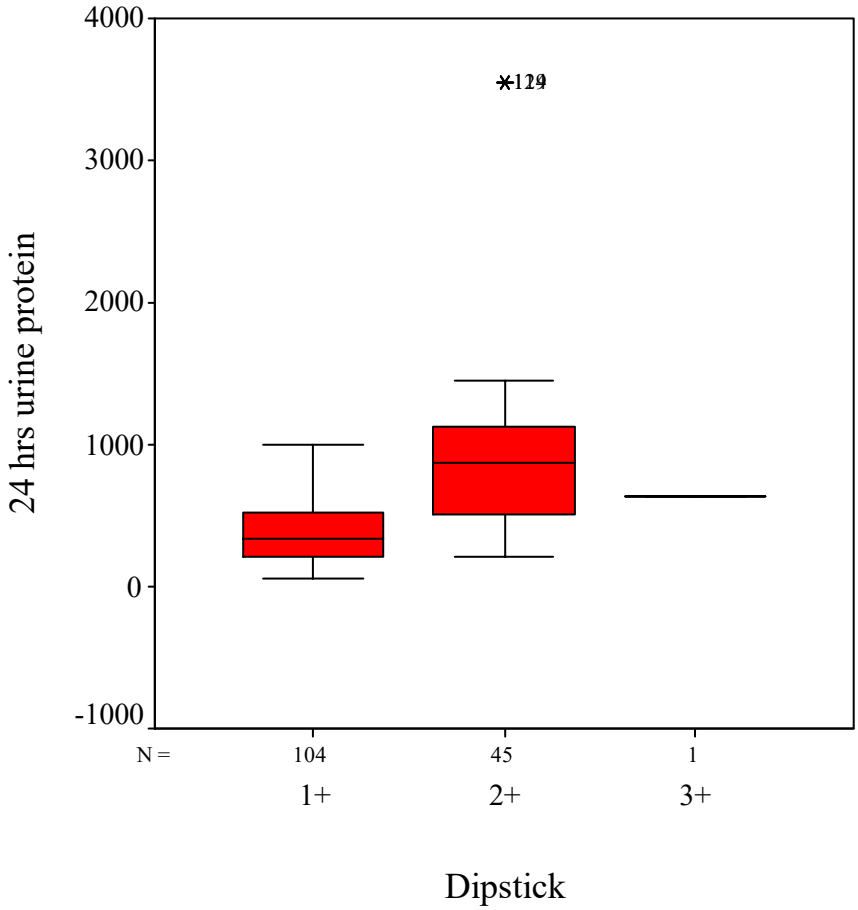


Figure 5 : comparison of urinary dipstick against 24 hours urine protein

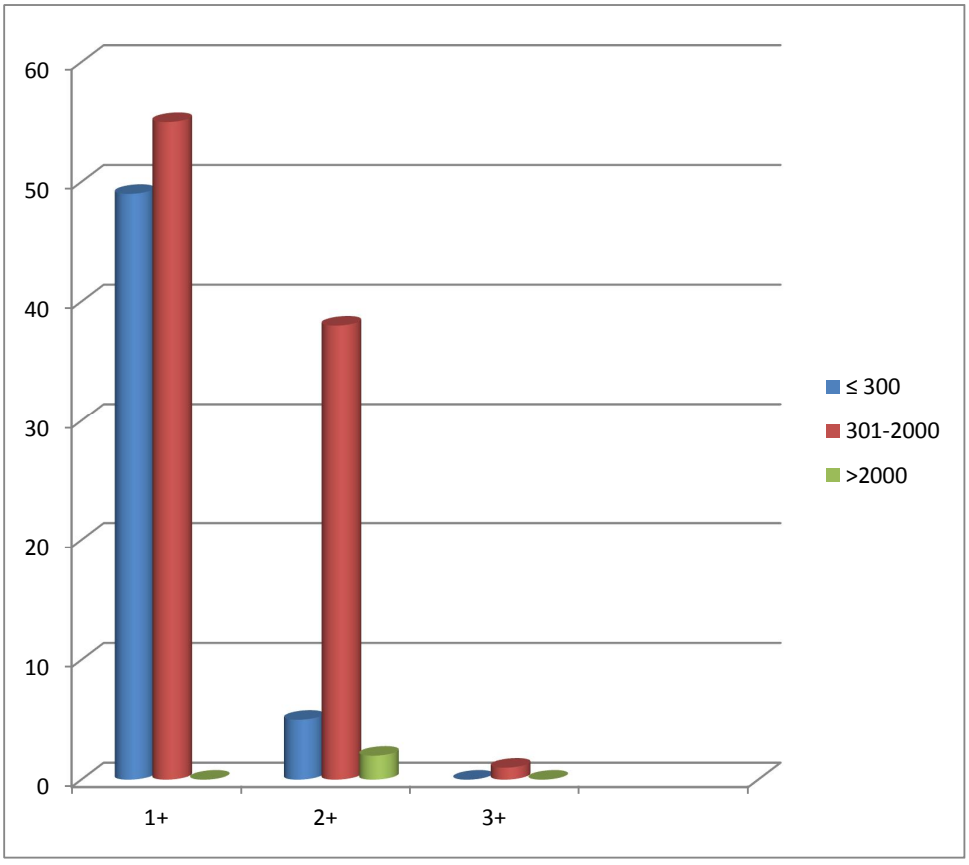
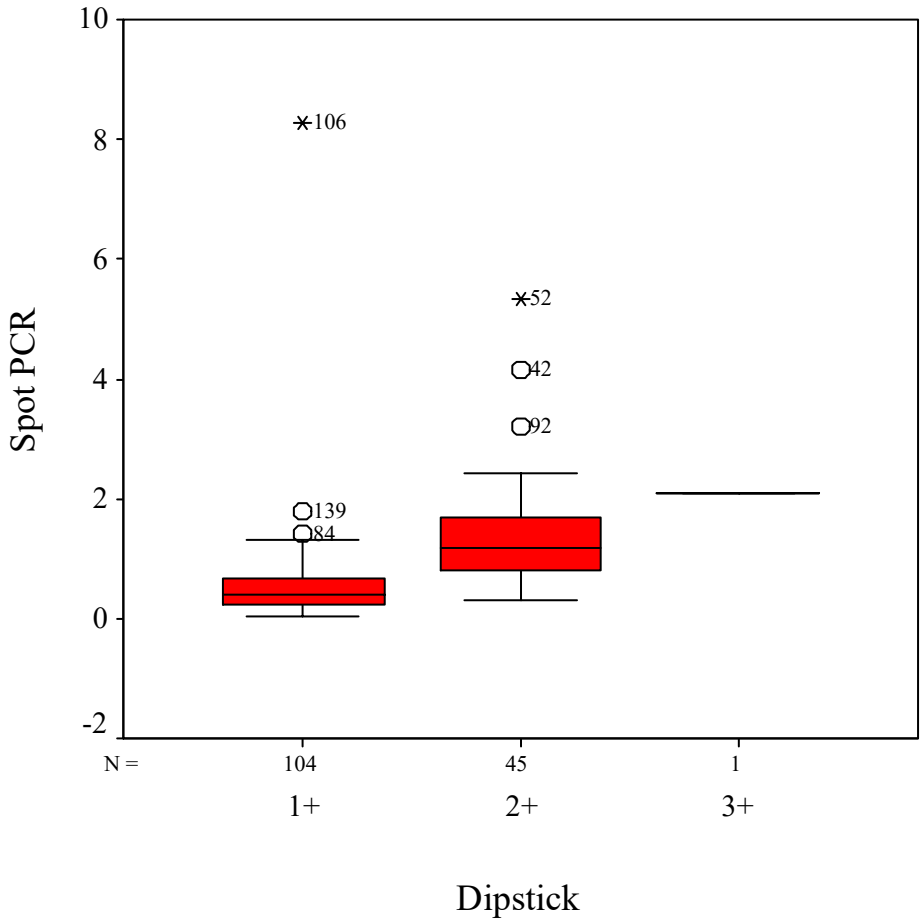


Table VI : Comparison of urinary dipstick against protein creatinine ratio

			Spot PCR		Total
			< 0.3	**> 0.3**	
DIPSTICK	1+	Count	42	62	104
		% within DIP	40.4%	59.6%	100.0%
		% within Spot PCR	100.0%	57.4%	69.3%
	2+	Count	0	45	45
		% within DIP	.0%	100.0%	100.0%
		% within Spot PCR	.0%	41.7%	30.0%
	3+	Count	0	1	1
		% within DIP	.0%	100.0%	100.0%
		% within Spot PCR	.0%	.9%	.7%
Total		Count	42	108	150
		% within DIP	28.0%	72.0%	100.0%
		% within Spot PCR	100.0%	100.0%	100.0%

The box plot analysis of spot protein creatinine ratio at different dipstick readings (Fig. 6) showed that the distribution of spot protein creatinine ratios is skewed at 2+ dipstick reading and more values were in the upper quartile of the median. However the degree of skewness was less in the dipstick value of 1+.

Figure 6 : Box plot analysis spot protein creatinine ratio at different dipstick values



Comparison of urinary dipstick against protein creatinine ratio

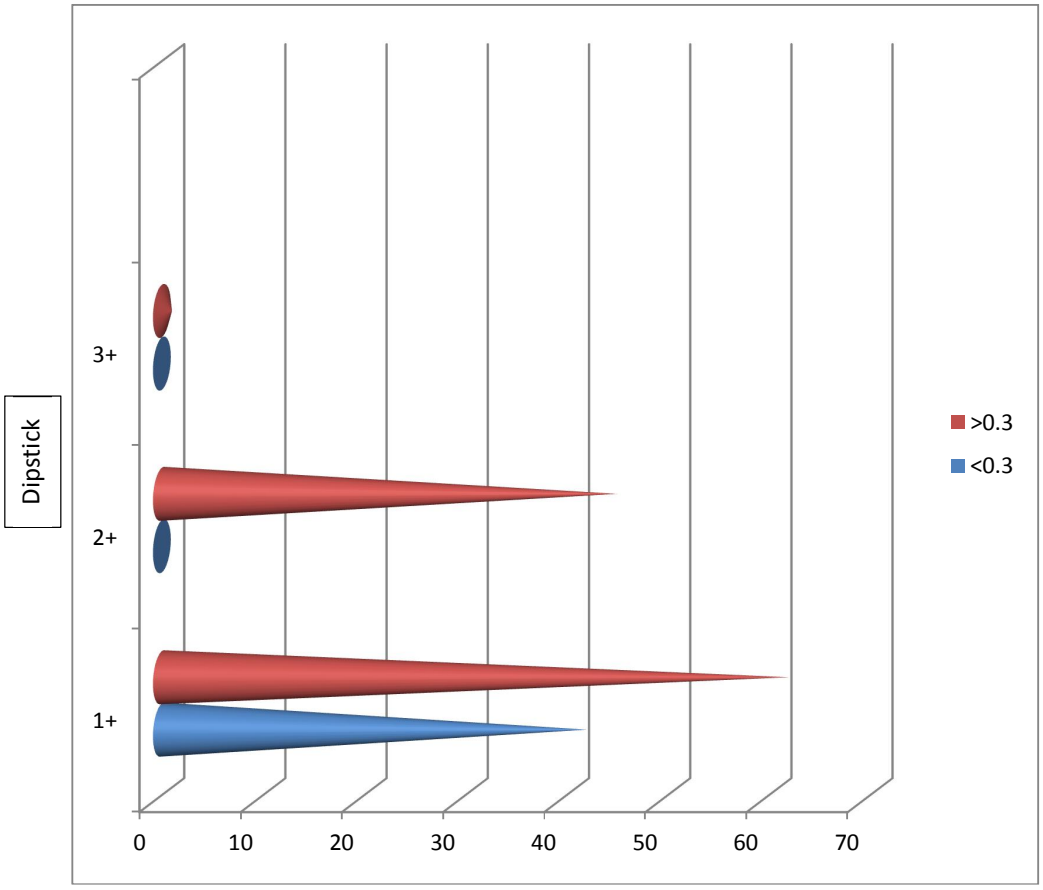


Table VII : Comparison of 24 hour urine protein and spot urine protein creatinine ratio

			Spot PCR		Total	P value
			< 0.3	**> 0.3**		
24 HUP	<= 300	Count	38	16	54	**<0.001**
		% within 24 HUP	70.4%	29.6%	100.0%	
		% within Spot PCR	90.5%	14.8%	36.0%	
	301-2000	Count	4	90	94	
		% within 24 HUP	4.3%	95.7%	100.0%	
		% within Spot PCR	9.5%	83.3%	62.7%	
	> 2000	Count	0	2	2	
		% within 24 HUP	.0%	100.0%	100.0%	
		% within Spot PCR	.0%	1.9%	1.3%	
Total		Count	42	108	150	
		% within 24 HUP	28.0%	72.0%	100.0%	
		% within Spot PCR	100.0%	100.0%	100.0%	

A good correlation of r = 0.469** (** Correlation is significant at the 0.01 level) was observed between the 24 hours urine protein and spot urine protein-creatinine ratio among the 150 subjects, which was significant at a P value of < 0.001

Figure 7 : Comparison of 24 hour urine protein and spot urine protein creatinine ratio

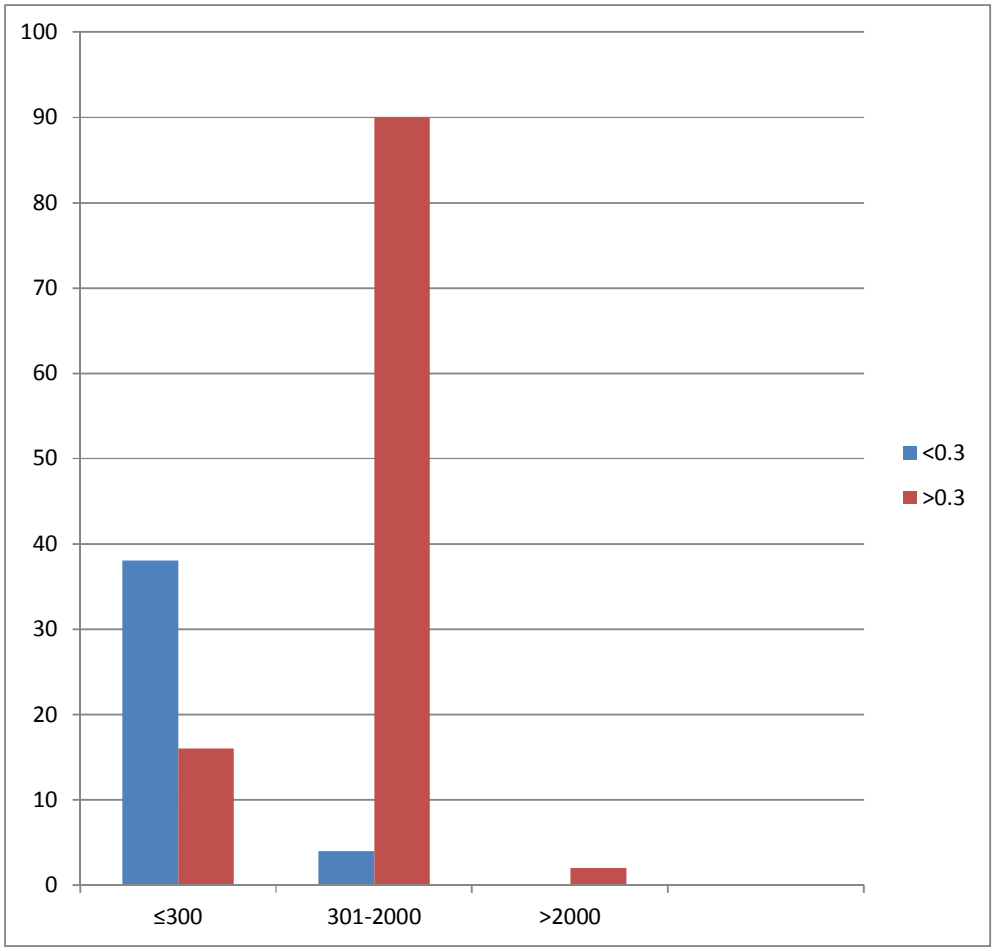


Figure 8: Scatter plot showing the distribution of 24 hour urine protein (mg) and spot urine protein creatinine ratio (all values)

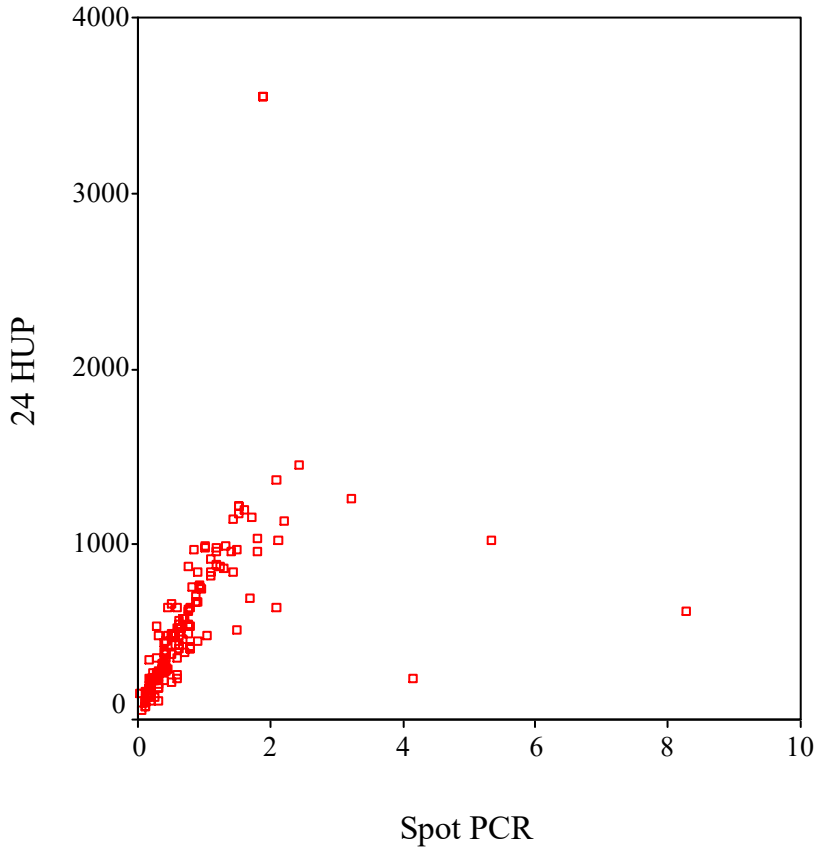
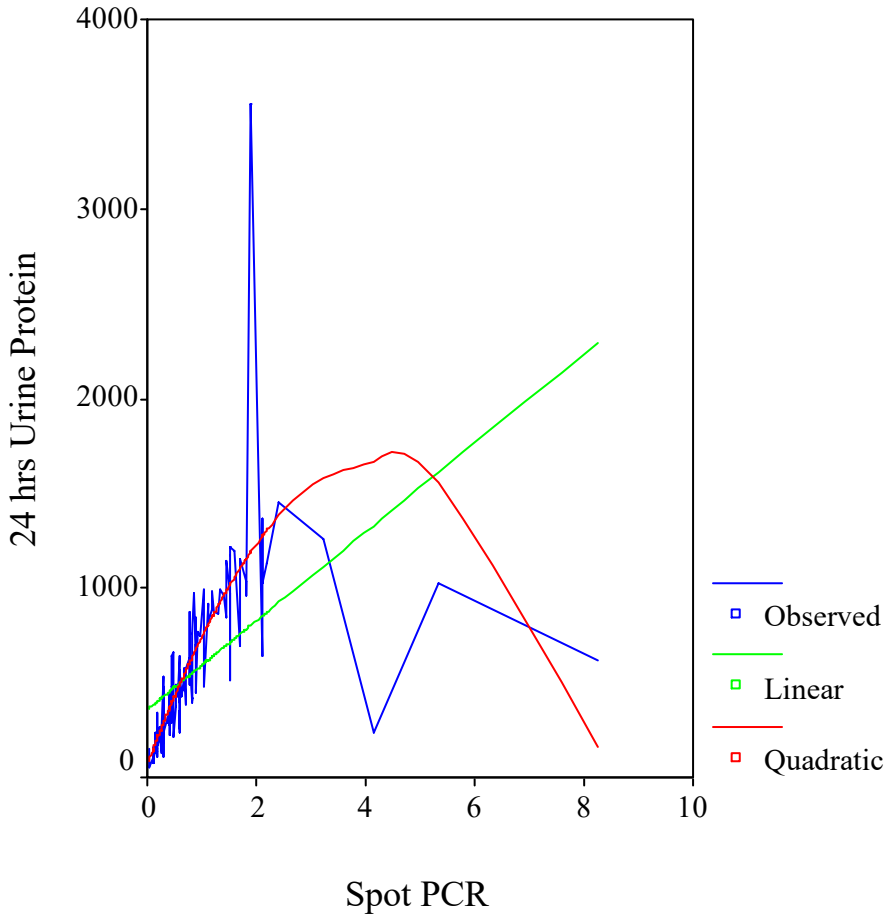


Figure 9 : Graph showing linear and quadratic relationship between spot urine protein ratio and 24 hour urine protein



When only the data for 24 hours urine protein < 2000 is analyzed, the simple linear correlation between 24 hours urine protein and spot urine protein creatinine ratio a shows better linear relationship (Fig. 9) and the P value is highly significant at 0.001 probability level. This is also illustrated by the linear and quadratic relationship between spoturine protein creatinine ratio and 24 hour urine protein as well as the observed values.

With the protein creatinine ratio of 0.3 taken as the threshold to detect significant proteinuria, the sensitivity and specificity were 95.7% and 90.5% respectively and the positive and negative predictive value were 83.3% and 100% respectively.

DISCUSSION

One of the frequently undertaken laboratory procedure is the quantification of proteinuria. Evaluation of hypertensive pregnant women is mandatory to establish the diagnosis and severity of preeclampsia. Twenty four hour urinary protein excretion , however, is considered to be inconvenient, cumbersome and subjective to collection errors .

This study was done to evaluate the correlation between twenty four hour urinary protein excretion and spot protein creatinine ratio on random urine samples and to determine its accuracy. A faster and more accurate test may avoid the patient's inconvenience and this will also avoid the delay in diagnosis and management.

This study was limited to the hospitalized nonambulatory patients. Postural changes influence the excretion of proteins. Excretion is more in the standing than in supine position and so the ambulatory status of the patient is important while interpreting the results.

In this study of 150 preeclamptic women, the sociodemographic variables shows that the peak age range was 21 – 30 years with the mean age being 24.30 years. The peak age of 21-30 years may be reflective of the fact that most first deliveries occur at that age and not necessarily of an special contribution of this age bracket to the etiology of the disease.

Primigravidae contributed the commonest parity (66.7%). Primigravidae was reported to be at high risk of developing preeclampsia. The mean gestational age of the patients under study was 34.75 weeks.

When the random urine protein creatinine ratios and the 24 hour urine protein were correlated,a good correlation was found, with correlation relation coefficient, $r = 0.469$ and p value at < 0.001 which is highly significant, when all the observations were considered.

Boler and associates analysed the two parameters among 54 patients. They found an excellent correlation ($r = 0.9935$, $p < 0.001$) between the two for normal pregnancies, multiple gestation and hypertensive pregnancies. They however did not mention the number of patients with preeclampsia. Similarly, Jaschevatzky study and associates on 70 healthy patients and 35 preeclamptic patients found better correlation ($r = 0.9278$, $p < 0.001$) between 24 hour proteinuria and

random urinary protein creatinine ratio. However, there is decreased degree of correlation in patients with proteinuria greater than 2 g. In both the studies, the sample size was smaller than in this study, and predictive values of the tests were not available.

In a study by Torng et al in 2001 to determine whether urine protein/creatinine ratio can be used as a predictor for 24 hour protein excretion in transplant patients, a good correlation could be established between the two variables at 0.5 – 2.0 g/day of proteinuria. But the precision and positive predictive value decreased as proteinuria increased >3g/day.

Careful interpretation of the results must be done specifically when decisions are made on the results since there is variation at severe degrees of proteinuria.

Out of 150 patients, only 2 patients had proteinuria greater than 2 g/24 hours. A poor degree of correlation at severe degrees of proteinuria could probably be due to the low prevalence of subjects with this range of proteinuria.

Given below is a table which shows the results of some similar studies in comparison with the present study.

Studies	**Correlation coefficient(r)**	**p-value**
Nissel et al	0.95	<0.001
Yamasmit et al	0.929	<0.001
Robert et al	0.94	<0.001
Boler et al	0.99	<0.001
Rodriguez – thompson et al	0.80	<0.001
Young et al	0.80	<0.001
Jaschevatzky et al	0.92	<0.001
Shahbazian et al	0.84	<0.001
Bansal et al	0.83	=0.000
Present study	0.469	<0.001

Future research should be focused on the cost effectiveness of the use of a spot urinary protein creatinine ratio for prediction of significant proteinuria and the evaluation of clinical outcomes. In addition, applying the test in an ambulatory outpatient basis should be further suggested in management of preeclamptic patient.

SUMMARY

The objective of this study is to know if a spot urinary protein/creatinine ratio would provide an accurate estimation of proteinuria and whether it could replace the use of the 24 hour urinary protein in preeclamptic women.

One hundred and fifty women with pre-eclampsia were recruited for this study. Patients with normal renal function was ascertained by estimating blood urea and serum creatinine levels. Instructions were given to the patients to collect the twenty hour urine initiating from the second urine sample in the morning to the first urine sample in the next day morning. A single voided urine specimen was obtained before the start of 24 hour collection to determine protein/creatinine ratio. The urine protein was measured using sulphosalicylic acid method. Urine creatinine was measured using modification of Jaffe's reaction which is commonly used to estimate creatinine.

Urine protein (mg/ml) was divided by urine creatinine (mg/ml) to obtain the ratio. Statistical method used was the Pearson's correlation coefficient.

In our study results were:

- A good correlation existed between the two variables with r = 0.469 with a highly significant p value = <0.001 when all the observations were considered.

- The correlation at high levels of proteinuria was very poor, hence the protein/creatinine ratios at severe degrees of proteinuria must be interpreted carefully.

CONCLUSION

Since the urinary protein excretion level has important clinical implications in the course of pregnancy, it is necessary to detect earlier even the smaller degrees of hyperproteinuria.

Dipstick analysis as a screening for proteinuria lacks reliability due to higher rate of false positives.

For years, 24 hour urine collection has been the gold standard to quantify proteinuria in managing a preeclamptic women. However, this method of quantification is inconvenient,cumbersome,incomplete due to collection errors, needs good compliance from the patient and results in the delayed diagnosis of > 24 hours till the time of collection. The value of the protein/creatinine ratio in a single random urine sample has potentially greater accuracy, as it avoids collection errors and gives us more physiologically relevant information.

Cost effectiveness and acceptability by the patient with good compliance makes spot protein creatinine ratio as an effective alternative in quantitating proteinuria .

Since preeclampsia is a progressive disorder affecting multiorgans, repeated laboratory examinations to quantitate proteinuria is necessary. Spot Protein/creatinine ratio would be a superior diagnostic tool when compared to the routine urinalysis which would otherwise be used for routine quantitation of proteinuria.

We conclude that a spot urine protein creatinine ratio has greater accuracy in predicting the amount of 24 hour urinary protein excretion based on the present study. This test could be a reasonable alternative to the 24 hour urine collection for detection of significant proteinuria in hospitalized antenatal women with suspected preeclampsia.

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PROFORMA

NAME :

AGE :

IP. NO. :

ADDRESS :

LMP :

EDD :

GESTATIONAL AGE :

PARITY :

ANY H / SUGGESTIVE OF PREECLAMPSIA :

H / O PREECLAMPSIA IN PREVIOUS PREGNANCIES :

FAMILY H / O PREECLAMPSIA :

H / O HYPERTENSION/RENAL DISORDERS / DIABETES / UTI

MEDICATIONS:

ANTIHYPERTENSIVES :

GENERAL EXAMINATION :

HEIGHT

WEIGHT

ANEMIA

ICTERUS

EDEMA

PULSE

BP

CVS

RS

OBSTETRIC EXAMINATION :

URINE MICROSCOPY :

URINE PROTEIN BY DIPSTICK TESTING :

24 HOUR URINARY PROTEIN :

SPOT PROTEIN CREATININE RATIO :

BLOOD UREA :

SERUM CREATININE :

HEMATOCRIT :

PLATELET COUNT :

LIVER FUNCTION TEST :

FUNDUS EXAMINATION :

USG:

DOPPLER (WHEREVER INDICATED) :

S.NO	NAME	AGE	IP NO	PARITY	SYS BP	DIAS BP	GEST AGE	DIP STICK	24 HUP	SPOT PCR
1	THUYAMATHI	25	9398	PRIMI	150	90	37	1+	275	0.4
2	EZHILARASI	29	9431	G2P1L1	140	90	36	2+	405	0.8
3	SUGANYA	19	9462	PRIMI	150	100	38	1+	260	0.6
4	KAVITHA	20	9402	G2A1	130	90	36	1+	340	0.18
5	HEMALATHA	19	9433	PRIMI	140	100	28	2+	580	0.72
6	LALITHA	25	9471	G3A2	150	90	36	2+	688	1.7
7	DHANALAKSHMI	27	9458	G2P1L1	150	94	27	1+	760	0.92
8	SANGEETHA	22	9516	PRIMI	150	100	34	1+	520	0.61
9	POOJA	23	9527	PRIMI	140	90	36	1+	844	0.9
10	JAYASHREE	22	9248	G3P1L1A1	140	90	33	2+	970	1.5
11	NITHYA	23	9693	G2P1L1	130	100	36	2+	544	0.61
12	MANASA	20	9761	G2A1	140	100	33	3+	640	2.1
13	SHANTHAKUMARI	25	9778	PRIMI	150	90	37	1+	660	0.5
14	DURGADEVI	22	9704	PRIMI	136	90	34	1+	103	0.1
15	CHANDAKUMARI	25	9778	PRIMI	130	94	34	1+	145	0.02
16	RENUKA	28	9836	G2P1L1	140	100	33	2+	920	1.1
17	RIYANA	30	9823	G3A2	150	96	36	1+	522	0.66
18	ANANDHI	28	9876	G3P1L1A1	140	100	35	2+	640	0.8
19	JANAKI	31	9880	PRIMI	150	100	32	2+	534	0.8
20	ANITHA	23	9915	G2A1	130	90	37	1+	78	0.1
21	EZHILARASI	19	9929	PRIMI	144	100	36	2+	453	0.9
22	ANITHA	28	9660	G2P1L1	130	100	34	1+	414	0.8
23	BRINDHA	30	9992	PRIMI	150	110	34	2+	990	1.02
24	UMA MAHESHWARI	23	10006	PRIMI	140	96	36	2+	1020	2.12
25	JAYALAKSHMI	23	9906	PRIMI	160	100	32	2+	1132	2.2
26	DEEPA	30	10046	PRIMI	160	90	34	1+	963	1.2
27	FAMIDHA BANU	21	10071	PRIMI	160	100	33	1+	630	0.76
28	ESWARI	27	10054	G2P1L1	150	104	36	2+	984	1.02
29	SELVI	27	10075	G2A1	140	110	34	1+	640	0.58
30	ANNAL	24	10086	PRIMI	160	100	33	1+	756	0.92
31	MENAKSHI	28	10095	G2P1L1	150	100	35	1+	386	0.4

S.NO	NAME	AGE	IP NO	PARITY	SYS BP	DIAS BP	GEST AGE	DIP STICK	24 HUP	SPOT PCR
32	PREETHA	20	10114	PRIMI	150	90	34	1+	482	0.52
33	LAKSHMI	25	10113	G2P1L1	160	90	38	1+	482	0.3
34	VIJAYA	23	10115	PRIMI	140	100	36	2+	960	1.4
35	SANGEETHA	20	10172	PRIMI	134	96	34	1+	110	0.3
36	SUGUNA	24	10236	PRIMI	140	90	36	1+	220	0.4
37	SUGANYA	25	10227	PRIMI	134	94	33	2+	380	0.7
38	GOMATHI	24	10317	PRIMI	150	90	37	1+	104	0.2
39	MUTHULAKSHMI	38	10423	G2P1L1	130	90	32	1+	180	0.3
40	UMA MAHESHWARI	27	10477	PRIMI	140	94	35	1+	320	0.4
41	RANI	25	10552	G3A2	144	100	33	2+	211	0.5
42	VENKATASUGANYA	24	10541	PRIMI	150	100	33	2+	230	4.14
43	PRIYA	21	10684	PRIMI	140	90	38	1+	110	0.1
44	RUKMANI	22	10691	PRIMI	160	100	35	2+	350	0.6
45	SELVI	27	10680	PRIMI	150	90	36	1+	420	0.8
46	BANUMATHI	21	11801	PRIMI	150	100	35	2+	510	1.5
47	RUBY	23	11778	PRIMI	146	94	30	1+	80	0.1
48	DHARMADEVI	23	11741	G2P1L1	130	90	38	1+	58	0.05
49	YASMIN	22	11748	PRIMI	154	100	31	2+	240	0.6
50	SHREESHA	23	11746	PRIMI	160	90	28	2+	400	0.8
51	ROJA	20	11732	PRIMI	140	90	36	1+	98	0.12
52	ANITHA	24	11717	PRIMI	144	90	28	2+	1020	5.33
53	AMARAVATHI	26	11701	G2P1L1	130	90	34	1+	155	0.1
54	MUNEESHWARI	26	11616	G3P1L1A1	150	86	34	1+	456	0.67
55	DIVYA	24	11564	PRIMI	140	90	34	1+	620	0.77
56	GANGAMMAL	18	11887	PRIMI	130	90	36	1+	188	0.19
57	GOKILAVANI	30	11566	G2P1L1	150	90	39	1+	440	0.39
58	BHARATHI	24	11543	PRIMI	140	90	24	1+	235	0.22
59	LAKSHMI	25	11531	G2P1L1	130	90	40	1+	175	0.19
60	RAMAYEE	30	11540	PRIMI	140	86	34	1+	242	0.3
61	MOHINI	23	11542	G2A1	140	90	34	1+	268	0.27
62	SARANYA	25	11480	PRIMI	150	94	24	1+	132	0.25

S.NO	NAME	AGE	IP NO	PARITY	SYS BP	DIAS BP	GEST AGE	DIP STICK	24 HUP	SPOT PCR
63	DHANABAGYAM	20	11491	PRIMI	144	84	35	1+	279	0.31
64	PALANISELVI	29	11497	PRIMI	140	90	34	1+	294	0.41
65	REKHA	27	11506	G3P2L1	130	84	35	1+	186	0.31
66	SONA	20	11448	PRIMI	150	94	33	1+	290	0.45
67	GOWRI	32	11443	PRIMI	140	84	35	1+	233	0.16
68	SHEELA	29	11387	G2P1L1	150	84	36	1+	274	0.41
69	MUMEENA	22	11290	G2P1L1	130	90	35	1+	200	0.31
70	PARIMALA	30	11399	PRIMI	150	86	34	1+	133	0.15
71	SOWJANYA	23	11826	PRIMI	140	90	36	1+	450	0.42
72	SUGUNA	29	11840	PRIMI	140	100	35	2+	842	1.1
73	DEEPA	26	9932	G2P1L1	140	90	36	1+	860	1.3
74	VANITHA	20	10038	PRIMI	130	96	37	2+	821	1.1
75	SUGANYA	23	10017	PRIMI	140	90	37	1+	525	0.6
76	PRIYA	22	10026	G3P1L1A1	150	90	37	1+	476	0.61
77	RUDRANI	27	9210	G3P2L2	130	90	37	2+	235	0.31
78	KAVITHA	24	10031	G3P1L1A1	130	90	27	1+	240	0.2
79	SUGANYA	21	10048	PRIMI	130	94	39	1+	266	0.3
80	GAYATHRI	23	9981	PRIMI	150	90	37	1+	376	0.42
81	NAGALAKSHMI	23	10029	PRIMI	140	100	35	1+	400	0.61
82	INBARASI	31	9902	PRIMI	150	100	36	2+	1450	2.42
83	INDIRANI	27	9582	G2P1L1	140	80	38	1+	180	0.17
84	SANGEETHA	21	9635	PRIMI	130	94	39	1+	842	1.43
85	BHUVANESHWARI	24	9997	G2A1	140	94	36	2+	1170	1.52
86	VANITHA	20	10038	PRIMI	130	90	27	1+	145	0.13
87	LAVANYA	29	9791	G2P1L1	150	94	35	2+	978	1.2
88	HEMALATHA	18	10043	PRIMI	150	90	35	2+	490	0.57
89	SUGANYA	21	10448	G2P1L1	140	90	34	1+	676	0.89
90	PRIYA	22	10026	G2A1	150	90	31	1+	176	0.18
91	RIANA	30	9823	PRIMI	140	80	26	1+	180	0.17
92	ARTHI	21	10042	PRIMI	150	100	36	2+	1254	3.21
93	INDIRANI	27	9582	G3P2L2	140	100	37	2+	1030	1.8

S.NO	NAME	AGE	IP NO	PARITY	SYS BP	DIAS BP	GEST AGE	DIP STICK	24 HUP	SPOT PCR
94	VINODHINI	23	10019	G2A1	130	94	37	2+	1190	1.6
95	REVATHY	26	10023	G2P1L1	130	90	29	1+	236	0.22
96	ESWARI	25	10054	PRIMI	140	90	37	1+	530	0.28
97	PARVEEN BANU	19	10028	PRIMI	150	100	36	2+	766	0.92
98	KALPANA	20	10056	PRIMI	154	90	37	1+	480	1.04
99	KAMATCHI	20	10121	PRIMI	144	80	38	2+	544	0.76
100	MUTHULAKSHMI	20	10059	PRIMI	150	84	37	1+	480	0.46
101	KANNIYAMMAL	25	10080	G2P1L1	130	100	37	1+	424	0.57
102	SELVI	27	10051	G3P1L1A1	140	90	38	2+	880	1.19
103	GEETHA	30	10078	G2P1L1	150	84	35	1+	490	0.76
104	DOWLATH	23	10009	PRIMI	150	90	36	1+	490	0.52
105	ANITHA	23	10013	PRIMI	136	90	38	1+	670	0.88
106	SANGEETHA	28	9920	G3P1L1A1	140	94	37	1+	620	8.27
107	SULOCHANA	28	9945	G2P1L1	130	90	26	1+	168	0.2
108	SASIKALA	24	9975	PRIMI	140	86	39	1+	380	0.43
109	MAHALAKSMI	19	9978	PRIMI	140	100	36	1+	476	0.53
110	RAMANI	19	9956	PRIMI	150	90	36	1+	560	0.61
111	SRIMATHI	22	9963	PRIMI	150	80	33	1+	154	0.19
112	RAJESHWARI	20	9981	PRIMI	150	94	38	1+	254	0.29
113	ANANDHI	22	9612	G2A1	140	90	32	1+	200	0.21
114	BRINDHA	21	9881	G2P1L1	130	96	34	1+	285	0.37
115	REVATHY	29	9527	PRIMI	140	90	35	1+	220	0.25
116	VIJAYALAKSHMI	30	9716	G2P1L0	154	90	35	1+	576	0.67
117	DHANALAKSHMI	30	9920	G2P1L1	140	86	36	1+	220	0.24
118	SEETHA	28	9930	PRIMI	140	90	35	1+	533	0.76
119	MEENA	19	9933	PRIMI	130	94	37	2+	3550	1.9
120	JAYALAKSHMI	26	9950	G2P1L1	150	100	36	2+	1220	1.52
121	THEBORAL	25	11009	G2A1	140	100	37	1+	970	0.84
122	SRIKUTTY	23	11502	PRIMI	140	94	36	1+	220	0.25
123	VANITHA	21	11401	PRIMI	150	100	36	2+	1220	1.52
124	NITHYA	24	11380	G2P1L1	150	94	37	2+	3550	1.9

S.NO	NAME	AGE	IP NO	PARITY	SYS BP	DIAS BP	GEST AGE	DIP STICK	24 HUP	SPOT PCR
125	MALATHI	26	11005	G3P1L1A1	140	90	35	1+	530	0.76
126	MADHAVI	34	11206	G3P2L2	140	86	36	1+	220	0.24
127	ALAMELU	22	11357	PRIMI	154	90	35	1+	576	0.67
128	SASIKALA	21	11561	PRIMI	150	90	32	1+	220	0.25
129	SWETHA	23	11209	G3A2	150	94	34	1+	285	0.37
130	LEELA	19	11005	PRIMI	140	90	35	1+	270	0.22
131	MANI	20	11074	PRIMI	140	90	38	1+	742	0.96
132	SUDHA	27	11096	G2P1L1	130	100	25	1+	138	0.19
133	KOKILA	29	11105	G2P1L1	150	94	40	1+	135	0.16
134	PARIMALA	24	11264	G2A1	140	100	36	2+	870	1.23
135	SOUJANYA	26	11351	PRIMI	140	86	37	1+	348	0.28
136	HEENA	30	11201	G2A1	150	90	38	1+	640	0.46
137	SHANTHI	22	11230	PRIMI	140	86	34	1+	700	0.88
138	KAVITHA	19	11297	PRIMI	130	96	38	1+	320	0.36
139	FARHANA	24	11300	G3A2	140	86	34	1+	960	1.8
140	DEVI	21	11312	PRIMI	140	100	36	2+	292	0.37
141	SARATHA	22	11327	G2P1L1	150	84	34	1+	376	0.51
142	GAYATHRI	27	11341	G2P1L1	140	100	36	1+	760	0.81
143	BABY	29	11261	G3P2L2	150	100	36	1+	996	1.32
144	RENUKA	24	11133	G2P1L1	150	90	35	1+	476	0.52
145	RAMYA	22	11388	PRIMI	150	100	36	2+	1154	1.72
146	YASMIN	20	11400	PRIMI	150	80	30	1+	356	0.41
147	PAVITHRA	26	11421	G2P1L1	150	94	38	2+	1370	2.1
148	BHARGAVI	29	11437	G3P2L1	140	90	39	2+	878	0.76
149	YUVARANI	19	11501	PRIMI	150	80	27	1+	422	0.63
150	NAGAPOOSHNAM	22	11681	PRIMI	150	90	39	2+	1140	1.45

ABBREVIATIONS

BP - Blood Pressure

EDD - Expected Date of Delivery

HELLP - Hemolysis, Elevated Liver enzmes Low Platelet

IUGR - Intra Uterine Growth Retardation

LDH - Lactate dihydrogenase

LMP - Last Menstrual Period

P value - Probability value

PCR - Protein to Creatinine Ratio

PVR – Pulmonary Vascular Resistance

POG - Period of Gestation

r - Pearson's Correlation Coefficient

SD - Standard Deviation

SE - Standard Error

SGOT - Serum Glutamate Oxaloacetate Transaminase

SGPT - Serum Glutamate Pyruvate Transaminase

USG - Ultrasonogram

UTI - Urinary Tract Infection

CONSENT FORM

I agree to participate in the study entitled '**SPOT URINE PROTEIN-CREATININE RATIO AND 24 HOUR URINE PROTEIN EXCRETION IN WOMEN WITH PREECLAMPSIA-A COMPARATIVE STUDY'**

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

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

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

Name of the participant :

Sign / Thumb print:

Name of the investigator: Dr.T.K.Madhumitha

Sign of Investigator :

சுய ஒப்புதல் படிவம்

இரத்த அழுத்தம் அதிகம் உள்ள கர்ப்பிணி பெண்களின் சிறுநீரில் உள்ள புரதம் - கிரியடினின் அளவு மற்றும் 24 மணிநேரமும் கழிக்கும் சிறுநீரில் உள்ள புரதத்தின் அளவையும் ஒப்பிடுதல்.

ஆய்வாளர் : மரு. த.க. மதுமிதா
முதுநிலை பட்ட மேற்படிப்பு மாணவர்
மகப்பேறு மற்றம் பெண்கள் நலத்துறை
ஆர்.எஸ்.ஆர்.எம்.மருத்துவமனை
ஸ்டான்லி மருத்துவ கல்லூரி - சென்னை

பெயர் : வயது : உள்ளிருப்பு எண் :

இந்த மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது என்னுடைய சந்தேகங்களை தீர்க்கவும் அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது

நான் இவ்வாய்வில் தன்னிச்சையாகத்தான் பங்கேற்கிறேன். எந்த காரணத்தினாலும் எந்த கட்டத்திலும் எந்த சட்டசிக்கலும் இன்றி இந்த ஆய்விலிருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.

நான் ஆய்விலிருந்து விலகிக்கொண்டாலும் ஆய்வாளர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கோ அல்லது உபயோகிக்கவோ என் அனுமதி தேவையில்லை எனவும் அறிந்து கொண்டேன் என்னை பற்றிய தகவல்கள் ரகசியமாக பாதுகாக்ப்படும் என்பதையும் அறிவேன்.

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும் பரிசோதனை முடிவுகளையும் ஆய்வாளர் அவர் விருப்பத்திற்கேற்ப பயன்படுத்திக் கொள்ளவும் அதனை பிரசுரிக்கவும் முழுமனதுடன் சம்மதிக்கிறேன்.

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன் எனக்கு கொடுக்கப்பட்டுள்ள அறிவுரைகளின்படி நடந்து கொள்வதுடன் ஆய்வாளருக்கு உண்மையுடன் இருப்பேன், என்றும் உறுதி அளிக்கிறேன்.

உடல்நலம் பாதிக்கப்பட்டாலோ வழக்கத்திற்கு மாறான ஏதேனும் நோய்குறி தென்பட்டாலோ அதனை தெரிவிப்பேன் என்றும் உறுதி கூறுகிறேன்.

இந்த ஆய்வில் எனக்கு எவ்விதமான பரிசோதனைகளையும் சிகிச்சைகளையும் மேற்கொள்ள நான் முழுமனதுடன் சம்மதிக்கிறேன்.

இப்படிக்கு,

ஆய்வாளரின் கையொப்பம் நோயாளியின் கையொப்பம்

INSTITUTIONAL ETHICAL COMMITTEE, STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work	: Spot Urine protein – creatinine ratio and 24 hours urine protein excretion in women with preeclampsia – A comparative study.
Principal Investigator	: Dr. T K Madhumitha
Designation	: PG, MS (O & G)
Department	: Department of O & G Government Stanley Medical College, Chennai-01

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 13.01.2016 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

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

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

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

MEMBER SECRETARY,
IEC, SMC, CHENNAI

MEMBER SECRETARY
ETHICAL COMMITTEE,
STANLEY MEDICAL COLLEGE
CHENNAI-600 001.