Original Research Article

A Study on Evaluation of Predictive Value of Microalbuminuria as a Screening Tool for Pre-eclampsia Among Patients Attending A Tertiary Care Centre Of Bihar

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Abstract

Introduction: Proteinuria is a defining dysfunction of Pre-eclampsia **(**PE) and repeated urinalysis to screen for the condition is part of the standard antenatal care. It has been proposed to be an indicator of both the severity of disease and the prediction of its outcome. Studies have shown that the presence of microalbuminuria earlier in pregnancy is associated with an increased risk of development of PE and severe adverse maternal and fetal outcome in PE. The aim of this study was to assess the role of microalbuminuria as a diagnostic marker in PE. **Methodology:** The current study was conducted by the Dept of Obstetrics and Gynecology, Nalanda Medical College & Hospital, Patna, Bihar, India during August 2021 to February 2022. Ethical clearance was obtained from the ethical committee of the institution. Informed consent was obtained from all the subjects. The study incorporated 25 normotensive pregnant women as controls and 25 pregnant women between 20 and 35 years of age were selected at 24 ± 4 weeks of gestation and had PIH diagnosed by the accepted criteria of the Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy with a blood pressure of >140/90 mm Hg and proteinuria (>300 mg/24-h). **Results:** The mean age (with SD) of patients from normotensive and PE group was 26.4 ± 3.4 years and 27.3 ± 4.1 years, respectively. The mean period of gestation was 32.2 ± 4.2 weeks and 29.7 ± 5.1 weeks respectively for both the study cohorts. The sensitivity and specificity of the various renal function parameters in PE was calculated. The sensitivity of micro albumin was 100% and the specificity was 78.2%, both being the highest among all renal function markers except creatinine, which had a higher specificity. Urea had a sensitivity of 80% and specificity of 65.7% while creatinine had a sensitivity of 72% but had a specificity of 81.2%. **Conclusion:** The current created evidence that microalbuminuria is a good diagnostic marker for PIH, although it may not be preferred for grading its severity.

Key Words: Microalbuminuria, Pre-eclampsia

Introduction

Pregnancy-induced hypertensive (PIH) disorders encompasses a whole spectrum of pathologies and disease states such as transient gestational hypertension, pre-eclampsia (PE), chronic arterial hypertension (CAH), PE superimposed on CAH, eclampsia and HELLP syndrome[1]. PIH contributes significantly to the maternal mortality, premature birth, and intrauterine growth retardation (IUGR) and perinatal mortality[2]. PE is observed in 10-20% of pregnant women. It is defined as hypertension of ≥140/90 mm Hg associated with proteinuria (≥300 mg/24 h or ≥1+/ran Dom sample dipstick test), with onset after 20 weeks of gestation, persisting up to 12 weeks after delivery[3]. The diagnostic work-up of PE patients includes renal function assessment by measurement of parameters such as proteinuria, urea, creatinine, uric acid, creatinine clearance, blood urea nitrogen (BUN), albumin and 24-h urinary protein. Liver enzymes, bilirubin and coagulation screening are performed to rule out hepatic involvement (HELLP syndrome). Other parameters such as serum magnesium and calcium are also measured[3, 4]. Radiological imaging to evaluate the fetal development and utero-placental circulation is also a part of the assessment[3].

Proteinuria is a defining dysfunction of PE and repeated urinalysis to screen for the condition is part of the standard antenatal care. It has been proposed to be an indicator of both the severity of disease and the prediction of its outcome[5].

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Microalbuminuria, albuminuria rates of 30-300 mg/g of creatinine and reduced estimated glomerular filtration rate (eGFR) have been proposed as useful integrated markers of sub-clinical target organ damage and renal endothelial injury resulting from local or systemic vascular damage[6, 7].

Studies have shown that the presence of microalbuminuria earlier in pregnancy is associated with an increased risk of development of PE and severe adverse maternal and fetal outcome in PE[8, 9]. The aim of this study was to assess the role of microalbuminuria as a diagnostic marker in PE.

Methodology

The current study was conducted by the Dept of Obstetrics and Gynecology, Nalanda Medical College & Hospital, Patna, Bihar, India during August 2021 to February 2022. Ethical clearance was obtained from the ethical committee of the institution. Informed consent was obtained from all the subjects.

The study incorporated 25 normotensive pregnant women as controls and 25 pregnant women between 20 and 35 years of age were selected at 24 ± 4 weeks of gestation and had PIH diagnosed by the accepted criteria of the Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy with a blood pressure of >140/90 mm Hg and proteinuria (>300 mg/24-h).

Cases of proteinuria due to other causes such as chronic hypertension, urinary tract infection, established renal diseases, diabetes mellitus, fever and acute inflammatory conditions and trauma were excluded from the study. Obstetric history including the last menstrual period, parity, period of gestation, previous obstetric history, complications and adverse outcomes of the patient were documented. Relevant medical history of the patients was also taken to rule out other causes

of proteinuria. Based on these details, subjects meeting the exclusion criteria were dropped from the study.

Values of the patients' serum creatinine measured by the Jaffe's method, serum urea measured by the urease method and uric acid measured by the uricase method were collected from the hospital laboratory data. Midstream early morning urine samples were collected from the patients and measurement of microalbuminuria was performed by the immune-turbidometric method in the semiautoanalyser. Blood pressure was recorded in the sitting position on two occasions about one week apart.

Data were analyzed by IBM SPSS version 20 software. Student's t-test was performed to compare the renal markers and PE markers between the cases and the controls. The correlation between microalbuminuria and systolic blood pressure in patients with mild-grade renal dysfunction was performed by Pearson's correlation analysis. The data were expressed as mean (standard deviation) and percentages. *P*-value <0.05 was considered to be statistically significant.

Results

The mean age (with SD) of patients from normotensive and PE group was 26.4 ± 3.4 years and 27.3 ± 4.1 years, respectively. The mean period of gestation was 32.2 ± 4.2 weeks and 29.7 ± 5.1 weeks respectively for both the study cohorts. Majority of the females were multigravida in both the groups. The average age, period of gestation and parity status were not statistically different between the two groups. Table 2 shows the comparison of the parameters of PE such as uric acid, proteinuria and microalbuminuria and renal function markers and blood pressures between the two study groups, and all the parameters showed a statistically significant difference between the study group and the controls. Microalbuminuria was significantly higher in the patients with PE compared with the control group, although it had no linear correlation with the grades of proteinuria**.**

Table 1: Comparison of the serum, urinalysis and blood pressure between patients of both the groups

Parameters	Control	PE	P value
Serum creatinine (mg/dL)	0.62 ± 0.3	1.3 ± 0.4	<0.05
Serum urea (mg/dL)	25.1 ± 12.1	49.5 ± 13.1	<0.05
Serum uric acid (mg/dL)	3.1 ± 1.3	6.2 ± 1.1	<0.05
Proteinuria (grades)	0.3 ± 0.05	3.4 ± 0.02	<0.05
Microalbuminuria (mg/L)	13.4 ± 5.1	46.2 ± 17.2	<0.05
SBP (mm of Hg)	116 ± 8.3	149 ± 10.2	<0.05
DBP (mm of Hg)	73.3 ± 5.5	99 ± 8.3	<0.05

The sensitivity and specificity of the various renal function parameters in PE was calculated. The sensitivity of micro albumin was 100% and the specificity was 78.2%, both being the highest among all renal function markers except creatinine, which had a higher specificity. Urea had a sensitivity of 80% and specificity of 65.7% while creatinine had a sensitivity of 72% but had a specificity of 81.2%.

Pearson's correlation coefficient was used to show the comparison of sensitivity and specificity of microalbuminuria with other markers of PE, such as uric acid and proteinuria. Microalbuminuria had the highest sensitivity and specificity. [Table 2]

Table 2: Sensitivity and specificity of various markers for PE

Parameter	Pearson's correlation coefficient	P value
Micro albumin	0.421	<0.05
Uric acid	0.615	<0.05
Proteinuria	0.691	<0.05

Discussion

The results of our study showed significant differences in all the parameters between the cases and the controls, as was expected. There was significant microalbuminuria in patients of PE compared with the normotensive patients. The presence of microalbuminuria in PE is due to the underlying pathology of the disease[5,10]. The mechanism for proteinuria in PE is not well understood. The glomerular basement membrane and podocytes typically appear normal[11, 12]. Layfette et al[13] stated that the impaired charge selectivity rather than the filtration diaphragm-related impairment of size selectivity is responsible for the heavy microalbuminuria.In PE, the glomerular barrier is certainly altered and there is an increased excretion of protein, including albumin. Generally, urine from PE has demonstrated a poor selectivity and has not differed significantly from other forms of primary renal disease. Glomerular proteins of intermediate size, such as albumin, have been identified alone or in combination with varying degrees of tubular proteins, such as β2-microglobulin, reflecting the tubular damage that can occur in severe PE[14,15,16].When total protein excretion exceeds 1 g/24 h, tubular protein reabsorption will be saturated and individual proteins excretion rates will be related to their molecular weights[5]. This non-selective proteinuria does not help in assessing whether it was due to glomerular damage or tubular dysfunction or both. Measurement of microalbuminuria on the other hand helps to exclude non-specific collateral damage.Bar et al[17] described a phase of microalbuminuria that preceded clinical proteinuria and that this test has some predictive value for severe disease. They also suggest that the accepted definition of gestational proteinuria should be reconsidered[5]. Furthermore, microalbuminuria preceded the development of hypertension in other studies; hence, it is a good predictor of PIH[18, 19]. Microalbuminuria is also used in the evaluation to rule out preexisting chronic hypertension[20]. However, its role in established PE is not well defined.

In our study, the patients with PE showed obvious signs of renal damage by an elevated serum urea and creatinine in comparison with the normotensive group. Studies show that early detection and treatment of kidney disease can slow, halt or even reverse its progression. [21,22]. In our study, microalbuminuria was found to have a significant correlation with systolic blood pressure in the hypertensive group. Microalbuminuria may correlate more closely with other clinical measurements of disease severity as it may more accurately reflect the glomerular dysfunction associated with the glomerular endotheliosis of PE[5].

Conclusion

The current created evidence that microalbuminuria is a good diagnostic marker for PIH, although it may not be preferred for grading its severity. It is also a better marker of renal dysfunction in PIH compared with the established markers. Microalbuminuria evaluation in the second trimester in high-risk patients can serve as a sensitive indicator of renal function.

References

1. Report of the national high blood pressure education program working group on high blood pressure in pregnancy. Am J Obstet Gynecol 2000;183:S1-22.
2. Anand S, Kirshnanand. Perinatal outcome in growth retarded babies born to normotensive and hypertensive mothers: A prospective study. Peoples J Sci Res 2012;5:24-6.

3. Cunningham FG, Leveno KJ, Bloom SL, Hauth J, Gilstrap LC, Wenstrom KD, eds. Hypertensive Disorders in Pregnancy, Williams Obstetrics. 22 nd ed. New York: McGraw-Hill;2005. p. 761-808.
4. Carson MP, Gibson PS. Hypertension and Pregnancy. Available from: http://www.emedicine.medscape.com/article/261435. [last accessed date in January 2022].
5. Maybury H, Waugh J. Proteinuria in pregnancy: Just what is significant? Fetal Matern Med Rev 2004;16:71-95.
6. Verdecchia P, Reboldi GP. Hypertension and microalbuminuria: the new detrimental duo. Blood Press 2004;13:198-211.
7. Van de Wal RM, Voors AA, Gansevoort RT. Urinary albumin excretion and the renin-angiotensin system in cardiovascular risk management. Expert Opin Pharmacother 2006;7:2505-20.
8. Chua S, Redman CW. Prognosis for preeclampsia complicated by 5 g or more of proteinuria in 24 hours. Eur J Obstet Gynecol Reprod Biol 1992;43:9-12.
9. North RA, Taylor RS, Schellenberg JC. Evaluation of a definition of pre-eclampsia. Br J Obstet Gynaecol 1999;106:767-73.
10. Davison, JM. Renal function during normal pregnancy and the effect of renal disease and pre-eclampsia. In: Andreucci VE, edr. The Kidney in Pregnancy. Boston: Martinus Nijhoff; 1986. p. 65-80.
11. Sanchez-Ramos L, Briones DK, Kaunitz AM, Delvalle GO, Gaudier FL, Walker CD. Prevention of pregnancy-induced hypertension by calcium supplementation in angiotensin II-sensitive patients. Obstet Gynecol 1994;84:349-53.
12. AbdAlla S, Lother H, el Massiery A, Quitterer U. Increased AT(1) receptor heterodimers in preeclampsia mediate enhanced angiotensin II responsiveness. Nat Med 2001;7:1003-9.
13. Lafayette RA, Druzin M, Sibley R, et al. Nature of glomerular dysfunction in pre-eclampsia. Kidney Int 1998;54:1240-9.
14. Hladunewich M, Karumanchi SA, Lafayette R. Pathophysiology of the clinical manifestations of preeclampsia. Clin J Am Soc Nephrol 2007;2:543-9.
15. Winkler U, Lison AE, Seitzer B, Niedner W. Urinary protein patterns for early detection of preeclampsia. Contrib Nephrol 1988;68:227-9.
16. Quaas L, Wilhelm C, Klosa W, Hillemanns HG, Thaiss F. Urinary protein patterns and EPH-gestosis. Clin Nephrol 1987;27:107-10.
17. Bar J, Hod M, Erman A, et al. Microalbuminuria as an early predictor of hypertensive complications in pregnant women at high risk. Am J Kidney Dis 1996;28:220-5.
18. Sonagra A, Biradar S, Dattatreya K, Murthy DS. Microalbuminuria in women with gestational hypertension. Int J Med Sci Public Health 2013;2:212-6.
19. Misiani R, Marchesi D, Tiraboschi G, et al. Urinary albumin excretion in normal pregnancy and pregnancy-induced hypertension. Nephron 1991;59:416-22.
20. Sibai BM. Hypertension in pregnancy. In: Gabbe SG, Niebyl JR, Simpson JL, (eds). Obstetrics: normal and problem pregnancies. 5 th edn. Churchill Livingston, New York:1996. pp. 935-96.
21. Koroshi A. Microalbuminuria, is it so important? Hippokratia 2020;11:105-7.
22. Caramori ML, Fioretto P, Mauer M. The need for early predictors of diabetic nephropathy risk: is albumin excretion rate sufficient? Diabetes 2001;49:1399-408.