

Urine Protein to Creatinine Ratio: An Early Predictor of Chronic Kidney Disease in A Group of Pre-Eclamptic Women

RUKHSHAN KHURSHID¹, ASAD MAHMOOD KHAN², LAIBA KHALID³, MUDDASIR ZIA⁴, MUMTAZ BEGUM⁵

ABSTRACT

Background: Preeclampsia is the most grave form of pregnancy complications due to hypertension. Although hypertension is usually observe in pregnancy, renal participation secondary to this circumstance has not been considerably explored.

Aim: To find out the role of urinary protein to creatinine ratio as an early predictor of chronic kidney disease.

Methods: Fifty pregnant women who met the criteria of preeclampsia were included in the study. The Blood pressure was noted by sphygmomanometer. Urinary protein was estimated by Lowery method. Serum creatinine was estimated by Jaffe reaction. Protein-to-creatinine ratio is calculated.

Results: Mean age of 31 cases was 26 and of 18 cases was 32 years. Blood pressure was 140/93 in 31 cases and 142/96 mmHg in 18 cases with gestational age was 25 weeks in both cases. All patients belong to poor and middle class. Obstetric complication including abortion and cesarean section were more common in 31 cases or young age compared to 18 cases or middle age group. It is observed that moderately increased urinary protein creatinine ratio was observed in 31 cases with value of 408.89 and in 18 cases, severely increased ratio was observed with a value of 453.58.

Conclusion: It is concluded that urinary protein to creatinine ratio may be use to detect kidney disease and damage early especially in preelamptic patients. The test may be use to minimize the damage and prolong kidney function.

Keywords: Preeclampsia, urinary protein creatinine ratio, chronic kidney disease.

INTRODUCTION

Preeclampsia is the 3rd leading reason of maternal mortality worldwide. It is also a main reason of perinatal morbidity and mortality, and related with retardation of fetal growth. Most of the deaths of pregnant women and complications are due to lack of hospital care, wrong diagnosis, lack of resources, and managing preeclamptic conditions especially in the developing countries¹.

Hypertensive pregnant women usually divided into two groups: Women with normal blood pressure but develop hypertension in pregnancy, which is distinguish by increase blood pressure, edema and proteinuria; and hypertensive women who become pregnant and are at an increase risk of developing superimposed preeclampsia².

Preeclampsia is the gravest form of pregnancy complications due to hypertension, However it is not a simple hypertensive disease; it is

a disarray due to the factors related with placenta. Preeclampsia is begin by abnormal placentation, which is associated with release of toxins and cytokines and may cause platelet activation and vasoconstriction and may be associated with endothelial dysfunction, and the complications are related with the vascular system^{3,4}. Although hypertension is usually observe in pregnancy, renal participation secondary to this circumstance has not been considerably explored⁵.

Proteinuria may reflect abnormal loss of plasma proteins due to glomerular proteinuria, or due to increase loss of proteins from the kidney (tubular damage) and lower urinary tract. It is suggested that proteinuria play an important role in the pathogenesis of progression of chronic kidney disease⁶.

The diagnosis of preeclampsia is based on increased blood pressure (140/90mmHg) and proteinuria (≥ 300 mg per 24 h) after the 20th week of gestation⁷. Urine protein-creatinine ratio has been taken as an predictor of proteinuria^{8,9}. Urine protein-to-creatinine ratio give an accurate measurement of the urinary protein and is not pretentious by hydration¹⁰.

Preeclampsia/eclampsia is associated with substantial maternal complications. There is a need of early finding and management of hypertension in

¹Asstt Prof. Biochemistry, Shalamar Medical & Dental College, Lahore

²Demonstrator Biochemistry, Shalamar Medical & Dental College, Lahore

³K. E. Medical University, Lahore

⁴Fatima Jinnah Medical University, Lahore

⁵Professor of Biochemistry, Shalamar Medical & Dental College, Lahore

Correspondence to Dr. Rukhshan Khurshi

Email: rakhshan99@yahoo.com Cell: 0331-2215323

the state of pregnancy for improved of maternal and perinatal outcome especially in our country.

Study was designed to find out the role of urinary protein to creatinine ratio as an early predictor of chronic kidney disease.

PATIENTS AND METHOD

Fifty pregnant women who met the criteria of preeclampsia were included in the study. Patients were taken from two local Government Hospitals. Duration of study was January 2017 to June 2017. The Blood pressure was noted by sphygmomanometer. Untimed or spot urine samples

were taken to find out proteinuria. Urinary protein was estimated by Lowery method. Serum creatinine was estimated by Jaffe reaction. Patients with a dipstick positive test (1+ or > 1) were included in the study. Protein-to-creatinine ratio is calculated. Study was approved by Ethical Committee of Institution. Letter of consent was taken from each patient.

Data was entered in SPSS 20. Quantitative variables were expressed as mean \pm SD. The values between groups are compared using student 't' test. P value of < 0.05 was considered statistically significant.

Table 1: Demographic profile of patients with different age range

Characteristics	Age range (31 cases)	Age range (18 cases)
Mean age (yrs)	26.16 \pm .08	32.44 \pm 2.69
Blood Pressure (mm Hg)	140.55/93.87 3.11 \pm 2.9	142.65/96.07 3.10 \pm 4.00
Married from (yrs)	3.00 \pm 1.41	8.00 \pm 4.11
Gravida	12 Multi gravida 10 Primary gravida	10 Multi gravida 02 Primary gravida
Parity	3.19 \pm 2.44	3.45 \pm 1.55
Gestational age	25.55 \pm 0.68	25.50 \pm 0.82
Socioeconomic status	24 Poor class 07 Middle class	10 Poor class 06 Middle class
Dietary habits	04 vegetarian 16 vegetable + chicken 13 vegetable + Meat	04 vegetarian 05 vegetable + chicken 07 vegetable + Meat
Obs complications	16 Abortions 02 PE/CS	04 Abortions 04 PE/CS

Table 2: Protein to creatinine ratio in patients

Variable	Moderately increased (31 cases)	Severely increased (18 cases)
Serum protein to creatinine ratio	429.34	453.58
Serum creatinine (mg/dl)	1.05 \pm 0.16	1.00 \pm 0.15
Urinary protein (mg/dl)	408.89 \pm 128.63**	453.58 \pm 129.4

**P< 0.001= Highly significant difference

RESULTS

It is observed that the mean age of 31 cases was 26 and of 18 cases was 32 years. Blood pressure was 140/93 in 31 cases and 142/96 mmHg in 18 cases. 31 cases were married from 3.00 and 18 cases were married from 8.0 years. 12 multigravida and 10 with primary gravida was observed in 31 cases. On the other hand in 18 cases the multigravida were 10 and of primary gravida were 02. Gestational age was 25 in both cases. Among 31 cases, 24 belong to poor and 07 were belonging to middle class. Among 18 cases, 10 belong to poor and 06 were belonging to middle class. Among 31 cases most of women used vegetable + chicken. However, among 18 cases most of the women used vegetable + mean. Obstetric complication including abortion and cesarean section

were more common in 31 cases or young age compared to 18 cases or middle age group (Table 1). It is observed that moderately increased ratio was observed in 31 cases with value of 408.89 and in 18 cases, severely increased ratio was observed with a value of 453.58 (Table 2).

DISCUSSION

Pregnant women with hypertension usually give up the follow-up procedure after delivery. However these women remain exposed to problems including sustained hypertension that may lead to chronic kidney disease, which may be asymptomatic until become to severe⁵.

According to our study most of the women (31 cases) were younger (mean age 26 years as compare to women (18 cases) with age of 32 years.

Majority of the women belong to poor or middle class. A study found the mean age of women with preeclampsia was 28 year and suggested that an increase risk of preeclampsia is known in younger age¹¹. Possible explanations of preeclampsia in young age may be of immaturity or poor socioeconomic status, economic factors, malnutrition and insufficient prenatal care^{12,13}.

We observed that obstetric complication including abortion and cesarean section were more common in young age compared to middle age group. It is explained the association between younger age and obstetric complication is due to improper blood supply to uterus and cervical region may cause increase risk of subclinical infection, increase synthesis of prostaglandin which may increase the incidence of preterm delivery¹⁴. However, a study reported that increase maternal age is a risk factor for pre-eclampsia, miscarriage, Cesarean section and gestational diabetes¹⁵.

We observed that mean blood pressure in age group 26 and of 32 years was 140/93 and 142/96 mmHg respectively. It is reported that person is said to be hypertensive with blood pressure 140/90 mmHg. It is suggested that pregnancy causes an alteration of some hormones and also cause a change in physical and psychological behavior results in stress, which may cause hypertension¹⁶. Another study proposed that increase blood pressure in pregnancy may be due to increase blood volume, which may be increases up to 45% during pregnancy. Changes are also occur in components of renin-angiotensin-aldosterone system (RAAS) in pregnancy. These changes related with endocrine secretions from the ovary, and the placenta. These hormonal secretions not only increase the levels of RAAS, they also the reason of physiological changes within the kidney and cardiovascular system. Thus, this complex combination of the secretions and effects of the circulating maternal renin-angiotensin system play an important role in pregnancy outcome¹⁷. It is reported that the levels of angiotensinogen (AGT) is increases during pregnancy and if the level of increase further in pregnancy, this may induced hypertension¹⁸.

Constantly increased proteinuria may show kidney damage or malfunctioning of kidney¹⁹. It is proposed that the increase excretion of urinary protein in preeclampsia, may alter the charge or size selectivity of the glomerular filter, causes an increases in glomerular capillary pressure, and compromise of reabsorption of proximal tubules. The lesion of kidney called "glomerular endotheliosis". It is experimentally proved that anti-angiogenic factors come from the placenta in preeclampsia is

responsible for glomerular endotheliosis, hypertension and proteinuria²⁰.

It is observed that moderately increased urinary protein creatinine ratio was observed in younger age where as in middle age group severely increased ratio was observed. A study reported that that urine protein: creatinine ratio (UPC ratio) is among the most commonly used tests to quantify and monitor proteinuria²¹. It is suggested that degree of proteinuria estimated by UPC ratio may be affected by nonrenal disease, corticosteroids, hyperthermia, and hypertension^{22,23}. Another study reported that Change in degree of proteinuria is used as a marker of response of treatment. According to some studies the association of blood pressure with the level urine protein or UPC is positive but, complicated while other studies reported no positive association²⁴. It is stated by studies that proteinuria may be a temporary increase due to an infection, pregnancy, medication, diet or neurological participation. Study suggested a repeat test to decide these conditions^{25,26}.

Limitation of study: Proteinuria is variable in pregnant women with or without kidney problem. Majority of studies find that the standard deviation is about 40 to 50% of the mean values. Proteinuria may be associated with some other than kidney diseases include urinary tract infection, Source of protein loss to pre-renal, renal, and post renal. These conditions are also important when choice the diagnostic test, prognosis of disease, and treatment.

CONCLUSION

It is concluded that urinary protein to creatinine ratio may be use to detect kidney disease and damage early especially in preelamptic patients. The test may be use to minimize the damage and prolong kidney function. However, further studies are needed on large number of preeclamptic patient to reach a better conclusion.

REFERENCES

1. Ghulmiyyah L, Sibai B. Maternal mortality from preeclampsia/eclampsia. *Semin Perinatol.* 2012 Feb;36(1):56-9.
2. Firoz T, Sanghvi H, Merialdi M, von Dadelszen P. Preeclampsia in low and middle income countries. *Best Pract Res Clin Obstet Gynaecol.* 2011 Aug;25(4):537-48.
3. Visser W, Wallenburg HC. Maternal and perinatal outcome of temporizing management in 254 consecutive patients with severe pre-eclampsia remote from term. *Eur J Obstet Gynecol Reprod Biol* 1995; 63:147-54
4. Churchill D; Perry IJ; Beevers DG. Ambulatory blood pressure in pregnancy and fetal growth. *Lancet* 1997; 349:7-10.

5. De Silva Junior GS, Morira SR, Nishida SK, Sass N, Kirsztajn GM. Urinary abnormalities and renal function in pregnant women with chronic hypertension. *J Bras Nefrol* 2016;38(2):191-202
6. Silva FG. The aging kidney: a review -- part I. *Int Urol Nephrol*. 2005;37:185-205
7. ACOG Committee on Obstetric Practice. ACOG practice bulletin. Diagnosis and management of preeclampsia and eclampsia. Number 33, January 2002. American College of Obstetricians and Gynecologists. *Int J Gynaecol Obstet*. 2002;77:67-75¹
8. Rodriguez-Thompson D, Lieberman ES. Use of a random urinary protein-to-creatinine ratio for the diagnosis of significant proteinuria during pregnancy. *Am J Obstet Gynecol*. 2001;185:808-811
9. Al RA, Baykal C, Karacay O, Geyik PO, Altun S, Dolen I. Random urine protein-creatinine ratio to predict proteinuria in new-onset mild hypertension in late pregnancy. *Obstet Gynecol*. 2004;104:367-371.
10. Dwyer, BK, Gorman M, Carroll, IR and Druzin M. Urinalysis vs urine protein-creatinine ratio to predict significant proteinuria in pregnancy *J Perinatol*. 2008 Jul; 28(7): 461-467.
11. Sovio U, Gaccioli F, Cook E, Hund M, Chamock-Jones S, Smith GCS. Prediction of Preeclampsia Using the Soluble fms-Like Tyrosine Kinase 1 to Placental Growth Factor Ratio. A Prospective Cohort Study of Unselected Nulliparous Women. *Hypertension*. 2017; 69:370-380
12. Stevens-Simon C, Beach RK, McGregor JA. Does incomplete growth and development predispose teenagers to preterm delivery? A template for research. *J Perinatol*. 2002;22:315-23.
13. Chen XK, Wen SW, Fleming N. Teenage pregnancy and adverse birth outcomes: a large population based retrospective cohort study. *Int J Epidemiol*. 2007;36:368.
14. Hediger ML, Scholl TO, Schall JI, Krueger PM. Young maternal age and preterm labor. *Ann Epidemiol*. 1997 Aug;7(6):400-6
15. Khalil A, Syngelaki A, Maiz N, Zinevich Y, Nicolaidis KH. Maternal age and adverse pregnancy outcome: a cohort study. *Ultrasound Obstet Gynecol*. 2013 Dec;42(6):634-43.
16. Soma-Pillay P, Catherine N, Tolppanen H, Mebazaa A, Tolppanen H, Mebazaa A. Physiological changes in pregnancy. *Cardiovasc J Afr*. 2016 Mar-Apr; 27(2): 89-94.
17. Lumbers ER, Pringle KG. Roles of the circulating renin-angiotensin-aldosterone system in human pregnancy. *Am J Physiol Regul Integr Comp Physiol*. 2014;306(2):R91-101.
18. Irani RA, Xia Y. The Functional Role of the Renin-Angiotensin System in Pregnancy and Preeclampsia. *Placenta*. 2008 Sep; 29(9): 763-771.
19. Robert Thomas, M.D.,^{1,2} Abbas Kalso, M.D.,^{1,2} and John R. Sedor, M.D.^{1,2} Chronic Kidney Disease and Its Complications *Prim Care*. 2008 Jun; 35(2): 329-vii.
20. Jeyabalan A¹, Conrad KP Renal function during normal pregnancy and preeclampsia. *Front Biosci*. 2007 Jan 1;12:2425-37.
21. Duffy ME, Specht A, Hill RC. Comparison between Urine Protein: Creatinine Ratios of Samples Obtained from Dogs in Home and Hospital Settings *J Vet Intern Med*. 2015 Jul-Aug; 29(4): 1029-1035.
22. Bacic A, Kogika MM, Barbaro KC, et al. Evaluation of albuminuria and its relationship with blood pressure in dogs with chronic kidney disease. *Vet Clin Pathol* 2010;39:203-209.
23. Herring IP, Panciera DL, Were SR. Longitudinal prevalence of hypertension, proteinuria, and retinopathy in dogs with spontaneous diabetes mellitus. *J Vet Intern Med* 2014;28:488-495
24. Buranakarl C, Ankanaporn K, Thammacharoen S, et al. Relationships between degree of azotaemia and blood pressure, urinary protein: Creatinine ratio and fractional excretion of electrolytes in dogs with renal azotaemia. *Vet Res Commun* 2007;31:245-257.
25. Lindheimer MD¹, Kanter D. Interpreting abnormal proteinuria in pregnancy: the need for a more pathophysiological approach. *Obstet Gynecol*. 2010 Feb;115(2 Pt 1):365-75
26. Indu Saxena Sangeeta Kapoor, Ramesh C Gupta. Detection of Proteinuria in Pregnancy: Comparison of Qualitative Tests for Proteins and Dipsticks with Urinary Protein Creatinine Index. *J Clin Diagn Res*. 2013 Sep; 7(9): 1846-1848.