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RESEARCH ARTICLE

CLINICAL SIGNIFICANCE OF URINARY MICROALBUMIN ESTIMATION IN DIABETIC PATIENTS WITH CO-MORBID OF HYPERTENSION AND RENAL INSUFFICIENCY

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ABSTRACT

Background: Microalbuminuria is a significant clinical outcome of diabetic nephropathy and related hypertension. Moreover, diabetes mellitus is a known dangerous metabolic disorders, resulting into induction of complications such as cardiovascular, glomerular hyperfusion and end stage renal disease (ESRD).
Aim and Objectives: Objectives of this study are 1) to determine the prevalence of microalbuminuria in selected age groups of diabetic patients, 2) to determine correlation of microalbumin with hypertension and renal insufficient in male and female patients.
Materials and Research Design: A total of 240 subjects (n = 160 diabetic patients, n = 80 controls) were selected for present study and classified according to gender, age, clinical categories (renal insufficiency and hypertension) and control groups. Urinary microalbumin was analyzed in 2nd morning urine of all selected patients and control groups by TINA-QUANT (Roche-Diagnostics) albumin methodology on Cobas 6000 c501 analyzer.
Results: Variable concentrations of microalbumin were detected in urine samples of male and female diabetic patients in both hypertensive and renal insufficiency co-morbids. Furthermore age-dependency on the correlation of microalbumin was noted, depicted by higher level of urinary microalbumin in older subjects as compared to younger ones.
Conclusion: Micro-albuminuria was noted to be more prevalent in renal insufficient diabetic patients as compared to hypertensive diabetics. Additionally age-dependency was also factor in higher levels microalbuminuria.

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INTRODUCTION

Microalbumin is a significant biomarker of diabetic nephropathy. Additionally, it is also a potent risk factor for cardiovascular disorders, hypertension and renal insufficiency (Defronzo, 1997; Silva *et al.,* 2008; Afkhami-Ardekani *et al.,* 2008). Moreover, diabetes itself is a potentially dangerous metabolic disorders, most of the times, rendering the complications of cardiovascular, glomerular hyperfusion and end stage renal disease (ESRD) (Afkhami-Ardekani *et al.,* 2008). Recent and past studies demonstrated an association between micro-albuminuria, cardiovascular and nephrotic diseases, including hypertension and renal insufficiency as co-morbids (Shekiba *et al.,* 2003; Viazzi *et al.,* 2010; Weir, 2004). Reported profiling and analysis of hypertensive patients showed 10 times increase in urinary albumin to creatinine ratio, thus increasing the risk of stroke and infarction by 30% in diabetic patients (Wachtell *et al.,* 2003). In this regard, the objectives of this study are 1) to determine the prevalence of microalbuminuria in selected age groups of diabetic patients, 2) to determine correlation of microalbumin with hypertension and renal insufficient in male and female patients.

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MATERIALS AND METHODS

Patient selection and research design

A total of 160 patients, divided (n = 80 each) equally into male and female groups with age and gender matched control groups of eighty individuals (male = 40, female = 40). Initially a total

of 200 patients were screened in each gender for presence of diabetes, with co-morbid of hypertension and renal insufficiency. Out of 200, 160 were included in the study as per diabetic patients primarily dividing in gender, with subdivision of hypertension and renal insufficiency, including of n = 40 males and n = 40 females, in each subdivision. Briefly the inclusion criteria were derived from a study reported earlier (Silva *et al.,* 2008). The study was conducted prospectively from Dec 2011 to Dec 2014 at Department of Biochemistry laboratory services and Chemical pathology, Liaquat National Hospital and Medical College, Karachi. Diabetic patients were those having fasting plasma glucose level of 125mg/dl, or with HbA1c greater than 8.0%. Those patients were considered hypertensive who manifest BP equal or higher than 140/90 mmHg or patient with earlier history of hypertension under treatment. Renal insufficiency in a patient was considered significant when protein to creatinine ratio is greater than 1.0 or nearer 0.9. It was made mandatory for inclusion of a patient in present study that he or she must be a diabetic with hypertension or renal insufficiency as co-morbids. Exclusion criteria were those patients aged less than 20 and greater than 86 years, patient's undergone surgeries. The patients in each gender were also subdivided into four age-groups to characterize the selected patients with age-based clinical or normal conditions.

Analysis of Micro Albumin

Urinary microalbumin was analyzed in 2nd morning urine of all selected patients and control groups. TINA-QUANT (Roche-Diagnostics) albumin methodology was used on Cobas 6000 c501 analyzer as per description of Hofmann and Guder (1989).

Statistical analysis

Data are presented in mean ± standard deviation. The variables and groups were compared with each other with SPSS version 13 (USA) and considered significant when $P < 0.05$.

RESULTS

A total of 240 subjects (n = 160 patients, n = 80 controls) were selected for present study and classified according to gender, age, clinical categories and control groups.

In males, a total of 80 diabetic patients were included and then divided into two separate co-morbids, hypertensive (n = 40) and renal insufficiency (n = 40), which were then subdivided into four age groups: 20-35 yrs, 36-50 yrs, 51-70 yrs and 71-85 yrs, each subgroups consisting of n =10 individuals. Similarly female diabetic patient groups had similar co-morbid groups and age-subgroups. Variable concentrations of microalbumin were detected in urine samples of male and female diabetic patients in both hypertensive and renal insufficiency co-morbids (Table I, Figs 1-4).

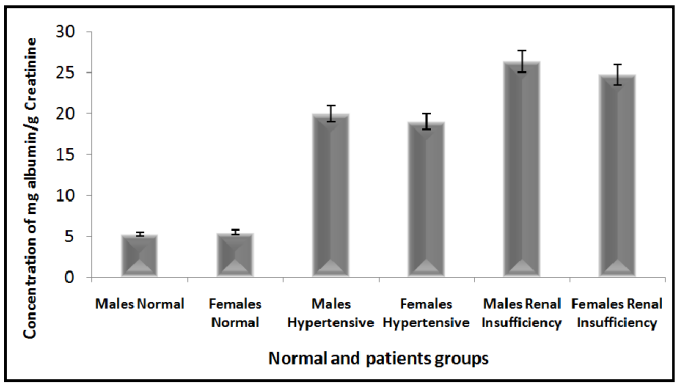

Fig. 1. Urinary micro albumin levels in selected patients of age group 20-35 years

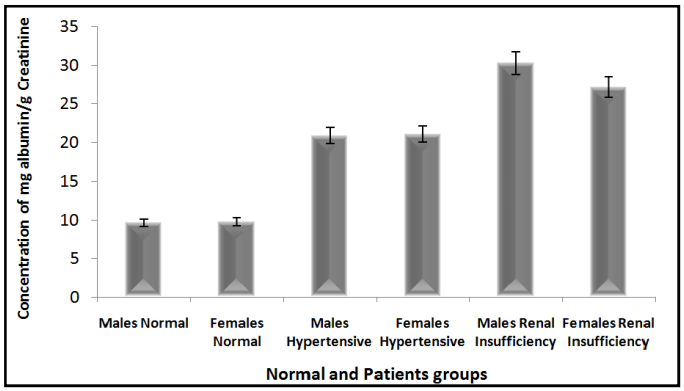

Fig. 2. Urinary microalbumin levels in selected patients of age group 36-50 years

Furthermore age-dependency on the correlation of microalbumin was noted, depicted by higher level of urinary microalbumin in older subjects as compared to younger ones. Urinary microalbumin ranged from 5.3 ± 0.65 mg/g of creatinine to 15.57 ± 2.10 mg/g creatinine in control group of young (20-35 yrs) and older (70-85 yrs) male groups, respectively (Table I).

Table I. Urinary micro-albumin mg/g of creatinine concentration in various control and co-morbid groups of diabetic patients

Groups Control and Co-morbid in Diabetic patients	Age-groups			
	25-35 yrs	36-50 yrs	51-70 yrs	71-85 yrs
Males Normal	5.3 ± 0.65	9.65± 2.10	12.24± 2.20	15.57± 2.45
Females Normal	5.5± 0.45	9.75± 2.30	12.25± 3.20	16.10 ± 3.45
Males Hypertensive	[a]19.96± 3.40	[b]20.95± 4.55	[c]24.58± 5.15	[a,b]33.01± 6.25
Females Hypertensive	[a]18.96± 3.65	[b]21.14± 6.75	25.28± 5.90	[a,b]33.51± 5.90
Males Renal Insufficiency	[a]26.3± 6.15	[b]30.28± 7.10	[c]33.14± 6.45	[a,b]36.32± 6.25
Females Renal Insufficiency	[a]24.7± 5.30	[b]27.16± 6.20	28.93± 6.11	[a,b]35.14± 6.40

Statistical analysis: a = $P < 0.001$, b = $P < 0.01$, c = $P < 0.05$

Moreover, both gender-based renal insufficiency subjects of all age groups showed higher than normal urinary micro-albumin ranging from 26.30 ± 6.10 mg/g creatinine to 36.32 ± 6.25 mg/g creatinine in males and 24.70 ± 5.30 mg/g creatinine to 35.14 ± 6.40 mg/g creatinine in females (Table I, Figs 1-4). In hypertensive groups, above normal urinary microalbumin was

detected only in groups that are older i.e. 51-70 yrs and 71-85 yrs, where as normal or near normal values were seen in age groups 20-35 yrs and 36-50 yrs (Table I).

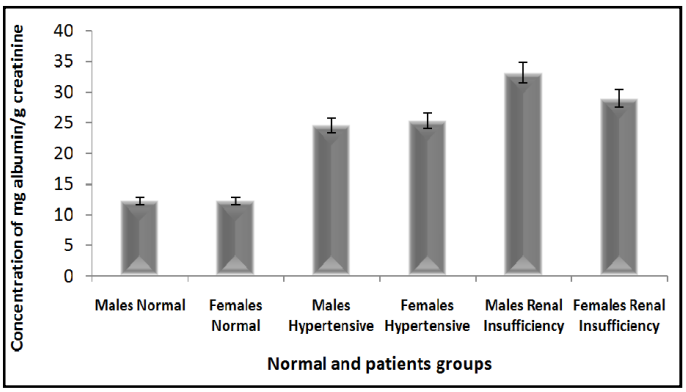

Fig. 3. Urinacy microalbumin in selected patients of age group 51-70 years

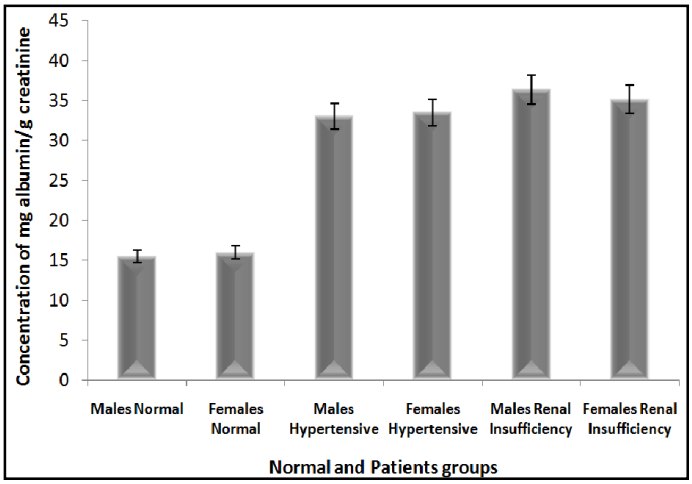

Fig. 4. Urinary microalbumin in selected patients of age group 71-85 years

Comparative analysis of co-morbids with age sub-groups depicted highly significant elevated levels ($P < 0.001$) of urinary micro-albumin in renal insufficiency group, aged 70-85 yrs of both gender, as compared to age group 20-35 yrs (Table I). Similarly male and female hypertensive group of older patients (70-85 yrs) showed significantly higher levels ($P < 0.001$) of urinary microalbumin than the younger (20-35 yrs) group. Comparison among age groups 31-50 yrs and 51-75 yrs versus older groups (70-85 yrs) in both renal insufficiency and hypertensive patients manifested mild to moderate significance in urinary microalbumin excretion levels.

DISCUSSION

It was reported that elevated urinary microalbuminuria occurs in 30-40% of patients suffering from diabetics, especially diabetes mellitus type 2 (Afkhami-Ardekani *et al.*, 2008). Moreover, this raised microalbumin is an early indicator of diabetic nephropathy, in addition to being a potent risk factor for indicating development of cardiovascular diseases (Battisti *et al.,* 2003; Afkhami-Ardekani *et al.,* 2008). Previous studies exhibited mild to significantly elevated levels of urinary micro-albumin in patients suffering from renal insufficiency and hypertensive cardiac-myopathies (Silva *et al*., 2008; Afkhani-Ardekani *et al.,* 2008). Our study describes the comparative analysis among diabetic patients with co-morbids of renal insufficiency and hypertension with age and gender dependent sub-classifications. The data and comparison reflected significantly elevated excretion of micro-albumin in male and female diabetic group of renal insufficiency patients in all age groups as compared to hypertensive groups and subgroups. However, urinary micro-albumin levels of patients in hypertensive groups were noted to significantly higher when compared with control groups. The outcome suggested progression of nephropathy in diabetic patients, causing marked albuminuria, as well as micro-vascular abnormalities and hypertension.

Previous studies regarding elevation of urinary micro-albumin in diabetic patients with moderate to severe co-morbids of renal insufficiency reported raising incidence of ESRD, mostly in type 2 diabetes mellitus (Mogenson, 1998; Raij, 2003). Documented data from other regions through various cross-sectional studies showed prevalence of micro-albumin upto 16.8% among type 2 diabetic patents in Saudi Arabia (Huraib *et al.,* 1995), whereas upto 22.7% prevalence of albuminuria was reported in young diabetic patients from Hong Kong (Ko *et al.,* 1999). Furthermore, in most of the previous studies, no specific correlation was found between prevalence of micro-albuminuria and age, except in very few cases (Varghese *et al.,* 2001: Shekiba *et al.,* 2003). A high incidence of urinary microalbuminuria upto 33% was also reported in patients with Coronary artery disease (CAD) (Tuttle *et al.,* 1999; Silva *et al.,* 2008). Moreover, several studies demonstrated correlation of micro-albumin with high blood pressure and its increase with the severity of diabetes (Cirillo *et al.,* 2005). A prevalence of 9.5% urinary microalbuminuria was noted in diabetic patients with hypertension (Silva *et al.,* 2008) and slightly higher prevalence in selected US population (Jones *et al.,* 2002).

Conclusion

The present study described the comparative analysis of prevalence of micro-albumin in diabetic patients that were suffering from either of the two co-morbid, hypertension and renal insufficiency. Micro-albuminuria was noted to be more prevalent in renal insufficient diabetic patients as compared to hypertensive diabetics. However, hypertensive patients did exhibited higher than normal micro-albuminuria when compared with normal controls. The results suggested progression of nephropathy in diabetic patients, as well as micro-vascular abnormalities and hypertension.

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