## Research Article

# Estimation of Urinary Protein/Creatinine ratio in Normal Pregnancy and Pre-Eclampsia and its importance as a diagnostic tool

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**Abstract:** Preeclampsia is a hypertensive condition that appears after the 20th week of gestation. There is an increased perinatal morbidity and mortality to fetus and mother in Preeclampsia condition. Proteinuria is the most common feature that is presented among Preeclamptic patients. The aim of the study is to estimate Urinary Protein/Creatinine ratio among Normal pregnancy subjects and Preeclamptic patients and comparison among them. This is a prospective study done for two years among 80 patients of among preeclampsia patients and normal pregnants by collecting 24 hours urine sample which is a gold standard method to detect urinary protein/creatinine ratio. Urine protein and Urine creatinine were measured by using turbidimetric method and alkaline picrate method respectively. The estimated mean value of urine protein was 224.4±310.2, urine creatinine was 87.72±47.5 and urinary protein/creatinine ratio was 2205.7±2286.9. Urinary protein/creatinine ratio shown statistically significant higher levels among normal pregnancy when compared to preeclampsia.Urinary Protein/Creatinine ratio shown wide variation of results among Preeclamptic patients. Estimation of urinary protein/creatinine is a feasible method with high accuracy to diagnose. It is a good screening method to predict preeclampsia which reduces perinatal morbidity and mortality. Proteinuria should not consider as single predictive value for preterm delivery in Preeclamptic patients.
**Keywords:** Preeclampsia, Normal Pregnancy, Urinary Protein/Creatinine ratio

## INTRODUCTION

The hypertensive disorders in pregnancy usually appear after the 20th week of gestation. These are common complications of gestation and form one of the great trial of complications that continue to be responsible for the majority of maternal deaths. The onset is usually insidious, but may be abrupt. The cardinal signs and symptoms of Pregnancy Induced Hypertension (PIH) are high blood pressure, oedema and albuminuria. Either all of them or combination of them may be present in a case but hypertension is the predominant feature of the disease. Hypertension is defined as diastolic blood pressure of atleast 90 mmHg and any increase of systolic blood pressure over and above 140 mmHg. Hypertension is the sinequanon of Pre-eclampsia and that from the moment blood pressure begins to rise, both the fetus and the mother are at increased risk.

Preeclampsia most commonly seen in Primigravida, obesity, diabetes mellitus, carrying more than one pregnancy,lupus, renal disorders etc. Vasospasm is basic to the disease process of preeclampsia - eclampsia. The vascular constriction imposes a resistance to blood flow and accounts for the development of arterial hypertension and inturn exerts a noxious effect on the blood vessels as well as the organs they supply. Intense vasospasm occurs probably in response to the higher sensitivity to all endogenous pressors, particularly angiotensin II [1]. Angiotensin II appears to have a direct action on endothelial cells, causing them to contract. The hypervolemia seen in normal pregnancy does not occur in Preeclampsia [2].

Proteinuria (> 300 mg of protein in 24 hr urine collection) occurs due to spasm of the glomerular capillaries results in anoxia of the glomeruli and this gives rise to endothelial damage. Proteinuria constitutes a sign of worsening hypertensive disease, and when the proteinuria is overt and persists, the risk to the fetus is increased even more.

Serum urea levels are higher in preeclampsia-eclampsia than in normal pregnancy. In normal pregnancy the lower levels of serum urea and creatinine compared with non pregnant women reflect increased glomerular filtration rate. Serum uric acid is usually raised in the stage of pre-eclampsia, and a rising level in a women with high blood pressure in the last trimester may be an indication of impaired fetal prognosis [3].

Creatinine clearance is generally high in normal pregnancy [4]. Pregnancy induced hypertension especially with proteinuria, is associated with a

creatinine clearance lower than in normal pregnancy but usually within normal non-pregnant range.

Deterioration of function in a number of organs and systems in pregnant women, presumably in large part as the consequence of vasospasm, have been identified in severe preeclampsia and eclampsia. Various organ damage occurred in PIH patients - Disseminated intravascular coagulation is a characteristic feature of PIH, pathologic erythrocyte destruction may further complicate cases. Corticosteroids secretion increased in normal pregnancy which gives rise to oedema, proteinuria and hypertension. Extra-adrenal Deoxycorticosterone formation may play a crucial role in the pathogenesis or perpetuation of PIH. Necrosis of the adrenal and the pituitary has been identified in some fatal cases of eclampsia [5]. Extravolume fluid in women with severe preeclampsia-eclampsia has expanded appreciably beyond the increased volume that characterizes normal pregnancy. In PIH, there is an alteration in tests of Hepatic function and Renal perfusion, glomerular filtration rate are reduced. Placental changes include increased syncytial knots, number of true infarcts, loss of synctium, villous necrosis etc. Retinal changes occurs. In brain haemorrhage ranging from petechiae to gross bleeding were present [6].

Proteinuria is the most common feature that is presented among Preeclamptic patients. Estimation of Urinary protein in 24 hrs sample and estimating the urinary protein/creatinine ratio will help as a diagnostic factor for preeclampsia and eclampsia patients. The present study is undertaken to estimate the urinary protein, creatinine and urinary protein/creatinine ratio in normal pregnancy and preeclampsia patients, also in comparison with normal non-pregnant women.

## MATERIALS AND METHODS

The present research work has done for two years as a prospective study on Urinary Protein/Creatinine ratio estimation and their comparison among normal pregnancy women and preeclampsia patients. Informed consent has taken from all patients and ethical committee has approved to do this work.

A total of 80 patients were considered for doing this study and divided them into groups

**Group 1 -** Study group - Preeclampsia patients with high blood pressure and oedema or oliguria, not having any history of Diabetes, renal, hepatic and bleeding disorders.Non-smoker, Not an alcoholic.

**Group 2 -** Control group - Normal Pregnancy women without any disorders of renal, hepatic, any evidence of diabetes, hypertension, thyroid, bleeding disorders.

Patients were advised to collect urine sample from early morning sample upto 24 hours. 24 hrs urine samples were collected in a leak proof container from all patients in study and control group and send it to Biochemistry department for estimation of Urinary Protein, Urinary Creatinine, Urinary Protein/Creatinine ratio.

Estimation of these by the following methods:

1. Estimation of Urinary Protein by Turbidimetric method
2. Estimation of Urinary Creatinine by Alkaline picrate method

Urinary Protein, Urinary Creatinine values were calculated and the ratio was analyzed in both the groups and the results were tabulated.

Using Graphpad software biochemical changes statistical significance has done. The Probability (P) value below 0.05 were considered significant.

## RESULTS

Among 80 patients, 40 of Normal Pregnancy women was selected such that their age, gestational age matches with Preeclampsia patients. The Average (SD) Maternal age of all patients were $26.3\pm7.8$. The Average (SD) Gestational age of all patients were $32.9\pm6.5$ days. Urinary protein and Urinary creatinine mean levels and their ratio were tabulated in Table no:1. All the tested biochemical changes were higher in Preeclampsia patients as compared to Normal pregnancy women. There is wide variation of urine protein levels among all Preeclampsia patients which inturn gave more standard deviation in urinary protein/creatinine ratio calculation.

**Table-1: Mean values of Urinary protein/creatinine ratio among normal pregnancy and preeclampsia patients**

| S.No. | Biochemical changes | Study Group (Mean±S.D) | Control Group (Mean±S.D) |
|---|---|---|---|
| 1 | Urinary Protein | 224.4±310.2 | 7.97±2.84 |
| 2 | Urinary Creatinine | 87.72±47.5 | 64.5±19.98 |
| 3 | Urinary Protein/Creatinine ratio | 2205.7±2286.9 | 122.8±31.6 |

S.D-Standard Deviation

All the variables (Urine protein, Urine creatinine, Urinary protein/creatinine ratio) correlation was estimated by comparing both the groups. Their significance has depicted in Table No:2. This shown that there is significant higher levels of these biochemical changes among preeclampsia patients when compared to normal pregnancy women.

**Table-2: Showing statistical significance of urinary protein/creatinine ratio among both groups**

| S.No. | Biochemical changes | t value | df | P value | Statistical significance |
|---|---|---|---|---|---|
| 1 | Urinary Protein | 4.4125 | 78 | less than 0.0001 | ESS |
| 2 | Urinary Creatinine | 2.8499 | 78 | 0.0056 | SS |
| 3 | Urinary Protein/Creatinine ratio | 5.7598 | 78 | less than 0.0001 | ESS |

ESS-Extremely Statistical Significant; SS-Statistical Significant

## DISCUSSION

Preeclampsia usually associated with increased maternal and fetal mortality and morbidity rate [7,8]. Preeclampsia can be clinically diagnosed by High blood pressure, Oedema, Oliguria. The changes in preeclampsia also include low platelet count, lower factor V, lower plasminogen, prolongation of prothrombin, partial thromboplastin and thrombin time, proteinuria. The cardinal manifestation of DIC, which correlates most closely with bleeding around venepuncture. The intravascular coagulation bears a relationship to the severity of the disease, being greatest in patients with preeclampsia and eclampsia. Howie PW[9] shown that the degree of intravascular coagulation strongly correlates with the severity of preeclampsia and the incidence of fetal death.

Proteinuria is a main component of preeclampsia and one of the diagnostic criteria of its severity. Diagnosing proteinuria is a feasible method, noninvasive, non-compliable which also gives accurate results.Urinary Protein/Creatinine ratio can be estimated by many methods like 24 hours urinary protein/creatinine ratio, random urinary protein/creatinine ratio, spot urinary protein/creatinine ratio, Urinary dipstick methods to estimate proteinuria. All these methods have their own advantageous and disadvantageous properties. It depends on clinician, severity of preeclampsia, compliance of patient which method should follow.

This study has done by routine 24 hours urinary protein/creatinine ratio which is a gold standard method and does not affected by patient's hydration status, diet, exercise. Urinary dipstick test even though it is a simple rapid test its results are inconsistent and poor correlation with 24 hours Urine estimation [10], also results varies throughout the day due to water intake, diet, exercise and improperly trained laboratory staff [11,12]. Jung-Hwa Park et al[13], Zadehmodarres S et al[14] observed that random urinary protein/creatinine ratio readily predicts proteinuria in preeclampsia. OyaDemirci et al[15], NazilHossain et al[16] reported spot urinary P/C ration in hospitalized women with suspected preeclampsia can be used as a screening test as a good predictor for significant proteinuria, which is a rapid alternative test.Jaschevatzky Oscar et al [17] documented that determination of the protein/creatinine ratio in random urine specimens may be a simple method for quantization of proteinuria in preeclampsia.

In the present study levels of Urinary Protein, Urinary Creatinine, Urinary protein/creatinine ratio were higher significantly among Preeclampsia when compared with normal pregnancy. The estimated mean value of urine protein was 224.4±310.2, urine creatinine was 87.72±47.5 and urinary protein/creatinine ratio was 2205.7±2286.9. There is wide variation of urine protein levels among all Preeclampsia patients which inturn gave more standard deviation in urinary protein/creatinine ratio calculation.

Papanna R et al[18] evaluated protein/creatinine ratio from 130 mg/g to 700 mg/g. For protein/creatinine ratio 130-150 mg/g, sensitivity ranged from 90-99%, and specificity ranged from 33-65%; for protein/creatinine ratio 300 mg/g and 600-700 mg/g with sensitivity of 81-98% & 85-87%, specificity of 52-99% & 96-97% respectively. Wheeler et al[19] documented P/C ratio was 100% sensitive and specific to detect the proteinuria >5 g/day in preeclamptic women.Guy et al [20] determined a pronounced correlation between 24-hour urine protein measurement and albumin-creatinine ratio when this was >1 g/day in a non-pregnant population with renal disease.

## CONCLUSION

Urinary protein/creatinine ratio analysis is more significant than proteinuria estimation. 24 hours urinary protein/creatinine ratio is a gold standard method which gives accurate results and the values independent of hydration status of patients. This ratio is highly significant among preeclampsia, so useful as a screening predictor and also diagnostic method for Preeclampsia. It helps to reduce the perinatal morbidity and mortality to the fetus and mother.

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