Screening of incidental kidney disease in normoglycemic, normotensive healthy adults

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Background and aim
Chronic kidney disease is a major public health problem with increased global incidence and prevalence, especially in Egypt, poor quality of life, and high risk of morbidity and mortality. The aim of the work was to determine the prevalence and the risk factors of incidental kidney diseases among apparently healthy adults.
Patients and methods
A total of 300 healthy normotensive and normoglycemic individuals were assessed for creatinine, proteinuria, and glomerular filtration rate, with correlation to their BMI and systolic and diastolic blood pressures.
Results
Microalbuminuria was positively correlated to age, BMI, and systolic blood pressure, with a significant *P*-value of less than 0.001.
Conclusion
The prevalence estimates and risk factors for those with microalbuminuria as a marker of occult renal disease include age, BMI, high systolic blood pressure, and family history of renal problems.

Keywords:
incidental kidney diseases, microalbuminuria, normotensive

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Introduction

Chronic kidney disease (CKD) is a major public health threat with high incidence and prevalence, leading to end-stage renal disease (ESRD), premature mortality, poor quality of life, and large burden for the healthcare system [1].

The prevalence of CKD varies widely among different study populations [2]. However, supplied population-based data on the prevalence of CKD offer the opportunity to develop stronger working relationships with the primary care teams, to plan health resource allocation, and also to detect and treat CKD in its early course [3].

Many factors are associated with the prevalence of CKD, including sex, occupation, education, marital status, diabetes, hypertension, cardiovascular disease, hyperuricemia, history of kidney stones, and the use of traditional medications [4].

The National Kidney Foundation-Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI) guidelines for CKD, which have been reviewed and endorsed by the 2006 Kidney Disease Improving Global Outcomes (KDIGO) Controversies Conference, recommended that all individuals should be assessed as part of routine health examinations to determine whether they are at an increased risk for developing CKD [5]. Patients who are at risk for developing CKD should be screened for proteinuria and a blood test for creatinine to estimate glomerular filtration rate (GFR). Patients who are at risk for glomerulonephritis should be screened for hematuria with a urinalysis [6].

Unfortunately, lack of information concerning epidemiologic characteristics of CKD and its contributing risk factors in the developing countries results in lost opportunities for appropriate intervention and prevention of the consequent ESRD [7]. Therefore, the current study aims to detect the prevalence of incidental CKD among normoglycemic and normotensive healthy Egyptian adults to predict the prevalence of subclinical renal diseases and point to it at an earlier more treatable stage, which will consequently slow the explosive growth of renal failure and ESRD complications.

Patients and methods

Study population

This prospective study was conducted in the period from September 2015 to March 2016. The screened population was randomly selected among the workers

and attendees to the Outpatient Clinic of Agouza Police Hospital, aged 18–60 years with a mean age of 36±11 years. There were 177 (59%) male and 123 (41%) female participants. Individuals with diabetes mellitus, hypertension, chronic liver disease, and heart disease were excluded; also, pregnant women, individuals who had been involved in vigorous exercise or competitive sport 12 h before the study, or patients with any kidney disease were omitted at the time of the study.

Methods

All studied populations were subjected to a stepwise screening program, including the following:

Full history taking and clinical examination

(1) Blood pressure (BP) was measured using mercurial sphygmomanometer in sitting supported position. Individuals were considered hypertensive if they met one of the following conditions: diastolic blood pressure (DBP) greater than or equal to 90 mmHg, systolic blood pressure (SBP) greater than or equal to 140 mmHg, or currently taking antihypertensive medications regardless of their actual BP measurement.
(2) Height was measured using calibrated height meters while participants stood erect and barefoot, with feet placed together and looking forward.
(3) Weight.
(4) BMI was calculated as follows: BMI=weight×height^2 (kg/m^2).

Laboratory investigations

Collection of blood samples: Blood samples were collected under complete aseptic conditions and immediately centrifuged (4°C) with serum stored at 20°C for the following assays:

(1) Random blood sugar (NHANES 2005–2006 laboratory methods):
Specimens were packaged (nonhemolyzed serum or plasma 'EDTA heparin or sodium fluoride') and shipped on cold packs and delivered directly to clinical laboratory and were stored at −70°C until analysis.
(2) Serum creatinine:
It was measured by the method of Henry (1974) using Randox Kit (Randox Laboratories Ltd, County Antrim, UK). A minimum of 0.6 ml of serum is needed for the multianalyte panel. Sample volume for individual test is 40 µl added to 1.27 ml of buffer reagent, and 40 µl added to 3.23 ml of reference reagent.
(3) Estimated glomerular filtration rate (eGFR):
It was calculated according to Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. The CKD-EPI creatinine equation is currently the most accurate method for estimating GFR for various populations. This equation is more accurate than the MDRD study equation, especially at a GFR more than 60 ml/min/1.73 m^2, and is replacing the MDRD study equation:
GFR=141×min(Scr/κ, 1)α×max(Scr/κ, 1)−1.209×0.993 age×1.018 [if female]×1.159 [if Black],

where Scr is serum creatinine (mg/dl), κ is 0.7 for females and 0.9 for males, α is −0.329 for females and −0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1.

Collection of urine samples

Urine samples were collected under complete aseptic conditions and examined for urinary albumin–creatinine ratio (ACR). Abnormal albuminuria was defined as a urine ACR more than or equal to 30 mg/g; albuminuria was measured by immunoturbidimetry.

Statistical analysis

Precoded data were entered into the statistical package for the social sciences software program, version 21 (SPSS Inc., Armonk, NY, USA), to be statistically analyzed. Data were summarized using mean and SD for quantitative variables and frequency and percentage for qualitative ones.

Results

The demographic and clinical data of the study participants are summarized in Tables 1 and 2.

The present study revealed that there was a significant relationship between the presence of microalbuminuria and older age, SBP, BMI, lower eGFR, and family history of renal problems ($P<0.001$), but there were no relations between microalbuminuria and sex, DBP, random blood sugar or serum creatinine, or family history of diabetes and hypertension, as shown in Table 3.

Regarding the correlation between the parameters of renal affection including serum creatinine, microalbuminuria, and eGFR and other variables, the study reported a significant positive correlation between ACR in urine and age, body weight, BMI, SBP, mean arterial blood pressure (MABP), and serum creatinine ($P=0.022$), but there was no

significant correlation between microalbuminuria and height, DBP, and random blood sugar (RBS), as demonstrated in Table 4.

Table 1 Clinical parameters of all studied participants

Variables	Mean±SD
Age (years)	36±11
Weight (kg)	78.9±9.8
Height (cm)	170±8
BMI (kg/m^2)	27.1±2.9
SBP (mmHg)	120±8
DBP (mmHg)	76±5
RBS (mg/dl)	108±13
Creatinine (mg/dl)	0.91±0.13
Urine ACR (mg/g)	12.1±7.2
eGFR (ml/min)	97±12

ACR, albumin–creatinine ratio; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure.

Table 2 Demographic data of the study participants

Variables	*N* (%)
History of smoking	110 (36.7)
Family history of diabetes mellitus	67 (22.3)
Family history of hypertension	127 (42.3)
Family history of renal disease	37 (12.3)
SBP	
Normal	220 (73.3)
Prehypertension	80 (26.7)
DBP	
Normal	282 (94)
Prehypertension	18 (6)
BMI	
Normal	63 (21)
Overweight	192 (64)
Obese class I	43 (14.3)
Obese class II	2 (0.66)

DBP, diastolic blood pressure; SBP, systolic blood pressure.

Discussion

The world population suffering from ESRD is growing. CKD has been recognized to be a underdiagnosed public health problem worldwide, with increasing incidence and prevalence, high costs, and poor outcome [8] associated with significant morbidity and mortality, and there is a steep increase in the number of patients reaching ESRD.

CKD is commonly asymptomatic early in the course of the disease and, as a result, awareness of CKD among the general population remains low [9]. Risk factors for CKD, which were identified in prospective studies, include age, hypertension, ethnicity, diabetes, smoking, low high-density lipoprotein cholesterol, proteinuria, and obesity [10]. However, the majority of studies have evaluated risk factors at, or near, the time of diagnosis of CKD when risk factor modification may be too late to prevent progression. It is likely that CKD risk factors are elevated decades before the diagnosis of CKD.

The current study aims to screen our community population to confirm whether these individuals are at a risk for subsequent nephropathy and to make every effort to detect subclinical renal disease at an earlier, more treatable stage, which will eventually slow the explosive growth of renal failure, and to assess prevalence of subclinical renal diseases in our community. All enrolled participants were clinically assessed and screened for serum creatinine, random blood sugar, and urinary ACR.

We used urine albuminuria as a marker of occult renal problem according to KDIGO definition of CKD.

Table 3 Relation of microalbuminuria with other variables among the study populations

Variables	Microalbuminuria (mean±SD)		*P*-value
	Yes (15)	No (285)	
Age (years)	54.5±4.8	34.6±10.0	<0.001
Sex [*n* (%)]			
Male	9 (60)	168 (58.9)	0.936
Female	6 (40)	117 (41.1)	
Body weight (kg)	87.7±12.6	78.4±9.4	<0.001
Height (cm)	169.4±8.6	170.2±8.5	0.940
BMI	30.6±4.5	27.0±2.7	<0.001
SBP (mmHg)	126.7±5.2	119.6±7.6	<0.001
DBP (mmHg)	78.3±5.9	76.0±5.3	0.158
RBS (mg/dl)	110.2±12.4	107.6±12.6	0.450
Creatinine (mg/dl)	1.0±0.1	0.9±0.1	0.151
eGFR (ml/min)	80.6±8.0	98.1±11.2	<0.001
Smoking [*n* (%)]	8 (53.3)	102 (35.8)	0.169
Family history of renal problems [*n* (%)]	7 (46.7)	30 (10.5)	<0.001
Family history of diabetes mellitus [*n* (%)]	5 (33.3)	62 (21.8)	0.294
Family history of hypertension [*n* (%)]	8 (53.3)	119 (41.8)	0.376

DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure.

Table 4 Correlation between microalbuminuria and estimated glomerular filtration rate and other variables among the study cases

Variables	Microalbuminuria		Serum creatinine		eGFR	
	r-value	*P*-value	*r*-value	*P*-value	*r*-value	*P*-value
Age	0.780	<0.001	0.645	<0.001	–0.674	<0.001
Weight	0.336	<0.001	0.364	0.05	–0.241	<0.001
Height	–0.004	0.94	–0.090	0.115	–0.089	0.125
BMI	0.411	<0.001	–0.169	0.003	–0.212	<0.001
SBP	0.276	<0.001	0.211	<0.001	–0.272	<0.001
DBP	0.094	0.104	0.133	0.021	–0.097	0.049
MABP	0.242	<0.001	0.229	<0.001	–0.241	<0.001
RBS	0.083	0.15	0.103	0.06	–0.104	0.072
Creatinine	0.132	0.002	–	–	–0.538	<0.001
Microalbuminuria	–	–	0.132	0.022	–0.598	<0.001
eGFR	–0.598	<0.001	–0.538	<0.001	–	–

DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure.

About 15 patients were found to have albuminuria 30 mg/g or more. It was found that microalbuminuric patients had higher age, weight, BMI, and lower eGFR with a high significance ($P<0.001$).

The study found a prevalence of microalbuminuria in 5% of our screened participants. This result is in agreement with other reports in Egypt. A study was conducted among participants of the EGIPT-CKD program (Egypt Information, Prevention, and Treatment of Chronic Kidney Diseases), a population-based screening program for microalbuminuria and CKD in Damanhur, Egypt. The screening tools included a questionnaire collating information on demographics, lifestyle, medical and family history of diabetes mellitus, hypertension, and CKD. The prevalence of microalbuminuria was 10.6% in the population screened and 6.2% in the nondiabetic and non-hypertensive participants. The prevalence of albuminuria increases with age, and it is significantly higher in diabetic patients, hypertensive patients, obese individuals, cardiovascular disease patients, and smokers. There was also a higher burden of microalbuminuria participants with low educational attainment (16 vs. 5.6%) and also those with a positive history of smoking (15.7 vs. 8.1%) [11].

In addition, our results conformed with those of El-Bahanasy *et al.* [12], who declared the prevalence of microalbuminuria to be 14.4% of 320 apparently healthy participants and the prevalence of CKD (eGFR<60 ml/min/1.73 m^2 and microalbuminuria) to be 15.6%, but those with elevated creatinine comprised 2.8% of the studied group. Microalbuminuria showed a trend with age. The prevalence of microalbuminuria was significantly higher among diabetic patients, hypertensive patients, obese individuals, cardiovascular disease patients, and smokers [12].

Our study showed a significant positive correlation between microalbuminuria and family history of renal problems; however, there was no relation as regards family history of hypertension and diabetes mellitus, which matches with a cross-sectional study carried out on 400 participants of the first-degree and second-degree adult relatives of those with ESRD who were subjected to measurement of proteinuria, serum creatinine, and eGFR. The study revealed that the prevalence of CKD among the relatives was 21% [13].

The present study demonstrated a statistically significant correlation between microalbuminuria and SBP, as well as mean arterial BP ($P<0.001$); these data conform with a recent study conducted in El-Sharkia, Egypt, which revealed that the main risk factor of renal disease is elevated BP [14].

We found that microalbuminuric patients had higher weight and BMI with a significant *P*-value of 0.013; this result is in agreement with other reports. Obesity, the epidemic of the 21st century, carries a markedly increased risk for comorbid complications, such as type 2 diabetes, cancer, hypertension, dyslipidemia, CKD, and its progression to ESRD [15]. Pinto-Sietsma *et al.* [16] showed that obesity was associated with a 70% increased risk of microalbuminuria compared with lean individuals. Components of the metabolic syndrome and CKD are strongly and consistently associated in many cross-sectional studies [17].

Although impaired glucose tolerance and smoking are considered to be risk factors for developing CKD, the current study found no relation between MA and random blood sugar or smoking.

There are several limitations to this study. First, as regards the small sample size, the results will need

confirmation in a larger scale of the population for early detection of CKD and for implementing the therapeutic intervention to eventually slow or prevent the progression to ESRD. Second, this study lacks the follow-up of kidney function tests to assess the predictability of the mentioned risk factors for developing CKD. Finally, it is better for screening of CKD in targeted populations, as nontargeted screening has poor positive predictive value and overestimates the prevalence of CKD.

In conclusion, this study reports the prevalence estimates and risk factors for those with microalbuminuria among normotensive, normoglycemic healthy adults, including age and increased BMI, and also among those with a family history of renal problems.

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Conflicts of interest
There are no conflicts of interest.

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