Frequency and possible associations of albuminuria in patients with essential hypertension: a single-center experience

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Background
Microalbuminuria is associated with a high incidence of morbidity and mortality. It is considered as an early marker of kidney damage and a predictor for end-stage renal disease and cardiovascular disease. Thus, it is of great importance to study albuminuria in high-risk groups such as the hypertensive patients to decrease the morbidity and mortality by decreasing the progression of kidney diseases on those groups.

Aims
The present study was undertaken to find out the frequency and association of microalbuminuria in newly diagnosed essential hypertension.

Patients and methods
This is a cross-sectional hospital analytic study enrolling all the outpatients nephrology and internal medicine clinics within the period from 2016 January to 2017 March. We enrolled all the patients with the positive inclusion criteria and divided them into two groups; those who are recently diagnosed as essential hypertensive patients (85 patients) aged between 25 and 65 years and (415 normotensive) as normotensive healthy participants with the same age groups. Exclusion criteria were age less than 25 years and more than 65 years, diabetes mellitus, chronic kidney disease, end-stage renal failure, nephrotic syndrome, pregnancy, and under steroid therapy.

Results
The study showed that 17% of the patients were hypertensive; 28.8% of hypertension cases and 13.1% of normotensive patients had microalbuminuria in the total population ($P = 0.000$). Twenty-two percent of the hypertensive cases had macroalbuminuria and 3% of the normotensive patients had macroalbuminuria with a P value of 0.000. Advanced age is associated with the increase in the albumin–creatinine ratio ($P = 0.000$).

Conclusion
By showing the strong association between microalbuminuria and hypertension, our findings suggest that microalbuminuria could be a useful marker to assess risk management of cardiovascular disease and renal disease.

Keywords:
hypertension, macroalbuminuria, microalbuminuria

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Introduction

Albuminuria is defined as the increased urinary excretion of albumin (>30 mg/24 h), which if present in the ratio (30–300 mg/24 h) cannot be detected by the routine protein dipstick method [1]. It is known that albuminuria is associated with a diffuse vascular dysfunction, thus it is considered to be a premier factor in the development of cerebrovascular and cardiovascular diseases, so its presence is associated with the increased morbidity and mortality especially for high-risk populations such as hypertensive patients and diabetics [2]. So it is useful to have a regular screening for microalbuminuria in hypertensive patients [3]. So the prevention of albuminuria whether occurrence or progression in the high-risk group can prevent or at least delay the progression of end-stage kidney disease and severe cardiovascular diseases. Therefore, characterization of the possible risk factors for the presence of microalbuminuria in hypertensive patients may provide valuable information for clinical intervention. It is well known that essential hypertension is one of the most common causes of end-stage kidney disease; however, the development of serious renal injury is relatively low [4]. Thus, the objective of our study was to find out the frequency, risk factors, and association of urinary microalbuminuria in essential hypertensive patients, hoping that our results would provide a basis for future development of intervention approaches to prevent and manage kidney diseases in this specific population.

Patients and methods

This hospital-based cross-sectional analytic study was conducted in the Department of Internal Medicine (Nephrology Unit), Assuit University Hospital from 2016 January to 2017 March. Consent was taken from the participants. We enrolled all the patients with the positive inclusion criteria and divided them into two groups; those who are recently diagnosed as essential hypertensive patients (85 patients) aged between 25 and 65 years and (415 normotensive) as normotensive healthy participants with the same age groups.

Data collection

A medical history was taken and a physical examination was performed by a physician. Age, sex, and weight were collected from the participants. BMI was calculated by weight (kg) divided by height (m^2). We measured the biochemical profile including total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol, triglycerides, and creatinine, from all participants. The urine sample was also processed on the same day and estimated for urinary microalbuminuria and creatinine. In spot urine sample albumin was measured quantitatively and adjusted to creatininuria and then interpreted as an albumin–creatinine ratio (ACR) of less than 3.4 mg albumin/mmol creatinine as normal albuminuria, more than or equal to 3.4–33.9 mg albumin/mmol creatinine as microalbuminuria, and more than 33.9 mg albumin/mmol creatinine as macroalbuminuria. Laboratory standard operation procedures were maintained for all laboratory analysis [5].

Inclusion criteria

Participants aged more than 25 years and less than 75 years with essential hypertension were enrolled as cases. Similarly, the age of more than 25 years and less than 65 years without hypertension were enrolled as a healthy control group.

Exclusion criteria

Participants having age less than 25 years and more than 65 years, diabetes mellitus, chronic kidney disease, end-stage renal failure, nephrotic syndrome, pregnancy, and under steroid therapy were excluded from study.

Definition

Hypertension was categorized according to blood pressure readings by JNC-VIII definitions: normal (systolic <120 mmHg and diastolic <80 mmHg), prehypertension (systolic 120–139 mmHg or diastolic 80–89 mmHg), hypertension stage I (systolic 140–159 mmHg or diastolic 90–99 mmHg), and hypertension stage II (systolic ≥160 mmHg or diastolic ≥100 mmHg) [6]. Estimated glomerular filtration rate (eGFR) was calculated using the EPI equation by using the national kidney foundation calculator (*http://www.kidney.org/professionals/kdogi/gfr_calculator.cfm*).

Statistical analysis

The data were analyzed using Excel 2003, R 2.8.0 Statistical Package for the Social Sciences (SPSS) for Windows, version 16.0 (IBM Corporation, USA).

Ethical approval

All participants in the study signed fully informed consent. Assiut Faculty of Medicine Institutional review board approved and oversaw the study.

Results

Table 1 shows that the mean age of the studied group was 42.93 ± 15.60 as in the following: 26, 18, 18, 19, 13, and 5% in the age range less than 30 years old, from 30 to less than 40 years old, from 40 to less than 50 years old, from 50 to less than 60 years old, and from 60 years to less than 70, and more than 70, respectively. Men represent 33% of the studied group while women represent 67%.

Table 2 shows that the mean and SD of the following: systolic blood pressure, diastolic blood pressure, BMI,

Table 1 Demographic distribution of the studied population including both hypertensive and normotensive population

Personal characteristics	*n*=500 [*n* (%)]
Age (years)	
<30	130 (26)
30-<40	90 (18)
40-<50	90 (18)
50-<60	95 (19)
60-<70	65 (13)
≥70	25 (5)
Mean±SD (range)	42.93±15.60 (20-94)
Sex	
Male	165 (33)
Female	335 (67)

Table 2 Clinical data and investigations of the studied population

Clinical data and investigations	Mean±SD	Range
Systolic BP (mmHg)	158.90±25.13	85-190
Diastolic BP (mmHg)	98.90±12.15	55-110
BMI (kg/m^2)	26.46±4.10	15.57-39.06
Serum creatinine (mg/dl)	1.19±0.60	0.70-4.50
eGFR (ml/min)	102.91±32.21	15.5-165.08

BP, blood pressure; eGFR, estimated glomerular filtration rate

serum creatinine, and eGFR among the studied samples were 158.90 ± 25.13, 98.90 ± 12.15, 26.46 ± 4.10, 1.19 ± 0.60, and 102.91 ± 32.21, respectively.

Table 3 shows that 22.0% of the hypertensive patients have macroalbuminuria, while only 3.5% of the normal healthy participants have macroalbuminuria; these differences have a statistically significant value where *P* value = 0.000.

Table 4 shows that 28.8% of the hypertensive patients have microalbuminuria while only 13.1% of the normal healthy participants have microalbuminuria, these differences have a statistically significant value where *P* value = 0.000.

Table 5 shows the comparison of the mean value of demographic, clinical, and biochemical characteristics to different levels of ACR group. With the increases in age ($P < 0.001$), the level of urinary ACR was also increased. Systolic blood pressure ($P < 0.001$) and diastolic blood pressure ($P < 0.001$) were significantly increased with the level of urinary ACR. Serum level of TC ($P = 0.178$) was found to be insignificantly increased with the increased level of urinary ACR. But serum level of HDL-C ($P = 0.013$) was found to be significantly decreased with the increased level of urinary ACR. We also found that the serum creatinine ($P < 0.001$) was found to be significantly increased with the increased level of urinary ACR, whereas the eGFR ($P < 0.001$) level was significantly decreased with increased level of urinary ACR.

Table 3 Relationship between macroalbuminuria and hypertension among the studied population

The studied population	Macroalbuminuria [*n* (%)]			*P*
	Present	Absent	Total	
Hypertension				
Hypertensive	19 (22.0)	66 (78.0)	85 (100)	0.000*
Normal	15 (3.5)	400 (96.5)	415 (100)	

*This means that the *P* value is statistically significant.

Discussion

Our study shows that out of the 500 patients included in the study, 85 patients were recently diagnosed to have essential hypertension. This represents 17% from the total sample. Hypertension is an important worldwide public-health challenge because of its high frequency and concomitant risks of cardiovascular and kidney disease. It has been identified as the leading risk factor for mortality, and is ranked third as a cause of disability-adjusted life years [7]. In 2008, the Egyptian Demographic Health Survey (EDHS) study showed that the prevalence of prehypertension and hypertension among the adult population aged from 25 to 59 years in Egypt were 57.2 and 17.2%, respectively; of those who were hypertensive 19.8% were from urban areas and 15.8% from rural areas. Our results were nearly similar to those of the EDHS, but our results also were slightly more than that in rural areas in EDHS; this can be attributed to the more age group included in our study unlike the sample in EDHS which included only till age 59 years, and also we performed our study in a tertiary center where cases come to us from every place when there is only a complain. To the best of our knowledge, no other studies were done in Egypt to detect the change in the prevalence of hypertension whether in rural or urban areas.

Table 4 Relationship between microalbuminuria and hypertension among the studied population

The studied population	Microalbuminuria [*n* (%)]			*P*
	Present	Absent	Total number after exclusion to those with macroalbuminuria	
Hypertension				
Hypertension	19 (28.8)	47 (71.2)	66 (100)	0.000*
Normal	52 (13.1)	348 (86.9)	400 (100)	

*This means that the *P* value is statistically significant.

Table 5 Demographic, clinical, and renal characteristics of participants with different levels of albumin-creatinine ratio

Characteristics	Normoalbuminuria (ACR <3.4 mg/mmol)	Microalbuminuria (ACR >3.4 and <33.9 mg/mmol)	Macroalbuminuria (ACR >33.9 mg/mmol)	*P*
Age	41.11±10.20 (40.35-43.86)	43.71±10.25 (42.18-47.24)	53.31±6.93 (50.09-58.53)	0.000*
BMI (kg/m^2)	21.6±2.32 (22.27-23.13)	22.3±2.60 (22.73-24.08)	23.83±1.23 (23.08-24.57)	0.08
Systolic arterial pressure (mmHg)	123.72±16.98 (121.82-127.64)	134.52±18.20 (131.04-139.99)	154±19.01 (143.49-166.5)	0.000*
Diastolic arterial pressure (mmHg)	81.4±12.45 (79.66-83.94)	88.82±12.1 (85.86-91.86)	96.88±9.46 (91.19-102.64)	0.000*
Serum creatinine (mg/dl)	78.9±16.44 (77.11-82.76)	105.14±23.23 (100.4-111.85)	128±30.54 (110.51-147.48)	0.000*
Total cholesterol (mg/dl)	4.80±0.85 (4.66-4.95)	4.97±1.02 (4.72-5.23)	5.22±1.02 (4.62-5.85)	0.167
HDL-C (mg/dl)	1.11±0.26 (1.078-1.168)	1.04±0.28 (0.98-1.12)	0.90±0.28 (0.73-1.08)	0.011
Glomerular filtration rate (ml/min/1.73 m^2)	94.3±26.24 (90.1-99.1)	82.59±19.99 (77.7-87.53)	72.75±17.9 (61.69-83.6)	0.000*

ACR, albumin-creatinine ratio; HDL-C, high-density lipoprotein cholesterol. *This means that the *P* value is statistically significant.

Our study shows that among the 85 hypertensive patients, 19 patients have microalbuminuria, 19 have macroalbuminuria, and 47 hypertensive patients have normoalbuminuria. In comparison of the hypertensive patients to other healthy participants we found that 51.88% of all hypertensive patients had microalbuminuria while 13.2% of the healthy participants had microalbuminuria. The high frequency of microalbuminuria in the healthy participants in our study can be attributed to other causes rather than hypertension and diabetes where some studies had reported an association of proteinuria with obesity [8] and hyperlipidemia [9]. A significant association was found between occurrence of proteinuria and essential hypertension; this proteinuria alarm us to the progression of endothelial dysfunction which will lead to hypertensive nephropathy [10].

There was significant relation between microalbuminuria and hypertension in our study, where 28.8% of hypertensive patients have microalbuminuria in comparison to 13.1% of the healthy participants who have microalbuminuria, in the absence of chronic kidney diseases, diabetes, and other risk factors of microalbuminuria. This may be attributed to the endothelial dysfunction associated with atherosclerosis present in essential hypertension [11]. No large population studies have specifically studied the prevalence of microalbuminuria in a hypertensive cohort. However, data from subgroup analyses of large general population studies have found microalbuminuria present in 11–16% of people with hypertension [12]. These findings suggest that microalbuminuria could be a useful marker to assess risk management of cardiovascular and renal damage. So the significant association of microalbuminuria with hypertension in our study should be an alarm to follow up these cases because of their increased risk of mortality. Obesity is a risk factor for the presence of proteinuria mostly due to the effect of obesity on the kidneys. Zheng *et al.*[13] reported a possible association between BMI and albuminuria. In our study, the mean value of BMI was found to be increased insignificantly ($P = 0.08$) with the increased level of ACR.

We found that the serum level of creatinine ($P < 0.001$) was increased with the increased level of ACR, despite the parameters fell well within the normal reference range. The higher level of creatinine with the increased level of ACR may be due to subclinical ultrastructural changes in the glomeruli of hypertensive patients [14]. Our study has shown that a higher level of ACR was associated with the advances of age ($P < 0.001$) which could be explained by the presence of the endothelial dysfunction which occurs in the elderly. Also, our study showed that decreased eGFR was associated with an increased level of ACR; this finding can be explained by several causes: first the effect of hypertension on the ultrastructure of the glomeruli and also the normal progression of hypertensive nephropathy. Some studies that reported the presence of microalbuminuria in the early stage of hypertension can be taken as an important independent predictor for the progression of renal disease [5].

Our study showed that there was an association between albuminuria and hyperlipidemia in hypertensive patients where the TC level increases with the increase of the ACR and the HDL-C decreases with the increase of the ACR. Actually, these changes have no statistically significant value, but they are obvious. These changes can be explained by the urinary loss of protein that may cause an increase in the serum levels of lipoproteins. This is supported by evidence that urinary losses of large amounts of proteins may lead to increased serum levels of total and low-density lipoprotein cholesterol as well as lipoprotein. An alternative explanation for the association between microalbuminuria and hyperlipidemia is that hyperlipidemia causes renal damage that results in increased urinary albumin excretion. Many authors believe that lipid abnormalities may contribute to renal damage by a mechanism analogous to atherogenesis. Recent studies have shown that hyperlipidemia may play a role in the progression of renal damage [9].

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Conflicts of interest
There are no conflicts of interest.

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