VOL. 18 | NO. 4 | ISSUE 72 | OCT.-DEC. 2020

Microalbuminuria as a Predictor of Pre-eclampsia in Pregnant Women Presenting in the Antenatal Clinic at Dhulikhel Hospital

Dongol A,[1] Timilsina N,[1] Bastakoti R,[1] Bhatta RD,[2] Risal P[2]

[1]Department of Obstetrics and Gynecology

[2]Department of Biochemistry

Dhulikhel Hospital, Kathmandu University Hospital,

Kathmandu University School of Medical Sciences

Dhulikhel, Kavre, Nepal.

Corresponding Author

Anjana Dongol

Department of Obstetrics and Gynecology,

Dhulikhel Hospital, Kathmandu University Hospital,

Kathmandu University School of Medical Sciences

Dhulikhel, Kavre, Nepal.

E-mail: anjanadongol@yahoo.com

Citation

Dongol A, Timilsina N, Bastakoti R, Bhatta RD, Risal P. Microalbuminuria as a Predictor of Pre-eclampsia in Pregnant Women Presenting in the Antenatal Clinic at Dhulikhel Hospital. *Kathmandu Univ Med J.* 2020;72(4):349-53.

ABSTRACT

Background

Pre-eclampsia is described as a pregnancy-specific syndrome that can affect virtually every organ system. The appearance of proteinuria remains an important diagnostic criterion. Proteinuria is an objective marker and reflects system-wide endothelial leak, which characterizes the pre-eclampsia syndrome.

Objective

To determine protein values using the spot urinary albumin/creatinine ratio amongst the pregnant women and to identify whether this test can be used as the investigation of choice for predicting pre-eclampsia in near future.

Method

A hospital based observational cross-sectional study conducted from February 2016 to August 2017. The study included pregnant women from 20-28 weeks of gestation. They were tested for spot urinary albumin and creatinine. They were all followed up till term, delivery and post partum.

Result

The mean age of the study patients was 28 years (N+335), the most common age group being 25 to 29 years (43.6%). Pregnant women with higher values of urinary albumin/creatinine ratio were found to develop hypertension compared to women with normal values of urinary albumin/creatinine ratio in the third trimester with insignificant difference ($p < 0.283$) statistically.

Conclusion

Microalbuminuria is one of the predictor of pre-eclampsia however it cannot be used as routine investigation for predicting pre-eclampsia in future; further studies in large scales are needed to prove whether urinary albumin/creatinine ratio can be utilized as predictor for pre-eclampsia or not.

KEY WORDS

Albumin creatinine ratio, Hypertension, Microalbuminuria, Pre-eclampsia

INTRODUCTION

Hypertensive disorders in pregnancy are associated with severe maternal obstetric complications and are a leading contributor to maternal mortality as well as fetal intrauterine growth restriction, low birth weight, preterm delivery and perinatal death.[1,2] Hypertensive disorders also pays foremost cause of maternal death in Nepal accounting for 30% of total deaths.[3] This disorder complicates 5 to 10% of all pregnancies, and together with hemorrhage and infection constitute the deadly triad contributing greatly to maternal morbidity and mortality.[4,5]

In pre-eclampsia, the appearance of proteinuria remains an important diagnostic criterion. It reflects a system wide endothelial leak. Abnormal protein excretion is arbitrarily defined by 24 hour urinary excretion exceeding 300mg; a urine protein:creatinine ratio ≥ 0.3; or persistent 30 mg/dl (1+dipstick) protein in random urine samples.[1,5] Significant proteinuria should be strongly suspected when urinary dipstick proteinuria is ≥ +2, and confirmed, if there is >300 mg of protein in a 24 hour urine collection.[6]

Prolonged renal hypo perfusion due to hypertension results acute tubular necrosis. Loss of both size and charge selectivity of the glomerular barrier contribute to the development of albuminuria.[7] Microalbuminuria is identified using the urinary albumin/creatinine ratio (uACR). Microalbuminuria is present when an abnormally increased excretion rate of albumin in the urine is in the range of 30-299 mg/g creatinine.[8] The 24 hrs protein measurement is a gold standard test but difficult to conduct and time consuming. Urinary albumin is usually done for the spot diagnosis and is less sensitive. Spot test for uACR as predictor may provide a practical screening tool for pre-eclampsia and eclampsia.

METHODS

This is an observational corss-sectional hospital based, non-interventional study conducted in the Department of Obstetrics and Gynecology of Dhulikhel Hospital, Kathmandu University School of Medical Sciences (DH, KUSMS). The total duration of study was 18 months after getting the approval from Institutional Review Committee (IRC) of KUSMS. The study was conducted between February 2016 and August 2017. The study population included pregnant women from 20-28 weeks of gestation who came for antenatal care (ANC) during the study period.

The final sample size was 335 patients, based on a sample size calculation of a prevalence of 7% of pre-eclampsia and a confidence interval of 95% with an error margin of 0.05. Pregnant women at gestational age of between 20-28 weeks of gestation visiting for ANC who gave consent and agreed to participate were enrolled for this study. Pregnant women with gestational age before 20 weeks or after 28 weeks, and women with medical disorders like gestational diabetes mellitus (GDM), chronic hypertension, acute or chronic kidney disease, nephritic syndrome, nephritic syndrome, diabetic nephropathy and liver disease were excluded from the study. Women who declined to co-operate or refused to give consent were also excluded.

The aim and objectives of the study were explained before consent was taken. After obtaining consent demographic details were collected this included age, place of residence, occupation, education, menstrual history, obstetrics history (gravid, parity, period of gestation), personal and family history, past medical and drug history. The information on ANC visits, calcium intake, dietary habits, exercise and ANC physiotherapy were also collected. Patient's weight was measured and they were allowed to rest for 5 minutes, then two consecutive blood pressure measurements were taken with an interval of 5 minutes at 20-28 weeks of gestation. Finally, were sent for the laboratory investigation of spot urinary albumin and creatinine. Random urine was collected and the parameters were immediately analysed using Biosystem analyser BA400. Urine albumin was measured using Turbidometry method and urine creatinine was measured using Jaffe's method at Clinical Biochemistry Laboratory, Dhulikhel Hospital. The urinary albumin to creatinine ratio was then calculated. The women then were followed up at term, delivery and postpartum. Blood pressure was recorded at term, during labour and in the postpartum period. Then the correlation between the level of microalbuminuria and development of any hypertensive disorders was assessed. All the data were recorded in the proforma and entered in an excel spread sheet as master sheet. Statistical analysis was performed using statistical package for the social science for windows version 16.0. Differences between two groups were compared by the student t-test. For non-parametric variables, the data were presented as median. The non-parametric Mann Whitney test was used for statistical comparisons. Categorical variables between groups were compared using Chi-square test. For all analyses, a two-tailed p value of < 0.05 was considered statistically significant.

RESULTS

During the study period, 335 cases were enrolled. The majority of patients in the study were in their twenties, 146 (43.6%) in the age group 25-29 years and 122 (36.4%) in the age group 20-24 ears. Total of 177 (52.8%) of cases were primigravida and 158 (47.2%) were multigravida. The majority were Hindu, 329 (98.2%) and 6 (1.8%) were Muslims. There were 143 (42.7%) cases from urban areas and 192 (57.3%) from rural areas. Total of 269 (80.3%) were literate while 66 (19.7%) were illiterate. In terms of antenatal care, 105 (31.3%) had total of ≤ 4 ANC visits while 230 (68.7%) cases had > 4 ANC visits. One hundred and seventy five women (52.2%) were doing exercises suggested by physiotherapist during pregnancy while 160 (47.8%) did not do any. Only 14 (4.2%) women got habit of

smoking while 321 (95.8%) were non-smokers. Dhulikhel Hospital ANC clinic has a protocol of prescribing Iron and Calcium tablets as supplementary medication. Most of the women 313 (93.4%) took the medication regularly while 22 (6.6%) were irregular with their medication. Many of the women were involved in agriculture 154 (45.9%), 110 (32.8%) were housewives, 38 (11.3%) were students, 30 (8.9%) were involved in business while only 3 (0.9%) were service holders. There were 300 (98.6%) women with normal body mass index while 10 (3%) were underweight and 4 (1.2%) were identified as obese.

During the study period, 30 (8.9%) patients developed gestational hypertension and none developed pre-eclampsia and eclampsia. The largest group of women were aged between 25-29 years 146 (43.6%), followed by 20-24 years 122 (36.4%), the hypertensive cases were also distributed in the similar proportions 13 (43.3%) in highest and 9 (30%) in second highest group.

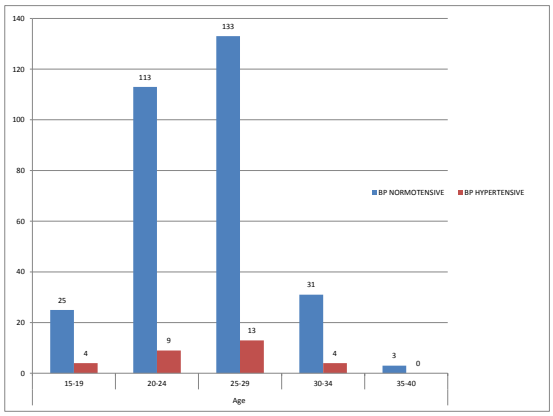

Figure 1. Statistical correlation of hypertensive with age groups

Risk factors for gestational hypertension such as geographical location, parity, education level, exercise, physiotherapy, smoking and intake of calcium intake is identified. However, the only statistically significant association was found between illiterate and hypertension and is presented in table 1. The clinical characteristics in pregnant women with or without hypertension are presented in table 2 below.

Table 1. Risk factors for hypertension in pregnant women

Risk factors	Hypertension		
	Present n=30	Absent n=305	p-value*
Primipara	19	158	0.241
Illiterate	19	47	0.001
Microalbuminuria	3	16	0.283
No Exercise	17	143	0.306
Non smoker	0	14	0.231
Irregular Calcium intake	0	22	0.128
Not doing physiotherapy	19	197	0.891
Rural area	20	172	0.278

*p-value is calculated using Pearson's Chi-square test.

Table 2. Clinical characteristics in pregnant women with or without hypertension

Characteristics	Hypertension		p-value
	Present (n=30)	Absent (n=330)	
Age (> 30 years)	24.90 (± 4.09)	24.96 (±3.78)	0.648
Obesity (BMI kg/m^2)	2.03 (± 0.36)	2.05 (±0.36)	0.159
MAP (mm of Hg)	94.66 (±12.79)	80.70 (±14.49)	0.003
Microalbuminuria (mg/g)	1.1(±0.30)	1.052 (±0.22)	0.083
Period of gestation (weeks)	24.70(±2.18)	25.30(±2.35)	0.052

Data are presented as mean ±SD; BMI, body mass index; MAP, mean arterial pressure

This study identified 316 (94.3%) women belong to group of normo albuminuria and 19 (5.6%) to group of microalbuminuria as presented in bar diagram. Higher values of urinary albumin/creatinine ratio were found in hypertensive pregnant women 3 (11.1%) as compared to healthy normotensive pregnant women 16 (5.5%) in the third trimester with insignificant difference (p<0.283) statistically. Total of 30 (8.9%) women developed gestational hypertension the statistical correlation of blood pressure with the level of miroalbuminuria was done which shows p value < 0.283 and is statistically not significant.

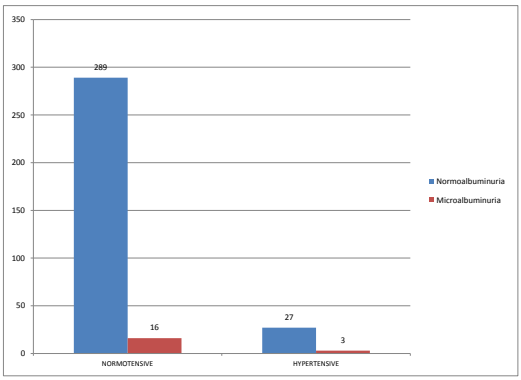

Figure 2. Statistical correlation of blood pressure with the level of microalbuminuria.

DISCUSSION

Hypertensive disorders are most common medical common medical complication in pregnancy affecting 7-15% of all gestation. It can lead to fetal intrauterine growth restriction, low birth weight, preterm delivery and perinatal death.[1,9] Appearance of proteinuria remains an important diagnostic criterion for pre-eclampsia. Thus, a lower limit of 30 mg/day was chosen for the definition of microalbuminuria as the average daily urine output of 1.5 l was multiplied by 20 mg/l. The upper limit of 300 mg/day was chosen as the sensitivity of the older dipsticks for albumin was 100 to 300 mg/l. This suggests that the limits chosen for microalbuminuria are arbitrary and the best cut offs still need to be identified.[4,10]

Kenny et al. reported that pre-eclamplsia occurs in extreme of reproductive age groups (> 40 yrs).[11] Pyane et al. reported that age was an independent risk factor for pre-eclampsia and it was more in advanced maternal age (> 35-40 years).[12] However, in this study most of the cases were found to be in between the age group 25-29 years i.e., 146 (43.6%) followed by 20-124 years 122 (36.4%) and very few women were found to be in extreme of age i.e., 35-39 years 3 (0.9%). Therefore hypertension was mostly identified in the age group of less than 30 years.

Sibai et al. in their review concluded that pre-eclampsia is the disease of first pregnancy and usually associated with increased risk due to limited sperm exposure.[13] Similar to Sibai a study by Pyane et al. showed that primigravida was the most common cause of pre-eclampsia.[12] Their findings correlated with this study which shows that hypertension is more frequent in primigravida women. In this study primigravida were 172 (52%) and among the primigravida 19 (12.04%) developed hypertension whereas 11 (7.48%) of multigravida developed hypertension. Bangal et al. showed that more pregnancy related complications due to hypertension are seen in people residing on rural areas.[14] Dhulikhel Hospital ANC clinic covers the rural 192 (57.3%) as well as urban areas 143 (42.7%). Similar to the Bangal et al. study the more cases developed hypertensive diseases from the rural areas 20 (11.62%) than from urban areas 10 (7.51%).[14]

Microalbuminuria has been suggested as a marker of endothelial dysfunction. A spot uACR cut off of > 30 mg/g (3.4 mg/mmol) is considered as positive for significant proteinuria and correlates well with 24 hours urine protein with sensitivity of 94%, specificity of 98% as against microalbuminuria alone which has sensitivity of 58% and specificity of 83%.[15,16] In studies by Jayaballa et al. and Kaur et al. they emphasize that antepartum peak uACR is a useful simple marker to help predict adverse maternal and fetal outcomes.[16,17] As the antepartum peak uACR level (in mg/mmol) increased from normoalbuminuria (uACR < 3.5) to microalbuminuria (uACR 3.5–35) to macroalbuminuria (> 35), the percentage of women with the primary composite outcome increased in a stepwise fashion (13.8% to 24.1% to 62.1, respectively, p < 0.001).[10,17] In contrast to these studies, 19 (5.6%) women who belong to group of microalbuminuria, none developed per-eclampsia and eclampsia in this study. This study therefore not been able to show that microalbuminuria has predictive value due to statistically non-significant (p-value 0.329).[10] This study suggests the need for further studies with larger sample size on uACR as a prognostic tool in pregnancy before it can be applied in clinical practice.

CONCLUSION

Pre-eclampsia is one of the commonest and most challenging problem in obstetrics. The 24 hour urine collection in patients with hypertensive disorders of pregnancy though considered as a gold standard for diagnosis of significant proteinuria, is time consuming, subject to collection error, and requires good patient compliance. There is demand for a predictive test so that the huge damage done by pre-eclampsia can be managed in the early antenatal phase. Spot uACR is easy, cheap, with good patient compliance that can be done during an ANC visit. This study explored uACR as a predictor of pre-eclampsia, with the aim to establish a simple and revolutionary change in the management of hypertensive disease in pregnancy. However, this study showed that antepartum peak uACR was not a useful marker to help predict adverse maternal and fetal outcomes. Further studies with larger sample size are required to establish uACR as a predictor of pre-eclampsia to apply in clinical practice.

REFERENCES

1. Dutta DC, Konar H. DC Dutta's Textbook of Obstetrics. 8th edition. Jaypee Brothers Medical Publishers (P) Ltd; 2015. Chapter 18, Hypertensive disorders in pregnancy: 255-81.
2. Say L, Chow D, Gemmill A, Tuncalp O, Moller AB, Daniels J, et al. Global causes of maternal death: A WHO systematic analysis. *Lancet Glob Health*. 2014; 2: 323-33.
3. Suvedi BK, Pradhan A, Barnett S, Puri M, RaiChitrakar S, Poudel P, et al. Nepal Maternal Mortality and Morbidity Study 2008/2009: Summary of Preliminary Findings. 2010.
4. Cunningham FG, Hauth JC, Lenevo KJ, Bloom SL, Spong CY, DasheJS, Hoffman BL. Williams Obstetrics. 24th edition. New York: MacGraw Hill Education; 2014. Chapter 40, Hypertensive Disorders: 728-79.
5. Roberts JM, Druzin M, August PA, Gaiser RR, Bakris G, Granger JP, et al. ACOG Guidelines: Hypertension in pregnancy. *American College of Obstetricians and Gynecologists.* 2012; 1-100.
6. Donald I. Hypertensive Disorders. In: Practical Obstetrics. Wolters Kluwer India Pvt Ltd. 2014; 142-75.
7. Momoh M, Dg Y. Accuracy of the spot urinary microalbuminuria: creatinine ratio compared to 24 hours urine protein in detecting proteinuria in pre-eclampsia. 2014; 1: 66-81.
8. Toto RD. Microalbuminuria: definition, detection, and clinical significance. *J Clin Hypertens*. 2004;6(11):2-7.
9. James D, Steer P, Weiner C, Gonik B. High risk pregnancy: management options. 4th ed. Elsevier; 2011. Chapter 35, Hypertension: 599-626.
10. Kaur IP, Shukla A, Gangopadhyay S, Gupta A, Sarkar G. Levels of microalbuminuria in prediction of pre-eclampsia: A hospital based study. 2016;3(4):354-6.
11. English FA, Kenny LC and Mccarthy FP. Risk factors and effective management of preeclampsia. *Integr Blood Press Control*. 2015;7-12.

12. Dadelszen PV, Ukah UV, Payne B, Cote AM, Hoodbhoy Z Dadelszen PV. The FIGO textbook of Pregnancy and Hypertension. The Global Library of Women's Medicine; 2016. Chapter 5, Risk factors and predictors of pre-eclampsia: 75-100.

13. Sibai B, Dekker G, Kupferminc M. Pre-eclampsia. *The Lancet.* 2005;365(9461):785-99.

14. Bangal VB, Giri PA, Mahajan AS. Maternal and foetal outcome in pregnancy induced hypertension: A study from tertiary care teaching hospital in India. *Int J Biomed Adv Res*. 2012;2(12):595-9

15. Minasyan AM, Gareginyan NA. Microalbuminuria as a predictor of cardiorenal syndrome. *New Armen Med J.* 2014;8(1):29-34.

16. Kaul I, Bhagat BR, Sharma D, Singh G. Comparison of single spot urinary albumin-creatinine ratio with 24 hour urinary protein excretion in women with preeclampsia. *Int J Reprod Contracept Obstet Gynecol.* 2018;7(5):1929-33.

17. Jayaballa M, Sood S, Alahakoon I, Padmanabhan S, Cheung NW, Lee V. Microalbuminuria is a predictor of adverse pregnancy outcomes including preeclampsia. *Pregnancy Hypertens*. 2015;5(4):303-7.