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Microalbuminuria: An Out of Sight Risk among Non-Diabetic Hypertensive Cases Residing In A Rural Area of Lahore

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Abstract
Background: *Microalbuminuria is an indicator of generalized vascular damage and a marker of cardiovascular complications in hypertensive. Early detection and prevention of microalbuminuria can help to control these related problems. The purpose of this pilot study was to determine urinary albumin creatinine ratio as measure of microalbuminuria in non-diabetic hypertensive patients residing in a rural area of Lahore.*
Method: *It was a cross-sectional study and was conducted in non diabetic hypertensive patients age >18 years, without a history of pre-existing kidney disease. A morning spot urine sample was obtained from each participant. Urinary albumin was estimated using in-house developed EIA kit for microalbuminuria and creatinine was determined using commercially available kit. Urinary albumin creatinine ratio ≤ 30mg/g was considered as normal.*
Results: *It was observed that urinary albumin creatinine ratios among hypertensive cases were considerably higher among hypertensive cases as compared to normotensive controls (p=0.003). The mean±SD of urinary albumin creatinine ratio (UACR) for normotensive controls, pre-hypertension, mild hypertension, moderate hypertension and that of severe hypertension cases were recorded as 13.7±6.7, 8.3±11.2, 15.5±12.6, 23.2±18.5 and 55.1±93.5 respectively. The comparison of UACR among these five stages were also found significant with p-value <0.001.*
Conclusion: *Screening for microalbuminuria should be practiced in routine management of non diabetic hypertensive patients in the basic health units of rural areas. Furthermore awareness program for general population residing in these rural areas should also be conducted to highlight the importance of screening for microalbuminuria among non diabetic hypertensive.*

I. Introduction

Hypertension is a major public health problem all over the world. In 1990-94 health survey of Pakistan reported 17.9% hypertension in adults 15 years and above.[1] In another study, reported prevalence of hypertension in a low-income community in Karachi was 26%.[2] Essential hypertension creates clinical albuminuria and a noteworthy reduction in renal function in 5–15% of patients.[3] The development of more sensitive methods to evaluate the UAE (urinary albumin excretion) has exhibited high rate of recurrence (25–100%) of microalbuminuria in patients with hypertension than in normotensive population.[4-6] This wide unpredictability in the incidence of microalbuminuria in these studies may be related to the severity of hypertension, selection criterion, racial diversity and due to differences in the methods used for detection.

The mechanisms and significance of microalbuminuria observed in some patients with essential hypertension are not clearly elucidated and the relation between albuminuria and renal function in non-diabetic hypertensive subjects is not well understood due to lack of simultaneous assessment of the relation between albuminuria and intra-renal hemodynamic and long-term follow-up studies. An increased urinary albumin excretion is associated with early and late renal functional abnormalities, such as hyper filtration and a diminished filtration in a non-diabetic population and these renal functional changes usually come to medical attention only after the development of renal damage.

Several studies have shown that proteinuria along with microalbuminuria are independent prognosticators of cardiovascular morbidity [7, 8] and mortality in patients with essential hypertension. The 2007 ESH/ESC guidelines recommend screening for microalbuminuria in all patients with hypertension both in patients with hypertension with or without diabetes because microalbuminuria has been shown to predict cardiovascular (CV) events. [9] Early identification of a patient at risk of CV events provides an opportunity for

early treatment, to slow the progression of disease. Moreover, 25% of patients with end stage renal disease have hypertension as the primary diagnosis.[3] For this reason; detection of microalbuminuria could be useful in selecting specific therapeutic strategies for reducing and preventing cardiovascular events in hypertensive patients.[10-12] Therefore in hypertensive subjects, microalbuminuria has now been considered as an essential component in the assessment of subclinical organ damage because its detection is easy and relatively inexpensive.[9]

Due to illiteracy the people in rural areas of Pakistan are unaware of the fact that hypertension leads to elevated UACR also called as microalbuminuria that can later cause kidney dysfunction and cardiovascular diseases. People in the rural area do not undergo proper consultation with doctors and have an improper treatment. The subjects taken were not having a proper treatment in consultation with the doctor for hypertension. Usually microalbuminuria is not tested among the people accessing the basic health unit in the rural area of Lahore. Microalbuminuria is tested in diabetic hypertensive patients but not the non-diabetic hypertensive patients being referred to the tertiary centers at the rural. The purpose of this pilot study was to determine urinary albumin creatinine ratio as measure of microalbuminuria in non-diabetic hypertensive patients residing in a rural area of Lahore.

II. Methodology

Setting

This study was conducted from January to June 2014 at Basic Health Unit Jallowana post office Cantt, Lahore.

Study Design

Cross-sectional study

Study Population

Non-diabetic subject's age >18 years, without a history of pre-existing kidney diseases participated in this study.

Inclusion Criteria

Patients with hypertension (defined by sitting blood pressure (BP≥140/90 mmHg) without history of diabetes and fasting glucose < 110mg/dl.

Exclusion Criteria

Patients with impaired kidney function (serum creatinine 1.4 mg/dl in male, or 1.2 mg/dl in female), or history associated with false positive albuminuria (fever, menstruation, urinary tract infection and post exercise).

Sample Selection

Normotensive consisted of 51 healthy volunteers, without history of hypertension (defined by sitting blood pressure (BP≤140/90 mmHg) and age and sex matched were also entered into the study. They were thoroughly screened for any disease especially hypertension, renal disease and diabetes mellitus. Hypertensive cases consisted of 126 diagnosed cases of hypertension that fulfilled inclusion and exclusion criteria of study.

Data Collection

The study was approved by SZPGMI IRB (IRB No. 1132). All participants gave written informed consent. A questionnaire was used for collecting information on demographics, current medical illness, and family history of cardiovascular disease, diabetes, kidney disease and duration of hypertension. Participants were also measured for weight and height.

Measurement of Blood Pressure

All participants have their BP measured after a 5 minutes rest with a calibrated digital BP monitor. Systolic and diastolic BP measurements were calculated as the mean of the last two visits. High blood pressure (or hypertension) was defined in an adult as a blood pressure greater than or equal to 140 mmHg, systolic pressure or greater than or equal to 90 mm Hg diastolic pressure.[13]

The hypertensive cases were further classified according to guidelines of European Society of Hypertension and Cardiology using following cutoff. [14]

Normal	120–129/80–84
Pre-hypertension (Pre-HT)	130–139/85–89
Mild hypertension (Mild-HT)	140–159/90–99
Moderate hypertension (Moderate-HT)	160–179/100–109

Severe hypertension (Severe-HT) > 180 / > 110
The study participants were categorized under the above criteria by looking at their systolic blood pressure.

Sample Collection

A morning spot urine sample was obtained from each participant according to the guidelines of The American Diabetes Association. [15] Three milliliter blood was also drawn from each participant for the estimation of fasting lipid profile.

Lipid profile

Serum cholesterol, triglycerides and HDL-cholesterol were determined using commercially available kits.

Urinary albumin measurements

Urinary albumin was estimated using in-house developed EIA kit for microalbuminuria and urine creatinine was determined using commercially available kit. Urinary albumin creatinine ratio ≤ 30mg/g was considered as normal.

Data analysis

Data was entered and analyzed using SPSS for windows version 20. P value of <0.05 was considered as significant.

III. Results

A total of n=177 study participants were enrolled in this study, out of which n=126 were hypertensive cases (BP≥140/90 mmHg) and n=51 were normotensive (BP≤140/90 mmHg). Demographic features of study participants are described in table 1. It was observed frequency of hypertension was higher among females 70(55.9%) as compared to 56(44.1%) in males (p= 0.001). Presence of hypertension in study subjects was significantly associated with family history of diabetes (p=0.026). (Table 1)

Table 1: Characteristics of study participants

Characteristics		Hypertensive		Normotensive		P value
		(n=126)	%	(n=51)	%	
Gender	Male	56	44.1	36	72	0.001
	Female	70	55.9	15	28.0	
Family history of hypertension		61	48.4	22	43.1	NS
Family History of Cardiac Disease		37	29.3	17	33.3	NS
Family history of diabetes		28	22.2	20	39.2	0.026
Self Smoking		10	7.9	8	15.7	NS

Clinical and biochemical characteristics were compared among hypertensive cases and normotensive controls. Hypertension was shown as the disease of older age (p<0.001). Most of the hypertensive cases were overweight as compared to normotensive controls (p=0.004). Serum cholesterol and triglycerides were estimated to be significantly higher among hypertensive cases as compared to normotensive controls (p = 0.022, 0.011 respectively). Further it was observed that urinary albumin creatinine ratios among hypertensive cases were considerably higher among hypertensive cases as compared to normotensive controls (p=0.003). (Table 2)

Table 2: Clinical and Biochemical characteristics of study participants

Characteristics	Hypertensive	Normotensive	P-value
	Mean ± SD	Mean ± SD	
Age (year)	48.6±13.6	40.9±11.5	<0.001
Body Mass Index (Kg/m^2)	28.02 ± 7.02	25.00 ± 5.83	0.004
Systolic Blood Pressure (mm of Hg)	154 ± 22	119 ± 8	<0.001
Diastolic Blood Pressure(mm of Hg)	92 ± 12	74 ± 7	<0.001
Total Cholesterol (mg/dl)	166.74 ± 105.13	136.87 ± 52.62	0.022
Triglycerides (mg/dl)	171.09 ± 102.39	140.91 ± 99.45	0.011
High Density Lipoproteins (mg/dl)	62.7 ± 15.7	58.7 ± 16.6	0.073
UACR (mg/g)	21.6±47.3	10.6±14.3	0.003

As per criteria of systolic blood pressure, out of total study population (n=177) there were 35(19.8%) cases having normal blood pressure, 16(9.0%) having pre-hypertension, 52(29.4%) with mild hypertension, 40(22.6%) with moderate hypertension and 34(19.2%) with severe hypertension. The mean±SD of urinary albumin creatinine ratio (UACR) for these groups were recorded as 13.7±6.7, 8.3±11.2, 15.5±12.6, 23.2±18.5 and 55.1±93.5 respectively. The comparison of UACR among these five stages were also found significant with

p-value <0.001 when Kruskull Wallis ANOVA was applied, which clearly shows the increasing tendency in UACR rate with severity of disease (Figure 1).

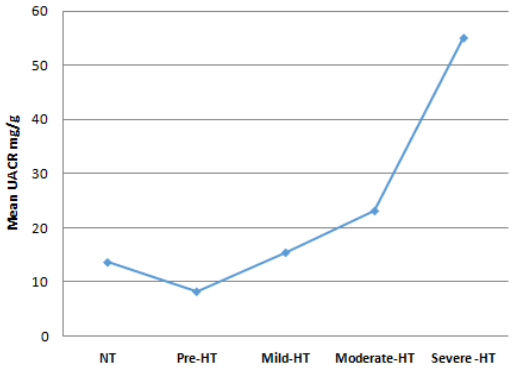

Figure 1: Association of high urinary albumin creatinine ratio with severity of hypertension

IV. Discussion

Nephropathy and heart diseases are intensely linked with microalbuminuria that is urinary albumin creatinine ratio (UACR) 30-300 mg/day or 20-200 µg/min which's a prognosticator for both of these diseases in both diabetic and non-diabetic patients [22, 23]. Previously, in a study microalbuminuria has been shown to be related with high risk of cardiovascular [16, 17] and progressive kidney disease [18–21] not only in diabetic but also in non-diabetic subjects. Recently, quantification of microalbuminuria in order to analyze the effects of hypertension on kidney has been on the go. Initially the term microalbuminuria was used by Viberti et al. to introduce the idea of subclinical rise in nephropathic diabetic patients [22, 23]. Parving et al. described the alliance between microalbuminuria and hypertension in 1974 [27].

In the present study clinical and biochemical characteristics were compared among hypertensive cases and normotensive controls. Hypertension was shown as the disease of older age (p<0.001). Hypertension and UACR being directly proportional to each other conclude that microalbuminuria is a disease of the older age. Previously, it has been proven that microalbuminuria is age dependant [35-38]. Earlier, alliance between albumin excretion rate and fatality in older age non-diabetic subjects along with an alliance between albumin excretion rate and heart diseases reflecting an age effect have been reported [8].

Most of the hypertensive cases were overweight as compared to normotensive controls (p=0.004). In a previously conducted study it was noticed among the four ethnic groups that the individuals with elevated BMI and waist circumference were more prone to hypertension. Compared to the other ethnic groups the indigenous individual's experienced grave elevation in hypertension. The difference in the risk for hypertension among white population and the indigenous individual's was due to difference in body compositions and the Asian population suffered hypertension more than the white population at the same levels of BMI and waist circumference [24]. A study in Uruguay showed 28.5% hypertension in a general population of 575 individuals and from these hypertensive individuals 74.4% had BMI higher than 25 kg/m^2 [25].

Serum cholesterol and triglycerides were estimated to be significantly higher among hypertensive cases as compared to normotensive controls (p = 0.022, 0.011 respectively). Our results are consistent with the results of a study conducted by Saha et al. in Bangladesh [26]. It is not a simple way of explaining that all hypertensive patients had high levels of total cholesterol. It is a continuous and graded relationship throughout the usual course of hypertension. Longer is the duration of hypertension more is the level of total cholesterol. In this study the same had been observed. Total cholesterol has been shown to have increasing trend. The same has been proved in tromso study conducted by Bonna and Thelle [29].

Further it was observed that urinary albumin creatinine ratios among hypertensive cases were considerably higher as compared to normotensive controls (p=0.003). Our result is supported by a previous study which also pointed out an interaction between hypertension and urinary albumin excretion rate not only in hypertensive patients and normal public [28, 29-31].

As per criterion of systolic blood pressure on the total study population the results match with the previous studies indicating that prehypertension is also associated with chronic kidney diseases [32-34].

A previously conducted study shows that the assurance of microalbuminuria in hypertensive patients hasn't fully been introduced. Many studies have shown that determination of microalbuminuria is an early marker for cardiovascular diseases for patients with or without diabetes and/or hypertension [17, 39, and 40]. Regardless of the working mechanism, the existence of microalbuminuria reveals bad prognosis. Hence, routine assurance should be practiced in patients suffering heart failure and its risks [41].

Spot UACR assessment has been shown to correlate well with CV risk and provides a simple and reliable method of microalbuminuria screening. Current challenges, therefore, should not preclude the inclusion of microalbuminuria screening in the routine management of hypertensive patients.

Concluding, microalbuminuria is a very easy and authentic method to detect cardiovascular morbidity, mortality and probably renal damage in both men and women with crucial hypertension [3]. Awareness among the general population to undergo screening of microalbuminuria should be created and routine checkup of microalbuminuria must be practiced in the normal people as well.

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