

## Pattern of urinary albumin excretion in non-diabetic first-degree relatives of type 2 diabetes mellitus patients

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### ABSTRACT

**Objectives:** To determine the pattern of urinary albumin excretion among non-diabetic first-degree relatives of patients with Type 2 DM residing in United Arab Emirates and to relate it to the socio-demographic profile and family history of chronic diseases.

**Materials and Methods:** Non-diabetic first-degree relatives of patients with Type 2 DM attending the Gulf Medical College Hospital (GMCH) or employed in the GMU/GMCH were invited to participate in the study. None of the participants had any known renal disorder. Data was collected using a pilot-tested, interviewer-administered questionnaire. Albumin/Creatinine ratio (ACR) was measured in urine. Data was analyzed using PASW 19.0 software.

**Results:** Among the 231 participants, 66.3% were males. 53.7% of the participants were in the 26-35 year age group. Forty (17.3%) had ACR higher than 10mg/g, of whom 10 had >30mg/g. ACR was >15mg/g in 9.9% of males and 18% of females. An increasing trend was seen with age. The percentage of participants having ACR 15-30mg/g was 6.2, 8.1, 11.4, 27.3 in ≤ 25, 26-35, 36-45 and above 45 years age groups; above 30mg/g in 3.8% and 13.6% in the 36-45 years and above 45 years age groups respectively. Among those with ACR >10mg/g, two reported a family history of kidney disorder, three stroke and seven CVD.

**Conclusion:** Among the non-diabetic first-degree relatives of Type 2 DM patients, urinary albumin excretion level was higher among females and in the older age group.

**Key words:** urinary albumin excretion, first-degree relatives, type 2 diabetes mellitus

### INTRODUCTION

Microalbuminuria is considered as one of the components of metabolic syndrome<sup>1</sup> (WHO), or as an additional metabolic criterion for research<sup>2</sup> and as a factor that increases the probability of Type 2 diabetes later<sup>1</sup>. Those with more components of metabolic syndrome have been found to have a higher risk for chronic kidney disease<sup>3</sup>. It is not clear whether microalbuminuria causes metabolic changes or results from some metabolic disturbance such as insulin resistance. It is suggested to occur with hyper filtration due to hyperglycemia and elevated blood pressure<sup>4</sup>. Urinary albumin excretion has been shown to be independently associated with fasting plasma glucose, triglyceride levels and systolic blood pressure, but not with other variables included in metabolic syndrome, such as HDL cholesterol, fasting plasma insulin, obesity or central adiposity<sup>4</sup>.

The relationship between insulin resistance and microalbuminuria is suggested to be partially dependent on blood pressure, glucose levels, and obesity. Those with microalbuminuria had lower insulin sensitivity and higher fasting insulin concentrations, independent of blood pressure<sup>5</sup>. Microalbuminuria has been found as a marker of a variety of disorders surrounding insulin resistance and glucose intolerance, evident before diabetes, and may serve as a marker of disease activity.

Urinary albumin excretion has been found to be heritable and genetically correlated to blood pressure in families with type 2 diabetes<sup>6</sup>, and is also an independent risk factor for developing diabetes<sup>7</sup>. A study conducted in the UK showed that it varies with ethnicity, and was more prevalent among South Asians than in the general population<sup>8</sup>.

The only study in the Arabian region, among young potential army/navy recruits in Saudi Arabia, showed a 10.3% prevalence of increased urinary albumin excretion with dipstick (N=204) and 6.2% (N=124) with 24-hr urine sample, independently associated with DM, hypertension (HT), obesity, male gender and hypercholesterolemia. The spot determination of microalbuminuria, easier to perform, has been shown to be at least 90% sensitive for determining microalbuminuria compared with a 24-hour urine collection, even after adjusting for age and gender<sup>9</sup>.

The UAE population is multiethnic with Emiratis accounting for less than 25% of the population<sup>10</sup>. As reported in a study conducted during 1998-2000 among those above 21 years of age, the UAE ranked second highest in the world for diabetes, with a prevalence of 19.6% of Diabetes (DM) and 15.2% of impaired glucose tolerance (IGT); among UAE nationals DM was 24% and IGT 17.9%, while among the expatriates DM was 17.4% and IGT 13.4%<sup>11</sup>. The number is increasing dramatically causing concern as regards prevention, early detection and lifestyle changes. At present, microalbuminuria is included in the national guidelines as an investigation for those detected to have diabetes, but not as a risk factor or predictor<sup>2</sup>. In this context, the present study was undertaken to determine the variation in urinary albumin excretion with respect to socio-demographic factors, family history of diabetes and metabolic factors in the UAE population. The present paper is the report of a preliminary analysis of the pattern of urinary albumin excretion with respect to socio-demographic factors and family history of related chronic diseases.

## MATERIALS AND METHODS

The research used a cross sectional study design, collecting data using a pilot-tested questionnaire for relevant socio-demographic details, medical history, family history, and laboratory investigations. A total of 231 first degree

relatives of patients diagnosed to have adult onset diabetes mellitus of both genders and any nationality, aged 20 years and above formed the study sample. The research assistants recruited the participants through the cooperation of the patients who attended the Internal Medicine Department of the Gulf Medical hospital and Research Centre (GMCHRC) or the employees in the university. Those with pregnancy, or history of diabetes, kidney disease and urinary infection were eliminated through medical history. The participants recruited were advised to report, fasting for at least 8 hours, on specific days at designated data collection points. The research assistants completed the questionnaire through direct interview. Urine and blood samples were collected by the assisting laboratory technician and analyzed at clinical laboratory in GMCHRC. The urinary albumin excretion was estimated by turbidimetric method to determine microalbuminuria.

The laboratory result was also recorded in the same questionnaire. The data was entered into Microsoft Excel sheets and analyzed on SPSS version 19.0 and presented as frequencies and proportions.

## RESULTS

Table 1. Profile of participants by age, gender and urinary albumin excretion

Variables	Male		Female		Total
	No	%	No	%	
Age (Years)					
<=25	22	14.4	10	12.8	32
26-35	84	54.9	40	51.3	124
36-45	35	22.9	18	23.1	53
>45	12	7.8	10	12.8	22
Total ACR (mg/g)					
<=5	92	60.1	20	25.6	112
6-10	43	28.1	36	46.2	79
11-15	8	5.2	8	10.3	16
16-20	3	2.0	4	5.1	7
21-25	1	0.7	5	6.4	6
26-30	--	--	1	1.3	1
31-35	1	0.7	2	2.6	3
>35	5	3.3	2	2.6	7

Table 1 shows the distribution of participants by age, gender and urinary albumin excretion. Among the 231 participants, 66.3% were males and 53.7% in the 26-35 age group. There

were 40 participants with ACR>10mg/g, of whom 10 had >30mg/g. The majority [112, (48.5%)] had a value of 10 mg/g or lower.

Table 2 gives the distribution of UAE in the different age groups. An increasing trend is seen with age. The percentage of participants having ACR >15mg/g is 6.2, 8.1, 11.4, 27.3 in ≤ 25, 26-35, 36-45 and more than 45 years age groups. Those

CVD. Table 3 shows the family history in detail.

## DISCUSSION

The study was conducted on 231 first degree relatives of individuals with Type 2 diabetes mellitus who were multiethnic UAE residents. Two thirds were males and more than half was in the age group 25-35 years.

Table 2. Urinary albumin excretion by age

ACR	≤25 years		26-35 yrs		36-45 yrs		>45 yrs		Total
	No	%	No	%	No	%	No	%	
≤5	20	62.5	65	52.4	20	37.7	7	31.8	112
6-10	7	21.9	43	34.7	21	39.6	8	36.4	79
11-15	3	9.4	6	4.8	6	11.3	1	4.5	16
16-20	1	3.1	3	2.4	1	1.9	2	9.1	7
21-25	1	3.1	1	0.8	3	5.7	1	4.5	6
26-30	-	-	1	0.8	-	-	-	-	1
31-35	-	-	3	2.4	-	-	-	-	3
>35	-	-	2	1.6	2	3.8	3	13.6	7
Total	32	100.0	124	100.0	53	100.0	22	100.0	231

Table 3. Urinary albumin excretion and family history of chronic disorders

ACR	Kidney Disorder		Stroke		CVD		Total
	No	%	No	%	No	%	
≤5	6	47.5	4	44.4	18	52.9	112
6-10	-	-	2	22.2	9	26.5	79
11-15	-	-	2	22.2	3	8.8	16
16-20	-	-	1	11.1	2	5.9	7
21-25	1	12.5	-	-	1	2.9	6
26-30	-	-	-	-	-	-	1
31-35	-	-	-	-	-	-	3
>35	1	12.5	-	-	1	2.9	7
Total	8	100.0	9	100.0	34	100.0	231

with higher levels of UAE are in those older than 35 years. For those in 36-45 years of age 18.9% had ACR in the 11-30 mg/g level, and 3.8% in >30mg/g level. Among those above 45 years of age 13.6% had ACR above 30mg/g.

The number of participants with family history of kidney diseases, stroke and CVDs was eight (3.5%), nine (3.9%) and 34 (14.7%) respectively. Among the 40 participants with UAE higher than 10mg/g, it was 38 against two for family history of kidney disorders, 37 against three for stroke and 33 against seven for

On examining the pattern of Albumin creatinine ratio, almost half of the group had ACR 10mg/g or lower, 17.3% had above 10mg/g of whom 10 (4.3%) had microalbuminuria (>30mg/g). In the Inter-Tribal Heart Project<sup>12</sup> among 15.2% of the nondiabetic native Americans surveyed had microalbuminuria and there was a twofold increase with Insulin resistance syndrome. The variation may be due to multiple ethnicities in the present study as was observed in the Strong Heart Study<sup>13</sup>, prevalence of microalbuminuria in adult Arizona, Oklahoma, and Dakota Indians

being 28.3, 15.2, and 13.8%, respectively. But it is suggested that in non-diabetic individuals the cut off should be taken as lower. In the HOPE study<sup>14</sup> on diabetic and non-diabetic individuals, any degree of albuminuria was found to be a risk factor for cardiovascular events in individuals with or without DM during a median period of 4.5 years of follow up. The risk is reported to increase with the ACR starting well below the microalbuminuria cutoff. The investigators in the PREVEND study (Prevention of Renal and Vascular end stage Disease)<sup>15</sup> in the Netherlands, while examining the pattern of urinary albumin excretion, considered 15-30mg/g as high normal albuminuria and found creatinine clearance elevated in this when compared to control group (ACR <15 mg/g) but decreased in those with micro and group macroalbuminuria. A significant linear increasing trend was observed with a positive family history for diabetes. With each increasing UAE level, male sex, age, plasma glucose, and a positive family history for diabetes all followed. In a study on 582 male non-diabetic first-degree relatives of patients with NIDDM in Finland, albumin excretion rate was 15-200 micrograms/min, and was associated with higher fasting glucose values. The rate of glucose metabolism was lower in those having abnormal compared to normal albumin excretion rate<sup>16</sup>.

ACR in our study is higher in the higher age group with an increasing trend even from the lower age category, similar to that reported by PREVEND study<sup>15</sup>. But contradictory to their finding a higher proportion of women had higher ACR than men. Lane JT in his extensive review<sup>17</sup>, quotes several studies where microalbuminuria is higher among women and also raises the contradictory findings regarding the later risk of cardiovascular disease in women with microalbuminuria. However, in either case the number in the present study is too small to make any conclusive inference. The gender differences are attributed to female hormones, and so, may vary with age. Among the 40 who had UAE more than 10mg/g, only two had a family

history of kidney disorders, three stroke, and seven CVD. Considering diabetes as a risk factor for stroke and CVD, it may be observed that one fourth of those non-diabetic first degree relatives of Type 2 diabetes mellitus with ACR more than 10mg/g had a family history of stroke or CVD. However, the number is too small to comment the study being on non-affected individuals, recruitment of subjects was more difficult than planned.

### **CONCLUSION**

Urinary albumin excretion in the non-diabetic first degree relatives in the multiethnic group studied showed 17.3% with albumin creatinine ratio higher than 10mg/g of whom 4.3% crossed the microalbuminuria threshold. There was a linear trend with age, and women were at greater risk.

### **RECOMMENDATIONS**

Urinary albumin excretion being a simple non-invasive investigation, it may be included in health checkup programs and packages, especially for those with a family history of diabetes or insulin resistance diseases.

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