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Microalbuminuria in Patients with Hypertension Visiting Tertiary Care Centre, Western Nepal

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ABSTRACT

Background: Renal complications of hypertension are associated with high morbidity and mortality. Prediction of such complications at the earliest is of utmost importance. We aimed to assess the prevalence of microalbuminuria in hypertensive patients.

Methods: A total of 130 clinically diagnosed hypertensive patients were enrolled in the study. Biochemical parameters that included serum creatinine, urinary albumin, and urinary creatinine were measured using standard methods. Albumin Creatinine ratio and estimated glomerular filtration rate were calculated. Albumin Creatinine ratio values between 30-300 mg/g were considered as microalbuminuria. Statistical analysis was performed on 120 samples after excluding frank proteinuria.

Results: The prevalence of microalbuminuria in hypertensive patients was 19.16%. Mean ranks of systolic blood pressure, pulse pressure, and serum creatinine levels were significantly higher in hypertensive patients with microalbuminuria. Mean estimated glomerular filtration rate was significantly low in hypertensive patients with microalbuminuria. Older age and increased duration as well as severity of hypertension were not associated with a higher prevalence of microalbuminuria.

Conclusions: The prevalence of microalbuminuria was high in hypertensive patients. Serum creatinine and estimated glomerular filtration rate were significantly altered in patients with microalbuminuria. Early screening of microalbuminuria in such patients might help prevent renal complications.

Keywords: ACR; creatinine; eGFR; hypertension; microalbuminuria

INTRODUCTION

Hypertension is one of the risk factors to renal dysfunctions which is associated with high morbidity and mortality.[1, 2] Long-term exposures to hypertension causes early renal damage resulting in the increased loss of albumin in the urine.[3, 4]

Microalbuminuria (MAU) can be assessed early to see the effect of hypertension on the kidney. MAU is an elevated urine albumin level of 30 - 300 mg/day.[5] Collection of 24 hours urine sample is cumbersome and error prone. Therefore, it has been suggested that a single spot urine sample is enough for the diagnosis of MAU.[6] To increase the accuracy, the urinary albumin can be adjusted to creatininuria. Thus, a urinary albumin-creatinine ratio (ACR) of 30-300 mg/g can be considered asMAU.[7]

A number of studies worldwide have highlighted the importance of measuring microalbuminuria in hypertensive patients. However, in context of Nepalese population, the relevant literatures are scarce. This study aimed to evaluate the prevalence of MAU in hypertensive patients and its association with stages of hypertension. Further, we aimed to correlate MAU with parameters of renal function.

METHODS

This hospital based cross-sectional study was carried in the department of Biochemistry in collaboration with the department of Internal Medicine, Universal College of Medical Sciences (UCMS), Bhairahawa, province no 5, Nepal from April 2019 to September 2019. Ethical approval was taken from the institutional review committee (IRC), UCMS (IRC/031/19) prior to the study. Both written and informed consent were obtained from the patients prior to sample collection.

Clinically diagnosed hypertensive patients by the

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Internal medicine department of UCMS were considered as the study population for this study. Those diagnosed with cardiac disease, diabetes mellitus, urinary tract infection, obesity, history of febrile illness, and pregnant women were excluded. Convenient sampling technique was used. Hypertension was categorized as per the World Health Organization (WHO)/ International Society of Hypertension (ISH) into three grades: Grade 1- Systolic Blood Pressure (SBP) 140-159 mm of Hg, Diastolic Blood Pressure (DBP) 90-99 mm of Hg); Grade 2- SBP 160-179 mm of Hg, DBP 100-109 mm of Hg; and Grade 3- SBP ^{3}180 mm of Hg, DBP ^{3} 110 mm of Hg hypertension respectively.[8] Previously diagnosed hypertensive patient still under medication whose blood pressure was normal at the time of measurement was additionally categorized as normal for analytical purpose. All the details including socio-demographic parameters, the anthropometric measurements, medical history regarding the inclusion and exclusion criteria were entered into the study proforma before the sample collection.

Five ml of blood and spot urine samples each were collected under the aseptic condition in a plain vial and clean container (without preservative), respectively, for the analysis of biochemical parameters. Anthropometric parameters like height (cm) and weight (kg) were also measured in parallel. The body mass index (BMI) was also calculated. The serum was separated by centrifugation at 3000 rpm for 15 minutes, and all the parameters were tested on the same day. Urinary albumin for microalbuminuria was measured by nephelometry method using a prefilled microalbumin cartridge (Mispa i3, India). Serum and urine creatinine (sCR and uCR) were estimated by modified Jaffe's kinetic method (Coral clinical system, India). Thenceforth, the albumin creatinine ratio (ACR) was calculated using formula: Urine albumin (mg/dL) / Urine creatinine (g/dl) = ACR in mg/g. Microalbuminuria was classified according to the reference range defined by the American Diabetes Association (ADA) and the National Kidney Foundation (NKF), i.e., 30-300 mg/g.[9,10] Samples with ACR more than 300 mg/g (frank proteinuria, n=10) were excluded. Estimated glomerular filtration rate (eGFR) was calculated by using Modification of Diet in Renal Disease (MDRD) equation: eGFR = 186.3 × (serum creatinine in mg/dl) $^{-1.154}$ × (age in years) $^{-0.203}$ × (0.742 for women). These values were entered into the study proforma as well.

The minimum sample size was calculated using the prevalence based formula z^2pq/d^2 (where z = 1.96, P=0.199 (prevalence)[11,12] ; Q = 1-P; d =0.075) and was calculated to be 108.86 (≈109). Initially, the study involved 130 hypertensive patients of which ten were excluded based on the presence of frank proteinuria (ACR > 300 mg/g). The final analysis was done on 120 samples.

Data were entered in Microsoft MS Excel 2007 and analyzed by Statistical Package for Social Sciences (SPSS); version16. The normality of the numerical data was analyzed by the Shapiro –Wilk test. All numerical variables except age and eGFR were not normally distributed. Non-normal data were expressed in median, 25th, and 75th percentile and normal data were expressed as mean ± standard deviation (SD). Non-parametric tests like the Mann-Whitney U test and Spearman's correlation analysis were performed for non-normal variables. Normal variables were analyzed by the independent Sample t-test. For categorical data Chi-square analysis and Binomial logistic regression were used. A p-value of < 0.05 was considered statistically significant.

RESULTS

The present study involved 120 hypertensive patients, among which 66 (55%) were male and 54 (45%) were female. Microalbuminuria was present in 23 (19.16%) participants. The mean age of the participants was 52.88 years and the median BMI was 24.67 kg/m^2. Most of the participants (50, 41.7%) had hypertensive duration of <1 year followed by 1-5 years (40, 33.3%), and 6-10 years (22, 18.3%) respectively. Majority of the study population (102, 85.0%) were under treatment of anti-hypertensive medications. The distribution of patients according to the stage of hypertension is depicted in figure 1.

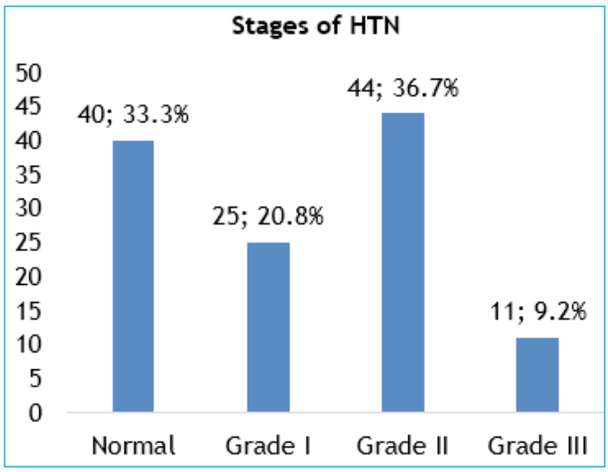

Figure1. Distribution of patients according to stages of hypertension.

The general characteristic of anthropometric, hemodynamic, and biochemical variables among the

microalbuminuria group is shown in table 1 where SBP, pulse pressure (PP), sCR, and eGFR were significantly different between them. Similarly, the categorical variables (sex, stage of hypertension, hypertension pharmacotherapy) are compared between the microalbuminuria groups (table 2). None of these variables were significantly different between the groups. Spearman Correlation analysis showed that ACR was positively and strongly correlated with sCR while negatively with eGFR (table 3).

Table 1. Association of microalbuminuria group with Anthropometric, Hemodynamic and Biochemical variables .

Variables	Total Subjects (n = 120)	Microalbuminuria		P-value
		No [ACR <30mg/g] (n=97)	Yes [ACR 30-300mg/g] (n = 23)	
Age (Years)	52.88 ± 12.64[a]	52.77 ± 12.13[a]	53.30 ± 14.89[a]	0.857[b]
BMI (Kg/m^2)	24.67 (22.24; 27.34)	24.74 (22.18; 27.95)	24.51 (22.31; 26.04)	0.163
SBP (mmHg)	150 (130; 160)	150 (130; 160))	150 (140; 180)	0.042
DBP (mmHg)	90 (90; 100)	90 (90; 100)	90 (80; 100)	0.964
PP (mmHg)	60 (40; 70)	50 (40; 60)	70 (50; 80)	0.018
Duration HTN (years)	2 (0.43; 5.75)	2 (0.41; 5)	3 (0.50; 10)	0.414
sCR (mg/dl)	0.90 (0.90; 1.08)	0.90 (0.90; 1.00)	1.20 (0.90; 1.60)	0.010
eGFR (ml/min)	74.69 ± 20.11[a]	77.17 ± 18.07[a]	64.21 ± 24.87[a]	0.026[b]

Abbreviations: BMI-Body Mass Index; SBP-Systolic Blood Pressure; DBP-Diastolic Blood Pressure; PP- Pulse Pressure; HTN-Hypertension; ACR-Albumin Creatinine Ratio; sCR-Serum Creatinine; eGFR-Estimated GFR (MDRD). a = Mean ± Standard Deviation [Median, with 25 and 75 percentiles in parentheses, for the rest]; b= p- values obtained from independent sample t-test (Mann-Whitney test for the rest). P-Value < 0.05 considered statistically significant (expressed in bold typing)

Table 2. Association of sex, stages of HTN and HTN pharmacotherapy with microalbuminuria group.

Parameters		Microalbuminuria		p-value
		No	Yes	
Sex	Male (66)	50 (75.8%)	16 (24.2%)	0.162[a]
	Female (54)	47 (87.0%)	7 (13.0%)	
Stage of HTN	Normal HTN (40)	34 (85%)	6 (15%)	0.086[b]
	Grade I (25)	19 (76%)	6 (24%)	
	Grade II (44)	38 (86.4%)	6 (13.6%)	
	Grade III (11)	6 (54.5%)	5 (45.5%)	
HTN Pharmacotherapy	No (18)	13 (72.2%)	5 (27.8%)	0.335[a]
	Yes (102)	84 (82.4%)	18 (17.6%)	

Abbreviation: HTN- Hypertension, a= P-values obtained from Fisher's Exact test; b = P-value obtained from Pearson's Chi-square analysis. P-value <0.05 considered statistically significant.

Table 3. Correlation of ACR with numerical variables in the total study population and microalbuminuria.

Subjects			Age	BMI	SBP	DBP	PP	sCR	eGFR	Durat-ion HTN
Total (120)		ρ	-0.068	-0.134	0.144	0.042	0.143	0.188	-0.197	0.011
P		0.231	0.073	0.058	0.325	0.059	0.020	0.015	0.454	
MAU	Yes (23)	ρ	0.134	-0.169	0.244	-0.007	0.255	0.211	-0.241	0.327
		P	0.272	0.220	0.131	0.487	0.120	0.167	0.134	0.064
	No (97)	ρ	-0.138	-0.061	0.016	0.060	-0.020	0.022	-0.087	-0.084
		P	0.089	0.275	0.439	0.282	0.422	0.415	0.198	0.208

Spearman Correlation analysis performed. Abbreviation: BMI- Body Mass Index, MAU-Microalbuminuria SBP- Systolic Blood Pressure, PP-Pulse Pressure, sCR- Serum Creatinine, eGFR- Estimated Glomerular Filtration Rate, HTN- Hypertension P-value < 0.05 considered statistically significant.

Binomial logistic regression analysis was performed to adjust the effect of covariates among the microalbuminuria group (table 4). After adjustment, only eGFR and sex (male) were found to be significantly associated with MAU.

Table 4. Association of microalbuminuria group with their covariates.

Variables		B	P-Value	Exp (B)	95% C. I. for Exp (B)	
				Lower	Upper	
Age		-0.048	0.082	0.953	0.903	1.006
SBP		0.019	0.593	1.019	0.951	1.092
PP		0.019	0.550	1.019	0.957	1.086
sCR		-0.472	0.347	0.624	0.234	1.666
eGFR		-0.053	0.011	0.948	0.910	0.988
BMI		-0.071	0.359	0.932	0.801	1.084
Sex (Male)		1.486	0.031	4.421	1.145	17.072
Duration HTN		0.103	0.085	1.108	0.986	1.246
Stage HTN	Grade I	0.505	0.737	1.658	0.086	31.784
	Grade II	0.186	0.877	1.204	0.115	12.602
	Grade III	-0.648	0.521	0.523	0.072	3.789

Binomial logistic regression analysis performed. Abbreviation: SBP-Systolic Blood Pressure, PP-Pulse Pressure, sCR- Serum Creatinine, eGFR- Estimated Glomerular Filtration Rate, BMI-Body Mass Index, HTN-Hypertension - Confidence Interval. Sex and Stage HTN are categorical variables. Reference HTN category is essential HTN P-value < 0.05 considered statistically significant.

DISCUSSION

The prevalence of microalbuminuria among hypertensive patients in this study was 19.16%. Several studies reveal an inconsistent prevalence of microalbuminuria among such patients ranging from 8-23%, or even higher.[13-15] One study conducted in Nepal also showed a high prevalence of 51.88%. Similarly, other studies done across various nations have shown seemingly disparate prevalence of 13%, 23.6%, 26.67%, 33.3%, 35.4%, 44%, 59.3% and 67.8%. [14, 16-22] There could be several reasons for this varied prevalence including non-exclusion of other independent factors like diabetes and obesity, diverse methods of estimation and urine collection, the inclusion of subjects with known albuminuria, and characteristics of study population among others.[22, 23] Furthermore, large-scale studies focusing on specific age groups, types of antihypertensive medications taken, and identification of other confounders may aid to minimize these discrepancies. Different variables such as age, sex, and BMI were evaluated for their role as possible risk factors for MAU. No such associations were found in the present study. Several other studies, however, have come up with variable conclusions.[16-20, 23]

In the present study, when ACR was categorized into the microalbuminuric group (ACR = 30-300mg/g) and normal (ACR < 30mg/g). We found no association between microalbuminuria and duration as well as the severity of hypertension. Correlation analysis also showed no significant association of ACR levels with the duration of hypertension. Hitha B et al, however, reported that MAU is significantly higher with longer duration and increasing severity of hypertension.[17] Sabharwal et al, in their research, found no association of urinary albumin excretion (UAE) with the duration of Hypertension.[18]

Age, sex, and BMI did not pose a significant risk for microalbuminuria in our study. However, when adjusted for possible confounders, males were likely to have microalbuminuria than females (exp B = 4.421, p = 0.031). Hitha B et al reported no significant association of gender with MAU, but patients with older age and higher BMI were more likely to have MAU.[17] Similarly, another study showed older age, but not higher BMI or gender to be significantly associated with MAU.[19] A study from Nepal by Poudel B et al reported that higher BMI, older age, and female gender was associated with MAU in hypertensive patients.[23]

In the present study, SBP and PP were significantly higher in hypertensive patients with MAU. However, they were not significantly correlated with ACR levels. Murai S et al reported SBP, but not DBP, correlated independently with abnormal albuminuria and urinary albumin.[19] Maggon RR et al also reported high mean SBP and DBP in patients with MAU, with the mean difference of SBP being statistically significant.[20] Several studies have found both SBP and DBP to be significantly elevated in hypertensive patients with MAU.[16, 23]

The classical view of MAU and frank proteinuria explained the phenomenon as a mere disruption of glomerular filtration. However, the modern view inclines towards the presence of large quantity albumin in the primary filtrate itself playing a major role in the pathophysiology of kidney dysfunction.[13] In the present study, the estimation of renal function was evaluated through measurements of sCR and calculated eGFR (MDRD). The mean sCR was significantly higher in patients with MAU (p = 0.010). There was also weak positive correlation between sCR and ACR levels (ρ = 0.188, p = 0.020). The eGFR was significantly lower in the microalbuminuric group (p=0.026). The eGFR values were also negatively

associated with the ACR in the overall study population (ρ = -0.197, p = 0.015). After adjustment for the possible confounders, however, eGFR was the only significant independent predictor of MAU. In a study by Murai S et al, mean sCR was significantly high in patients with abnormal albuminuria, but did not correlate independently when multivariate regression analysis was performed. Similar results were found with eGFR as well where it negatively correlated with abnormal albuminuria but not independently when multivariate analysis was done.[19] Poudel et al, found increased ACR levels with higher levels of sCR.[23]

CONCLUSIONS

The prevalence of microalbuminuria in hypertensive patients was 19.16%. SBP, PP, and sCR were significantly higher in the hypertensive patients with microalbuminuria whereas eGFR was significantly lower. However, older age and increased duration as well as severity of hypertension did not pose the risk for microalbuminuria. Even after adjustment for the confounders, eGFR, and male sex were found to be independently associated with microalbuminuria.

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REFERENCES

1. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. Prevention, Detection , Evaluation , and Treatment of High Blood Pressure. The JNC 7 Report. JAMA 2003; 289 (19): 2560-72. [Article]
2. Burt VL, Whelton P, Roccella EJ, Brown C, Cutler JA, Higgins M, et al. Prevalence of hypertension in the US adult population: results from the Third National Health and Nutrition Examination Survey, 1988-1991. Hypertension. 1995 Mar;25(3):305-13.[Article]
3. Perneger TV, Nieto FJ, Whelton PK, Klag MJ, Comstock GW, Szklo M.A Prospective Study of Blood Pressure and Serum Creatinine Results From the Clue. JAMA 1993; 269: 488–93. [Article]
4. Badiger S, Sandeep HM , Satish C Talikoti BM. A Study of Microalbuminuria and Target Organ Damage in Patients with Essential Hypertension. Int J Biol Med Res 2012; 1(3): 1351–5. ISSN (Online): 2393-915X. [Download PDF]
5. Tobe SW, Mcfarlane PA, Naimark DM. Microalbuminuria in diabetes mellitus. CMAJ 2002;167 (5):499–503. [Article]
6. Pugliese G, Solini A, Fondelli C, Trevisan R, Vedovato M, Nicolucci A, et al. Reproducibility of albuminuria in type 2 diabetic subjects. Findings from the Renal Insufficiency and Cardiovascular Events (RIACE) study. Nephrol Dial Transplant 2011; 26 (12):3950–4.[Article]
7. Croal BL, Mutch WJ, Clark BM, Dickie A, Church J, Noble D, et al. The clinical application of a urine albumin : creatinine ratio point-of-care device. Clin Chim Acta 2001; 307: (1-2); 15–21. [Article]
8. World Health Organization (WHO)/International Society of Hypertension (ISH) statement on management of hypertension. J Hypertens 2003; 21(11): 1983-92. https://journals.lww.com/jhypertension/Abstract/2003/11000/2003_World_Health_Organization__WHO__International.2.aspx
9. American Diabetes Association: Nephropathy in diabetes (Position Statement). Diabetes Care 27 (Suppl. 1): S79–S83, 2004.[Article]
10. Keane WF, Eknoyan G. Proteinuria, albuminuria, risk, assessment, detection, elimination (PARADE): a position paper of the National Kidney Foundation. Am J Kidney Dis 1999; 33: 1004-10.[Article]
11. Hasan M, Sutradhar I, Akter T, Das Gupta R, Joshi H, Haider MR, et al. Prevalence and determinants of hypertension among adult population in Nepal: Data from Nepal Demographic and Health Survey 2016. PLoS One. 2018; 13(5): e0198028.[Article]
12. Who.int. 2020. Hypertension. [Online] Available at: https://www.who.int/news-room/fact-sheets/detail/hypertension
13. Zeeuw DD, Parving HH, Henning RH. Microalbuminuria as an Early Marker for Cardiovascular Disease. J Am Soc Nephrol 2006. 17: 2100–5.[Article]
14. Schrader J, Luders S, Kulschewski A, Hammersen F, Zuchrer C, Venneklaas U, et al. Microalbuminuria and tubular proteinuria as risk predictors of cardiovascular morbidity and mortality in essential hypertension: final results of a prospective long-term study (MARPLE Study). J Hypertens 2006; 24 (3): 541-8.[Article]

15. Flynn JT. Microalbuminuria in children with primary hypertension. J ClinHypertens2016; 18 (10): 962-5.

16. Leoncini G, Sacchi G, Ravera M, Viazzi F, Ratto E, Vettoretti S, et al. Microalbuminuria is an integrated marker of subclinical organ damage in primary hypertension. Journal of human hypertension. 2002 Jun;16(6):399-404.[Article]

17. Hitha B, Pappachan JM, Pillai HB, Sujathan P, Ramakrishna CD, Jayaprakash K, et al. Microalbuminuria in Patients with Essential Hypertension and its Relationship to Target Organ Damage: An Indian Experience. Saudi J Kidney Dis Transpl 2008; 19 (3):411-9.[Article]

18. Sabharwal RK, Singh P, Arora MM, Somani BL, Ambade V. Incidence of microalbuminuria in hypertensive patients. Indian J Clin Biochem 2008; 23 (1) 71-5.[Article]

19. Murai S, Tanaka S, Dohi Y, Kimura G, Ohte N. The prevalence, characteristics, andclinical significance of abnormal albuminuria in patients with hypertension. Sci Rep 2014; 4: 3884.[Article]

20. Maggon RR, Malik R, Jain N, Isser HS. Study of the Prevalence of Microalbuminuria in Patients of Essential Hypertension and Its Correlation with Left Ventricular Hypertrophy and Carotid Artery Intimamedia Thickness. J Clin Prev Cardiol 2018; 7; 11-6. [Article]

21. Kangwagye P, Rwebembera J, Wilson T, Bajunirwe F. Microalbuminuria and Retinopathy among Hypertensive Nondiabetic Patients at a Large Public Outpatient Clinic in Southwestern Uganda. International journal of nephrology. 2018 Jun 6;2018.[Article]

22. Habbal R, Sekhri AR, Volpe M. Prevalence of microalbuminuria in hypertensive patients and its associated cardiovascular risk in clinical cardiology: Moroccan results of the global i-SEAR CH survey – a sub-analysis of a survey with 21 050 patients in 26 countries worldwide. Cardiovasc J Afr 2010; 21 (4): 200-5.

23. Poudel B, Yadav BK, Nepal AK, Jha B, Raut KB. Prevalence and association of microalbuminuria in essential hypertensive patients. N Am J Med Sci 2012; 4 (8): 331-5. [Article]