ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 9, Issue 4, 2016

Online - 2455-3891
Print - 0974-2441

Research Article

URINE ALBUMIN EXCRETION IN NON-DIABETIC NORMOTENSIVE HEALTHY ADULTS WITH NORMAL RENAL FUNCTION

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Received: 25 April 2016, Revised and Accepted: 04 May 2016

ABSTRACT

Objectives: The aim of our study is to measure the urine albumin excretion in apparently healthy adults, to find out the prevalence of elevated urine albumin excretion, and to correlate urine albumin excretion with anthropometric parameters.

Methods: For this, cross-sectional study was conducted where healthy adults of age group 35-50 years were taken. Systolic, diastolic blood pressures, fasting plasma glucose, 2 hrs postprandial glucose, serum urea, serum creatinine, serum cholesterol, serum high-density lipoprotein cholesterol, serum low-density lipoprotein cholesterol, estimated creatinine clearance, body mass index, body surface area, mid arm circumference, waist circumference, hip circumference, wasit: hip ratio, mid-thigh circumference, mid-calf circumference, urine albumin, urine creatinine, and urine albumin creatinine ratio were measured. The relationship between urine albumin creatinine ratio and the individual anthropometric measures was studied using spearman rank correlation analysis.

Results: 2 out of 54 participants had a urine albumin creatinine ratio in excess of 30 µg/mg which signifies microalbuminuria. This corresponds to a prevalence of 3.7%.

Conclusion: Urine albumin creatinine ratio correlated positively with the waist circumference and waist hip ratio. The relationship with other anthropometric measures was negative. None of them found to be significant.

Keywords: Proteinuria, Microalbuminuria, Renal function.

INTRODUCTION

Urine provides a vehicle for the excretion of many physiological substances. The excretion of many of these substances can be regulated to maintain the body's internal mileu. In clinical practice, urinalysis provides valuable information. Proteinuria is common in patients suffering from kidney disease. Diabetic individuals are at high risk of developing renal function impairment. Diabetes is the most common cause of End Stage Renal Disease in the United states and Europe [1]. The presence of microalbuminuria in a diabetic individual signifies an increased risk of developing overt kidney disease [2]. It also increases the cardiovascular disease risk and the overall mortality risk is also more [3,4]. Microalbuminuria has been found to occur in 40% of the patients with diabetes and without known kidney disease [5]. Some studies reported microalbuminuria to enhance the risk for cardiovascular mortality in patients with an essential hypertension [6]. An increased urinary albumin excretion has been found in patients suffering from malignancies, and this increased excretion could be due to local renal causes rather than generalised endothelial dysfunction [7]. The prevalence of albuminuria increases gradually with uric acid elevation and serum uric acid is an independent risk factor of elevated urinary albumin excretion especially in females [8].

The data available on the utility of urinary albumin excretion as a predictor of renal function impairment is very much restricted to diabetic population. A study published in 2004 reported increased albumin excretion in the general population as a predictor of renal function impairment [9]. In routine clinical practice, the functioning of kidneys is considered as being normal on finding a normal serum urea and creatinine values and if the glomerular filtration rate estimated (GFR) is more than 90 ml/min. Blood urea levels can get altered by nonrenal causes. Serum creatinine is not sensitive to early renal dysfunction and the Jaffe's assay used for its estimation is not precise at lower concentrations of creatinine. GFR has its own limitations in that it can remain normal in the initial stages of chronic renal disease.

Although albumin excretion can be measured using an overnight or timed urine specimen, its measurement in a 24 hrs collection or in firs void urine specimen is preferred. Measuring the albumin excretion rate in a first void specimen is more convenient than a 24 hrs urine collection which is also prone for collection errors. The urine flow rate in an individual is variable and is affected by the hydration status. This variability is corrected by expressing albumin as a ratio to creatinine. A first void urine sample also has the advantage of having the lower within-person variation for the albumin creatinine ratio and it also eliminates the possibility of orthostatic proteinuria. To the best of our knowledge, there is no study available from India that reports the urine albumin excretion rate in the general population.

It is hence decided to study the urinary albumin-creatinine ratio in the first void urine sample of individuals belonging to Indian population and assessed as having normal renal function based on serum creatinine and serum urea concentrations in an attempt to find out if there is any increase in the same in these apparently healthy individuals which could signify a renal disease in the early stage.

METHODS

This cross-sectional observational study has been carried out in the Department of Biochemistry of a Tertiary Care Teaching Institution Chennai Medical College, Trichy. This study has been approved by the Institutional Ethics Committee.

The subjects who participated in the study were apparently healthy volunteers in the age group of 35-50 years and belonged to both sexes. Individuals who performed regular physical exercise were not

included in the study as urine albumin excretion can be increased by exercise. Also not included in the study were pregnant women for similar reasons. Individuals who reported smoking and regular alcohol intake were excluded as this could affect urine protein excretion. Individuals with a history of renal disease, past renal surgery, injury to kidneys or urinary tract, and illnesses involving the excretory system in the past were not included. Individuals, who were known diabetics and/or hypertensives, were also excluded. Individuals with a blood pressure exceeding 140/90 mm Hg and those with a body mass index (BMI) exceeding 30 kg/m^2 were also excluded. Individuals with a fasting plasma glucose concentration equal to 126 mg/dl and 2 hrs postprandial plasma glucose concentration equal to or exceeding 200 mg/dl and with increased serum urea and creatinine were also excluded from the study.

The remaining subjects then had their blood pressure recorded in their left upper arm in the supine position and anthropometric measures taken. Weight was measured using digital scales and recorded to the nearest mm in the standing position using a free standing stadiometer. The BMI was calculated as the ratio of body weight in kg to the height in m^2. The body surface area was calculated using the Dubois and Dubois formula.

Body surface area = (W0.425 × H 0.725) × 0.007184

The following measures were recorded as per the guidelines of the National Health and Nutrition Examination Survey III. The hip circumference was measured at the level of the maximum extension of the buttocks with the individual in the standing position. Waist circumference was measured at the level of the highest point of the iliac crest. The remaining measures were taken on the right side of the body and perpendicular to the long axis of the segment. The mid arm circumference was recorded midway between the most upper edge of the posterior border of the acromion process of the scapula and the tip of the olecranon process. The mid-thigh circumference was recorded midway between the inguinal crease and the upper border of the patella. The maximum girth between the knee and ankle joints was recorded as the mid-calf circumference.

The individuals were instructed to collect a midstream specimen of the first void morning urine sample. On the day of urine collection, blood specimens were obtained from individuals under fasting conditions and 2 hrs postprandial. The blood specimens were assayed for plasma glucose concentrations. The fasting specimen was used for the estimation of serum urea, creatinine, total cholesterol, high-density lipoprotein-cholesterol, and triglycerides.

The urine specimen was analyzed for creatinine concentration using a kinetic Jaffe's procedure after suitable dilution. The albumin concentration was measured using a commercial immunoturbidimetric kit. The sensitivity of the procedure was 3 mg/L. Both these assays as well as the assays carried out using the plasma and serum specimen were carried out using a fully automated chemistry analyzer. The ratio of urine albumin to creatinine was calculated and reported as mg of albumin/G of creatinine. A urine albumin creatinine ratio exceeding 30 was taken to be a case of microalbuminuria.

The creatinine clearance was estimated using the Cockroft-Gault algorithm and recorded for all the subjects.

Estimated creatinine clearance = (140-age in y) × (body weight in kg) × 0.85 if female/(72 × Plasma creatinine in mg/dl)

A statistical analysis was performed using the SPSS software. The descriptive data are presented as a mean±standard deviation (SD). The ranges are also given in parentheses for chosen variables. The prevalence of increased urine albumin excretion was reported as percentage. The relationship between urine albumin creatinine ratio and the individual anthropometric measures were studied using spearman rank correlation analysis.

RESULTS

Descriptive statistics for urine albumin excretion and other variables are presented in Table 1. The mean age of the subjects was 39.7 and the SD was 4.8. The mean±SD for urinary albumin concentration was 4.6±6.8 mg/ml, whereas the mean±SD for urinary creatinine concentration was 92.0±88.0 mg/dl. The urine albumin creatinine ratio ranged from 0.0 to 100 and it had a mean and SD of 8.3±15.6. 2 out of the 54 participants had a urine albumin creatinine ratio in excess of 30 µg/mg which signifies microalbuminuria. This corresponds to a prevalence of 3.7%. The Spearman's rank correlation coefficients for urinary albumin creatinine ratio with the anthropometric measures are given in Table 2 along with the p values. The relationship with other anthropometric measures was negative. None of them were found to be significant.

DISCUSSION

Urine albumin excretion in the general population is gaining attention as increased excretion has been shown to increase risk for cardiovascular disease and renal failure. It is also reported to increase the risk for hypertension and all cause mortality.

Table 1: Descriptive statistics for the variables

Variable	Values
Age, year	39.7±4.8
Systolic blood pressure, mm Hg	114.7±11.4
Diastolic blood pressure, mm Hg	73.1±7.3
plasma glucose (fasting), mg/dl	89.0±8.3
Plasma glucose (2 hrs post prandial), mg/dl	101.5±17.3
Serum urea, mg/dl	21.0±6.2
Serum creatinine, mg/dl	0.9±0.2
Serum cholesterol, mg/dl	186.1±37.6
Serum HDL cholesterol, mg/dl	44.1±7.5
Serum LDL cholesterol, mg/dl	119.1±30.5
Estimated creatinine clearance, ml/min	91.2±15.9
Height, cm	159.2±9.9
Weight, kg	62.3±11.5
BMI, kg/m^2	24.5±3.3
Body surface area, m^2	1.6±0.2
Mid arm circumference, cm	27.5±3.0
Waist circumference, cm	83.8±10.0
Hip circumference, cm	95.5±7.3
Waist: Hip ratio	0.9±0.1
Mid-thigh circumference, cm	48.2±5.7
Mid-calf circumference, cm	32.8±3.2
Urine albumin, mg/ml	4.6±6.8
Urine creatinine, mg/ml	92.0±88.0
Urine albumin creatinine ratio, micro g/mg	8.3±15.6

Data are given as mean±SD. HDL: High-density lipoprotein, LDL: Low-density lipoprotein, BMI: Body mass index, SD: Standard deviation

Table 2: Spearman rank correlation coefficients of urinary albumin creatinine ratio with anthropometric measures and the p values

Variable	Correlation coefficient	p values
Height, cm	−0.003	0.981
Weight, kg	−0.154	0.265
BMI, kg/m^2	−0.134	0.332
Body surface area, m^2	−0.095	0.495
Mid arm circumference, cm	−0.174	0.209
Waist circumference, cm	0.018	0.897
Hip circumference, cm	−0.153	0.270
Waist: Hip ratio	0.139	0.317
Mid-thigh circumference, cm	−0.169	0.221
Mid-calf circumference, cm	−0.075	0.592

BMI: Body mass index

The urine albumin creatinine ratio in the present study ranged from 0.0 to 100 and it had a mean and SD of 8.3±15.6. The prevalence of microalbuminuria was found to be 3.7%. Wattari study reported a prevalence of 5.5% among the people of Wattari town Japan [10] and Fan *et al*. reported a prevalence of 12.9% in Pingghu district, Beijing [8]. The Hermex study found out a prevalence of 4.7% in the population of Extremadura Spain while Repisco *et al*. reported a prevalence of 7.65% in a representative Spanish population. Cirillo *et al*. reported a prevalence of 4.75% and 11.1% for non-diabetic men and women, respectively, in the gubbio population study conducted in the town of Gubbio, in North-Central Italy [11]. The Prevend study documented a prevalence 7% in the general population and 6.6% in non-diabetic and nonhypertensive subjects [12]. The epic Norfolk study reported the prevalence as 11.2% [13]. Zacharias *et al*. in their study on a Canadian first nation population at high risk for End Stage Renal Disease and dialysis found out the prevalence of microalbuminuria to be 15% and that of proteinuria to be 5% [14]. The lower prevalence of microalbuminuria in our study could well be due to the fact that some of the studies mentioned above did not exclude diabetics and hypertensives in the general population and included individuals who happened to be smokers and consumed alcohol. The difference in the analytical methodology for detecting microalbuminuria could contribute to this prevalence variation. Furthermore, the albumin excretion parameter measured in these studies were also not the same. The urine creatinine excretion varies among different races which could influence the urine creatinine ratio.

In this study, no significant correlation was found between urine albumin creatinine ratio and anthropometric measures. The relationship between BMI and urine albumin excretion is the one extensively reported and the reports are contradictory. The Epic-Norfolk study had reported a borderline association with BMI while Zacharias *et al*. found out an independent association between BMI and urine albumin excretion [13,14]. Afsar *et al*. found no association between the two in their study [15]. A positive relationship between urine albumin excretion and hip circumference has been reported by Ganie *et al*. [16].

The current study is likely to be the first study to report the prevalence of microalbuminuria in an apparently healthy Indian population and the first one to have studied the relationship between the urine albumin creatinine ratio and the anthropometric measures. Since the studied population is small, it may not be possible to draw generalised conclusions. The study may be carried out in multiple centres to be representative of the diverse Indian population. The effect of sex on urine albumin excretion can also be studied.

ACKNOWLEDGMENTS

We sincerely acknowledge Indian Council Of Medical Research Short term Studentship (STS) programme under which the work is carried out. (N0.01512). We are grateful to Dr. P. Thirumalai Kolundu Subramanian and Mr. M Ismail for their immense support and help offered throughout this work. We also thank authors/editors/publishers of all those articles, journals and books from where the literature for this article has been received, discussed, cited and included in references of this manuscript.

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