ORIGINAL RESEARCH PAPER

Volume-8 | Issue-5 | May-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

MICROALBUMINURIA AND ITS ASSOCIATION WITH RENAL FUNCTION AND SERUM URIC ACID LEVEL IN PREHYPERTENSION

Biochemistry

Shivani Godara M.Sc.(Medical) Biochemistry

Dr. Bushra Fiza* Professor, Mahatma Gandhi Medical college and Hospital, Jaipur. *Corresponding Author

Dr. Maheep Sinha Head of Department, Mahatma Gandhi Medical college and Hospital, Jaipur.

ABSTRACT

Microalbuminuria (MA) develops from progressive, subclinical, structural and functional changes within the kidney and represents a sensitive marker of early renal disease. Therefore, this study planned to explore the association of MA with renal variables in patients of prehypertension. For the study, 100 patients with prehypertension visiting the Medicine out-patient department of Mahatma Gandhi Medical College and Hospital, Jaipur were selected based on the predefined inclusion and exclusion criteria. Of total prehypertensive patients 32% exhibited MA. On comparing the renal profile it was observed that S. Urea, Creatinine and Uric acid were significantly higher in the microalbuminuric group. (P=0.000, P=0.004, P=0.002) respectively. On applying Pearson's correlation, the present study reported a significant association between S. uric acid & AC and between uric acid and urinary albumin. Findings of the present study suggest that microalbuminuria may be an independent risk factor in prehypertension. Increased prevalence of microalbuminuria and its significant correlation with renal function test indicates significant association between prehypertension and renal dysfunction.

KEYWORDS

INTRODUCTION

Hypertension is one of the leading causes of the global burden of disease. No single or specific cause is known for most cases of hypertension, and the condition is referred to as primary in preference to essential. Persistent hypertension can develop in response to an increase in cardiac output or a rise in peripheral resistance. (Lawes CMM et. al., 2008).

Prehypertension is a precursor of clinical hypertension and is closely related with increased incidence of cardiovascular disease (Ferdinand KC et. al., 2007; Vasan MG et. al., 2001). Prehypertension was formerly defined as high-normal and above-optimal Blood Pressure (BP). In a normotensive person, prehypertension is defined as a systolic BP 120-139 mmHg and/or diastolic BP 80-89 mmHg based on properly measured seated BP readings on each of two or more office sittings. Compared with normal BP, hypertension is associated with an increase in cardiovascular morbidity and mortality (Qureshi AI et. al., 2005; Mainous AG et. al., 2004). Prehypertension is a warning sign of developing hypertension in future. High blood pressure increases the risk of heart attack, stroke, coronary heart disease, heart failure, and kidney failure.

Microalbuminuria (MA) develops from progressive, subclinical, structural and functional changes within the kidney and represents a sensitive marker of early renal disease (Newman DJ et. al., 2005; Ogensen CE et. al., 1995). Microalbuminuria is typically defined as 24-hour urine albumin excretion of 30-300 mg or urinary albumin creatinine ratio (UACR) of 2.5- 30mg/mmol in men, 3.5-30 mg/mmol in women (Karalliedde J et. al., 2004).

Albuminuria is a well known predictor of poor renal outcomes in patients with type 2 diabetes and in essential hypertension (Keane WF et. al., 2003; Pinto-Sietsma SJ et., 2000). Albuminuria has also been shown more recently to be a predictor of cardiovascular outcomes in these population (Anavekar NS et. al., 2004; Gerstein HC et. al., 2001). The kidneys play a central role in the homeostatic mechanisms of the human body. Reduced renal function strongly correlates with increasing morbidity and mortality. Quantitation of overall functions of kidneys are based on the assumption that all functioning nephrons are performing normally and that a decline in renal function is due to loss of functioning nephrons, quantitatively related to the loss (Tietz 4th edition; 2008).

The present study was therefore planned to explore the association of MA with renal variables in patients of prehypertension.

AIM AND OBJECTIVE

1. To assess the renal function i.e. Urea, Creatinine and Uric acid levels in prehypertensive patients.
2. To estimate Microalbuminuria in such patients.
3. To study the relationship of hyperuricemia, Urea and Creatinine with microalbuminuria in prehypertension.

MATERIAL AND METHOD

The study was conducted in Department of Biochemistry in association with Department of General Medicine of Mahatma Gandhi Medical College & Hospital, Jaipur.

This study was approved by the Institutional Ethics Committee. Total 100 subjects were enrolled. Patients enrolled in the study were recommended not to have heavy exercise at least 24 hours before examination.

1. Inclusion criteria

Clinically diagnosed and biochemically confirmed cases of Prehypertension.

Age upto 60 years, either gender. Patients who were willing to participate and submitted a signed consent.Patient willing to comply with the protocol requirements.

2. Exclusion criteria

Patients on anti hypertensive and cholesterol lowering drugs.
Diagnosed cases of renal failure and cardiac failure.
Pregnant and lactating women.
Malignant patient.
Patients on drugs known to cause hyperuricemia or nephrotoxicity.
Gout.

Clinical Investigations

Renal Function Test viz. Urea, S. Creatinine and Uric acid.
Urine albumin level
Urine Creatinine level

STATISTICAL ANALYSIS

The prehypertensive subjects enrolled for the study (n=100) were grouped on the basis of ACR as :
Normoalbuminuria ACR $\leq$ 30µg/mg (n=68)
Microalbuminuria ACR > 30µg/mg (n=32)

Different variables in the groups were presented as mean± SD. For statistical comparison, students 't' test was applied between the two groups. To analyze the association of ACR with variables of RFT and Pearson's Correlation was applied. To exhibit the correlation X-Y scatter plot were plotted. For all test $P < 0.05$ was considered as statistically significant.

RESULT AND DISCUSSION

Table:1 Distribution of Urea, S. Creatinine, uric acid, Urine Albumin, Urine Creatinine and ACR in groups formed on the basis of microalbuminuria (n= Nuber of Patients).

Parameters	Normal group (n=68)	Microalbuminuria group (n=32)	t value	p value
Urea(mg/dl)	30.04±12.43	41.12 ±18.24	-3.559	0.0000
S. Creatinine (mg/dl)	0.91 ±0.44	1.26± 0.76	-2.909	0.004
Uric Acid (mg/dl)	4.68±0.95	5.53± 1.73	-3.171	0.002
Urine Albumin (mg/dl)	12.25 ±16.42	82.24± 72.23	-7.622	0.000
Urine Creatinine (mg/dl)	85.17 ±87.26	75.31±65.07	0.569	NS
ACR (µg/dl)	15.13±7.34	115.81 ±82.6	-10.024	0.000

Table:2 Coefficient correlation

Test Coefficient	correlation (r)	P-value
ACR Vs Uric Acid	0.362	0.000
ACR vs Urea	0.361	0.000
ACR Vs Creatinine	0.384	NS
ACR Vs Microalbuminuria	0.715	0.000
Ur Albumin Vs Uric Acid	0.231	0.020
Ur Albumin Vs Urea	0.314	0.001
Ur Albumin Vs creatinine	0.349	0.000

The present study was planned to study the association of renal function including serum uric acid with microalbuminuria in prehypertension. For the study, 100 patients with prehypertension visiting the Medicine out-patient department of Mahatma Gandhi Medical College and Hospital, Jaipur were selected based on the predefined inclusion and exclusion criteria. After obtaining informed consent, all patients were subjected to blood pressure measurement; routine blood chemistry and spot urine examination for Albumin Creatinine Ratio(ACR). While urinary albumin was measured by immunoturbidometic assay, urinary creatinine was measured by Jaffe's method.

Of total prehypertensive patients 32% exhibited MA.

In a study by Sabarwal RK et. al., 2008, the prevalence of MA in hypertensive patients was observed to be 33.3%. The mean ACR for normoalbuminuria group was 15.13±7.34µg/mg whereas that for MA was 115.8±82.6 µg/mg.

On comparing S. Urea & creatinine levels between thenormo alb uminuria & microalbuminuria it was observed that the results were significantly higher in the prehypertensive subjects with Microalbuminuria.

Previous studies have reported that hypertension is a clear risk factor of CKD (O'seaghda CM et. al., 2009; Yamagata K et. al., 2007; Iseki k et. al., 2004). Chronic Kidney Disease is recognized as a major public health problem (Levey AS et. al., 2007; Schiffrin EL et. al., 2007).
The mean S. Uric acid levels in two groups. It was observed that S. Uric acid levels were significantly higher (P=0.002) in pre-hypertensive subjects with Microalbuminuria.

This finding is in accordance with study of Meena et. al., 2013 who demonstrated a strong independent association between uric acid level & microalbuminuria in prehypertensive subjects without a history of cardiovascular disease, diabetes and decreased renal function.

In the present study, the mean uric acid level in MA was 5.53 ±1.73 mg/dl which was significantly higher than that of normoalbuminuria group i.e. 4.68± 0.95 mg/dl (P=0.002).

In recent study by Lee JE et. al., 2006, it has been observed that increased S. Uric acid level is an independent factor for microalbum inuria in prehypertension group.

The excretion of urinary microalbumin is suggestive of generalized endothelial dysfunction which in turn is associated with a varied range of risk factors (Zeeuw D et. al., 2004). In other words, MA can be considered as a risk factor for cardiovascular complications & hence for patients at high risk & who require more intensive therapy (Yuyun MF et. al., 2005).

In various studies conducted on hypertensive subjects, hyperuricemia has been suggested as an independent risk factor for target organ damage & hence in combination with prehypertension, it might be associated with MA (Svetkey LP et. al., 2005; Vasan RS et. al., 2001).

Several animal experiments have exhibited hyperuricemia induced hypertension, renal arteriolopathy and impairment of Nitrogen oxide generation (Sanchez Lozada LG et. al., 2007; Khosla UM et. al., 2005). Further oxidative stress due to hyperuricemia leads to vascular endothelial dysfunction (George J et. al., 2009). The association between S. uric acid levels and cardiovascular disease has been controversial (Fang J et. al., 2000; Culleton BF et. al., 1999).

Previous studies suggested hyperuricemia is an independent risk factor for cardiovascular and renal diseases, particularly in patients with hypertension, heart failure or diabetes (Baker JF et. al., 2005).

On applying Pearson's correlation, the present study reported a significant association between S. uric acid & ACR (r=0.362) and between uric acid and urinary albumin (r=0.231). Excretion of proteins in urine even in minute quantities is indicative of microvascular changes. The probable cause of initiation of these changes is endothelial dysfunction leading to damage of the blood vessels linings. Besides endothelial dysfunction, elevated levels of S. uric acid also induce proliferation & pro-inflammation of smooth muscles, due to some hormonal cytokinase effects (Sanchez-Lozada LG et. al 2006). Uric acid has been reported to be associated with various inflammatory markers including CRP and IL-6 (Ruggiero C et. al., 2006). The present study recommends further evaluation of levels of such inflammatory markers such as CRP, IL-6 etc in association with prehypertension.

A positive association was also noted between ACR & S. urea (r=0.361). S. urea is the end product of protein metabolism that is excreted through kidneys. It is an important marker of renal function. However compared to S. urea, there are other parameter which have been studied thoroughly in relation to MA. The suggested association of MA with S. Urea may be interesting to explore further.

SUMMARY AND CONCLUSION

Hypertension is a sustained elevation of systemic arterial pressure. Hypertension is one of the most common cardiovascular disorders. Like hypertension, prehypertension is associated with cardiovascular disease. Prehypertension remains an important public health challenge all over the world. It has been defined as systolic blood pressure (SBP) 120 to 139 or diastolic blood pressure (DBP) 80-89 mmHg, based on two or more properly measured seated blood pressure (BP) readings on each of two or more office visits. Prehypertension tends to increase in severity over time and associates with increased incidence of cardiovascular disease (CVD). Microalbuminuria has been proposed as a potential atherosclerotic risk factors in hypertensive individuals. Increased urine albumin excretion is associated with an unfavourable cardiovascular risk profile and prognosis in primary hypertension. Microalbuminuria has been proposed as an integrated marker to identify patients with subclinical organ damage. The present study was performed to assess the association of S. RFT with microalbuminuria in prehypertension. A total of 100 patients diagnosed for prehypertension visiting the OPD of Department of Medicine at Mahatma Gandhi Hospital were included in the study. On the basis of presence or absence of microalbuminuria, the subjects were grouped as:
Normoalbuminuria ACR ≤30 µg/mg (n=68)
Microalbuminuria ACR >30 µg/mg (n=32)

On comparing the renal profile it was observed that S. Urea, Creatinine and Uric acid were significantly higher in the microalbuminuric group. (P=0.000, P=0.004, P=0.002) respectively.

The mean urine albumin levels were nearly seven times higher in microalbumin group than in normal group (P=0.000).
The mean urine creatinine levels were non significant in microalbuminuria group and in normal group (P=NS).

The mean ACR levels were high in microalbuminuria group as compared to normal group (P=0.000).

Findings of the present study suggest that microalbuminuria may be an independent risk factor in prehypertension. Increased prevalence of microalbuminuria and its significant correlation with renal function test indicates significant association between prehypertension and renal dysfunction. The study therefore recommends screening of pre-hypertensive patients for microalbuminuria.

REFERENCES

1. Baker JF, Krishnan E, Chen L, Schumacher HR. Serum uric acid and cardiovascular disease: recent developments, and where do they leave us? Am J Med. 2005;118:816–26.
2. Ferdinand KC, Pacini RS. New evidence confirms risks associated with prehypertension and benefits of therapeutic lifestyle changes in management. Journal of the Cardiometabolic Syndrome. 2007;2(2): 302–4.
3. George J, Struthers AD. Role of urate, xanthine oxidase and the effects of allopurinol in vascular oxidative stress. Vasc Health Risk Manag. 2009;5:265–72.
4. Gerstein HC, Mann JF, Yi Q. Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals.JAMA. 2001;286:421-6.
5. Karalliedde J, Viberti G. Microalbuminuria and cardiovascular risk. Am J Hypertens. 2004;17:986-93.
6. Khosla UM, Zharikov S, Finch JL et. al. Hyperuricemia induces endothelial dysfunction. Kidney Int. 2005;67:1739–42.
7. Lee JE, Kim YG, Choi YH, Huh W, Kim DJ, Oh HY. Serum uric acid is associated with microalbuminuria in prehypertension. Hypertension. 2006;47:962–7.
8. Mainous AG III, Everett CJ, Liszka H, King DE, Egan BM. Prehypertension and mortality in a nationally representative cohort. Am J Cardiol. 2004;94:1496–1500.
9. Newman DJ, Mattock MB, Dawnay AB et. al. Systematic review on urine albumin testing for early detection of diabetic complications. Health Technol Assess 2005;9:iii-vi, xiii-163.
10. Ogensen CE. Microalbuminuria in prediction and prevention of diabetic nephropathy in insulin-dependent diabetes mellitus patients. J Diabetes Complicat. 1995;9:337-49.
11. Qureshi AI, Suri MF, Kirmani JF, Divani AA, Mohammad Y. Is prehypertension a risk factor for cardiovascular diseases? Stroke 2005;36:1859-63.
12. Ruggiero C, Cherubini A, Ble A et. al. Uric acid and inflammatory markers. Eur Heart J 2006;27:1174–81.
13. Sanchez-Lozada LG, Tapia E, Lopez-Molina R et. al. Effects of acute and chronic L-arginine treatment in experimental hyperuricemia. Am J Physiol Renal Physiol. 2007;292:F1238–44.
14. Svetkey LP. Management of prehypertension. Hypertension. 2005;45: 1056–61.
15. Tietz, Textbook of Clinical Chemistry and Molecular Diagnostics. Ed. 4th., 2008.
16. Vasan RS, Larson MG, Leip EP, Kannel WB, Levy D. Assessment of frequency of progression to hypertension in non hypertensive participants in the Framingham heart study: a cohort study. The Lancet. 2001;358:1682-6.
17. Yamagata K, Ishida K, Sairenchi T et. al. Risk factors for chronic kidney disease in a community-based population: a 10-year follow-up study. Kidney Int. 2007;71:159–66.
18. Yuyun MF, Adler AI, Wareham NJ. What is the evidence that microalbuminuria is a predictor of cardiovascular disease events? Curr Opin Nephrol Hypertens. 2005;14:271–6.