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Early screening of chronic kidney disease patients among the asymptomatic adult population in Bangladesh

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Abstract

Introduction: Early identification of chronic kidney disease (CKD) provides valuable opportunities for effective interventions that reduce the risk of outcomes, particularly renal failure.

Objectives: This study aimed to screen the Bangladeshi asymptomatic adult population for CKD to identify potential risk factors for its development.

Patients and Methods: The screening program was carried out among the 400 subjects in the Thakurgaon district of Bangladesh to identify people with the risk of CKD. All the subjects were asymptomatic and previously been never diagnosed with kidney diseases. Demographic data were collected by a structured questionnaire. Urinary protein was tested by dipstick method, and serum creatinine was measured by an auto-analyzer. Estimated glomerular filtration rate (eGFR) was calculated by using standard formula. CKD was diagnosed and classified according to the National Kidney Foundation (NKF) Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines.

Results: A total of 18.2% respondents were found to have likely CKD to whom 82% were in stage 1 and 18% were in stage 2. The majority of the likely CKD respondents (30.1%) were in age >60 years. The prevalence of proteinuria was significantly (P=0.0001) higher among previously documented CKD patients compared to the control group. Logistic analysis revealed that after adjustments, CKD showed a significant association with diabetes mellitus (ORs: 7.46, P=0.00), smoking (ORs: 2.36, P=0.02), obesity (ORs: 3.98, P=0.00) and hypertension (ORs: 1.16, P=0.66) compared to control.

Conclusion: A substantial number of adults were found to be unaware of the existence of CKD hence, large-scale prevention programs should be undertaken to reduce the classical risk factors of these disorders.

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Introduction

Chronic kidney disease (CKD) is a serious public health concern that is the major cause of morbidity and mortality worldwide. CKD is defined by the kidney damage that is usually detected through certain markers including albuminuria or estimated glomerular filtration rate (eGFR <60 mL/min/1.73 m^2) (1). The prevalence of CKD among the general population worldwide was estimated at around 11%-13% (2), whereas the prevalence was reported to be higher in developing countries compared to developed countries (3). According to an earlier report (4), in 2015 around 109.9 million people from developed countries had CKD while these numbers were around 387.5 million for developing and lower income countries. In South-East Asia, the prevalence of CKD was ranging from 10.6% in Nepal to 23.3% in Pakistan (3). Bangladesh is also experiencing huge burdens in the total number of CKD patients. In Bangladesh, the overall prevalence of CKD was estimated at around 14% (5), while these numbers varied substantially depending on age and other

Key point

In a screening program among the 400 subjects in the Thakurgaon district of Bangladesh to identify people with the risk of CKD, 18.2% of subjects with CKD were f asymptomatic in our study. Since a substantial number of adults were found to be unaware of the existence of CKD hence large-scale prevention programs should be undertaken to reduce the classical risk factors of these disorders.

factors (5). According to a study conducted in Dhaka, the prevalence of CKD was 26% for people aged 30 years or above (6), and 13% for people aged 15 years or above (7).

CKD is influenced by several factors including age, gender, socioeconomic conditions, and health risk factors like cardiovascular diseases (CVD), diabetes, hypertension, obesity, etc (8-10). According to previous reports, the prevalence of CKD among the diabetic patients was 34% (11), around 26.8% to 47.2% among the CVD patients (12,13), around 30.1% among the young obese people (14). Along with the effect on health, CKD also impacts social life (15), whereas financial burden is identified as the most common form of social burden. Most of the CKD patients are at higher risk of developing end-stage renal diseases (ESRDs) that often require kidney transplantation and dialysis (16).

Substantial number of people in Bangladesh are at risk of CKD without being diagnosed (8). Many patients in their early stage of CKD are asymptomatic and they do not take any measures to treat which posed them serious health risks (17). Therefore, the actual number of people with CKD cannot be determined as the first and second stages of CKD are not easily detectable. Thus, the screening of CKD patients in their early stages could offer valuable opportunities for effective interventions that could reduce the risk of possible CKD outcomes. However, no such study has been conducted so far showing early detection of CKD among the Bangladeshi population. Only the overall prevalence of CKD among the Bangladeshi population and its associated risk factors were reported by few studies so far (6,10,18).

Objectives

Here, this study attempted to screen CKD patients in their early asymptomatic stage among the adult Bangladeshi population. This study will also consider the association between CKD with other risk factors including demographic and baseline factors, lifestyle and clinical factors among the Bangladeshi population. We also aimed to perform logistic analysis to find out the adjusted associations between CKD with other risk factors.

Patients and Methods

Study participants

This study was conducted to generate epidemiological data of CKD among the asymptomatic adult population from Thakurgaon district in Bangladesh. This screening program was conducted between January 2013 to December 2013 among 400 subjects who were willing to participate in the study. All the participants were chosen randomly. However, participants with previous history of kidney diseases, or taking drugs that could affect kidney functions were excluded from the study. Then we interviewed all the participants using a close-ended structured questionnaire. The questionnaire included several questions regarding demographic information, lifestyle factors like smoking habit and alcohol consumption habit.

Sample size

Sample size was calculated using the formula: n= z^2p (1-p)/ d^2; where z= Standard normal deviation at 95% confidence level, p= assumed target proportion to have a particular characteristic, d= margin of error and n= sample size.

Considering the proportion of patient with particular characteristics (p) = 50% =0.5 (since the actual number is unknown), z = 1.96, margin of error (d) = 5% = 0.05; then at 95% confidence interval, sample size (n) becomes 384. However, due to 5% non-response, we added 16 samples for conducting this study. So, total sample size was 400.

Biochemical measurement

The participants' blood pressure, waist and hip circumference, weight and height were measured at the time of hospital visit and then body mass index (BMI) and waist-hip ratio (WHR) were calculated accordingly. Blood samples (5 mL) were collected for the measurement of serum fasting blood glucose, serum albumin and serum creatinine. Blood specimens were centrifuged to separate serum and were preserved immediately at -20°C for the future analysis.

Serum glucose (fasting and 2 h after breakfast) was measured by glucose oxidase (GOD-PAP) method (19) (Randox Laboratories Ltd., UK). Serum creatinine was estimated by colorimetric method using an auto-analyzer (20). Proteinuria was assessed by Dipstick method in most outpatient settings to measure the urine protein concentration (21). Urine albumin was measured by BNII ProSpec nephelometer, and urine creatinine was measured by Jaffe method using the Modular-P chemistry analyzer (Roche/Hitachi, Switzerland) (22). For determination of estimated glomerular filtration rate (eGFR), modification of diet in renal disease (MDRD) formula version 4 was used (23,24). According to K/DOQI and Kidney Disease (25), we should have at least three months history or three positive test results. Since we conducted a screening program and tested only once, we used the term "likely CKD" instead of CKD.

Definition and classification

The severity of the CKD was classified into five stages based on the recommendation by Kidney Disease Outcome Quality Initiative (K/DOQI) (25): stage 0: eGFR>90 mL/min/1.73m^2, and no proteinuria, stage 1: eGFR of > 90 mL/min/1.73 m^2 with evidence of kidney damage; stage-2 (mild renal insufficiency with eGFR of ≥60–89 mL/min.1.73 m2); stage-3 (moderate renal insufficiency with eGFR of ≥30–59 mL/min/1.73 m2); stage-4 (severe renal insufficiency with eGFR of ≥15–29 mL/min/1.73 m2) and stage-5 (renal failure with eGFR of <15 mL/min/1.73 m^2.

Proteinuria was classified as trace and (1+, 2+, and 3+) based on earlier study (20). BMI was categorized into underweight (BMI <18.5), normal weight (18.5-25) and overweight (>25) according to WHO classification (26). Diabetes was considered when subjects fasting blood glucose was found >7.0 mmol/L or >126 mg/dL) (27). Hypertension was considered when systolic blood pressure (SBP) >130 mm Hg or diastolic blood pressures (DBP) >80 mm Hg were found (21).

Ethical issues

The study was performed according to the ethical standards of human experimentation in accordance with the Helsinki Declaration. Here, written consent was taken from each respondent and the study was approved by the appropriate Ethics committee. The participants were notified about the aim and purpose of this study. Anonymity, confidentiality and voluntary participation were ensured. The participants' safety was assured by not doing any kind of harm to them. Sensitive and polite wording were used.

Statistical analysis

Data analysis was done using SPSS program version 24 software (SPSS Inc., Chicago, USA). Quantitative variables were presented as mean ± S.D. Categorical variables were shown in number and percentage. Since, the data followed normal distributions, for analysing categorical variables, Pearson's $\chi 2$ (chi-square) test was performed and for continuous variables, student's t-test was performed. The level of significance of each result was set at $P < 0.05$. All statistical tests were 2-sided. Binary logistic regression analysis was also performed to determine the adjusted associations between CKD and other risk factors.

Results

Demographic characteristics of the study subjects

Table 1 showed the demographic characteristics of the study subjects. Here, the likely CKD subjects were termed as CKD group and non-CKD subjects as control group. Among the total 400 subjects, 73 (18.2%) subjects were diagnosed with likely CKD, and the rest 327 (81.8%) were control. The mean age of the subjects was found 48.94 ± 11.00 for control, and 53.09 ± 11.11 for the CKD group, which differed significantly ($P = 0.01$). Within the age categories, most participants in the control group were belonged to 30-40 years (29.1%), followed by 41-50 years (28.4%), 51-60 years (26.6%) and >60 years (15.9%). Whereas, most of the participants in the CKD group were belonged to >60 years (30.1%), followed by 51-60 years (27.4%), 41-50 years (26%), and 31-40 years (16.4%). Almost half of the subjects in both groups (67.3% for control and 63% for CKD group) were found male. The mean BMI for the control group was 21.40 ± 5.25, and that for the CKD group was 24.75 ± 5.14, which was significantly higher ($P = 0.00$). Among the BMI categories, most of the subjects belonged to normal weight (59% in the control group, and 41.1% in the CKD group). Regarding

Table 1. Demographic characteristics of the CKD and control subjects

	Control (n=327)	CKD (n=73)	*P* value
Age	48.94 ± 11.00	53.09 ± 11.11	
30-40 years	95 (29.1%)	12 (16.4%)	
41-50 years	93 (28.4%)	19 (26%)	0.01*
51-60 years	87 (26.6%)	20 (27.4%)	
>60 years	52 (15.9%)	22 (30.1%)	
Gender			
Male	220 (67.3%)	46 (63%)	0.46
Female	107 (32.7%)	27 (37%)	
BMI	21.40 ± 5.25	24.75 ± 5.14	
Underweight	86 (26.3%)	07 (9.6%)	
Normal weight	193 (59%)	30 (41.1%)	0.00
Overweight	37 (11.3%)	21 (28.8%)	
Obesity	11 (3.4%)	15 (20.5%)	
Education			
Illiterate	87 (26.6%)	18 (24.7%)	
Primary	173 (52.9%)	38 (52.1%)	0.51
Secondary	35 (10.7%)	12 (16.4%)	
Graduate	32 (9.8%)	05 (6.8%)	
Occupation			
Professional	25 (7.6%)	05 (6.8%)	
Housewife	17 (5.2%)	03 (4.1%)	
Business	25 (7.6%)	06 (8.2%)	0.98
Unemployed	13 (4.0%)	02 (2.7%)	
Domestic helper	108 (33%)	27 (37%)	
Day labourer	139 (42.5%)	30 (41.1%)	
Marital status			
Married	309 (94.5%)	70 (95.9%)	0.63
Single	18 (5.5%)	03 (4.1%)	
WHR			
Normal	190 (58.1%)	40 (54.8%)	
Moderate risk	48 (14.7%)	7 (9.6%)	0.26
High risk	89 (27.2%)	26 (35.6%)	

*Statistically significant.

educational qualification, over half of the subjects (52.9% in control, and 52.1% in CKD) in both groups were found with primary level education. Most of the subjects in both groups were domestic helper (33% in control, and 37% in CKD group) and day labourer (42.5% in control, and 41.1% in CKD group). Furthermore, most of the study subjects were found married (94.5% in control, and 95.9% in CKD group). Finally, the WHR was within normal category for 54.8% of CKD subjects and within low and high-risk categories for 9.6% and 35.6% of CKD subjects respectively, whereas in case of control group, the WHR categories belong to normal, low and high-risk were 58.1%, 14.7% and 27.2%, respectively.

Prevalence of CKD among the asymptomatic adult subjects

Here, among the total 400 subjects, 82% (327) were in the control group that means their eGFR was found >90 mL/min/1.73m^2 with no proteinuria and kidney damage. On the other hand, 15% (60) of total subjects were found with stage 1 (eGFR of > 90 mL/min/1.73 m^2 with evidence of kidney damage). Only 3% of total subjects were found with stage-2 (mild renal insufficiency with eGFR of ≥ 60–89 mL/min.1.73 m^2). Since we conducted our study only among the undiagnosed populations, we did not find any subjects with stage 3, 4 and 5 (Figure 1).

Proteinuria and albumin-creatinine ratio significantly affected CKD

All subjects were tested for proteinuria, albuminuria and urine creatinine. Table 2 showed overall proteinuria status and albumin-creatinine ratio (ACR) among the CKD and control subjects. Among the 73 CKD subjects, over half (58.9%) exhibited +1 proteinuria, 24.6% exhibited +2 proteinuria, and 6.5% exhibited +3 proteinuria, while these proportions represented only 7.6%, 1.5% and 0.4%, respectively in case of control subjects. The difference in proteinuria status between the CKD and control groups was statistically significant ($P = 0.00$). On the other hand, ACR was found less than 30 mg/g for 92% of control subjects, but this proportion belonged to only 8.2% in case of CKD subjects. About 78% of subjects with CKD had ACR within 31-300 mg/g, and 13.8% subjects had ACR >300 mg/g. However, in case of control subjects, only 08% subjects had ACR within 31-300 mg/g range, and none had ACR >300 mg/g. The differences in ACR between the CKD group and the control group were significant as well ($P < 0.01$).

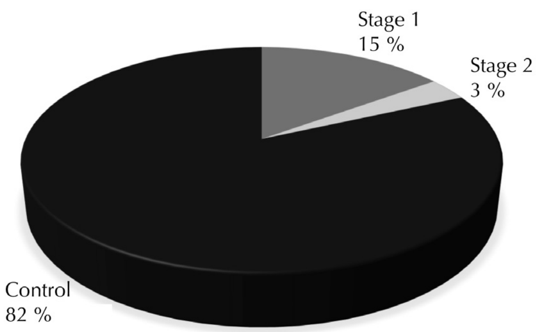

Figure 1. Number of subjects according to CDK stages. Here, pie chart represented total number of subjects according to CDK stages. No stage 3, 4, and 5 CKD subjects were found in our study.

Table 2. CKD stages and proteinuria status among the CKD and control subjects

	Normal (n=327)	CKD (n=73)	*P* value
Proteinuria			
Trace (<30 mg/dL)	296 (90.5%)	08 (10.0%)	
+1 (30-100 mg/dL)	25 (7.6%)	43 (58.9%)	0.00*
+2 (100-300 mg/dL)	05 (1.5%)	18 (24.6%)	
+3 (300-1000 mg/dL)	01 (0.4%)	04 (6.5%)	
ACR			
<30 mg/g	301 (92%)	06 (8.2%)	
31-300 mg/g	26 (08%)	57 (78%)	0.00*
>300 mg/g	00	10 (13.8%)	

*Statistically significant.

Association between CKD with other risk factors

We also investigated the association between CKD with other risk factors (Table 3). Here, we observed that smoking, diabetes, obesity, and hypertension were significantly ($P < 0.05$) associated with CKD. According to our study, the risks of developing CKD increased 1.8 times due to smoking, 10.68 times due to having diabetes, 7.43 times due to obesity, and 2.08 times due to hypertension. However, our study didn't find any significant correlation between CKD and alcohol consumption.

Logistic regression analysis

Finally, we performed a logistic regression analysis to find out the adjusted association between CKD and other risk factors. Here in our study, the presence or absence of CKD was considered as dependent variable, and age, gender, BMI, diabetes, smoking habit, hypertension, and WHR were considered as independent variables. Independent variables were further categorized considering age (30-40 years), gender (male), BMI (normal weight), smoking habit (non-smoker), alcohol consumption (non-consumer), WHR (normal), hypertension (no), diabetes (no) as reference group.

Here, CKD groups showed a positive association with age, BMI, smoking, diabetes, and hypertension after adjustments for all the risk factors. According to the results, adjusted ORs was found highest for diabetes (ORs = 7.46), followed by obesity (ORs = 3.98), overweight (OR = 3.78), age >60 years (ORs = 3.39), smoking habit (ORs = 2.36), age (51-59 years) (ORs = 1.77), age (41-50 years) (OR = 1.43), and hypertension (ORs = 1.16). However, significant association was observed for only age (>60 years), overweight, obesity, smoking, and diabetes.

Table 3. Association between CKD with risk factors

	Control (n=327)	CKD (n=73)	*P* value	OR (95% CI)
Smoking status				
Non-smoker	216 (66.1%)	38 (52.1%)	0.03*	1.18 (1.07-2.99)
Smoker	111 (33.9%)	35 (47.9%)		
Alcohol consumption status				
Never	301 (92%)	65 (89%)	0.41	1.42 (0.61-3.29)
Alcohol consumer	26 (08%)	08 (11%)		
Diabetes				
Non-diabetic	309 (94.5%)	45 (61.6%)	0.00*	10.68 (5.46-20.87)
Diabetic	18 (5.5%)	28 (38.4%)		
Obesity				
No	316 (96.6%)	58 (79.5%)	0.00*	7.43 (3.25-16.98)
Yes	11 (3.4%)	15 (20.5%		
Hypertension				
No	144 (44%)	20 (27.4%)	0.009*	2.08 (1.19-3.65)
Yes	183 (56%)	53 (72.6%)		

*Statistically significant.

Alcohol consumption and WHR were not found positively associated with CKD after adjustments (Table 4).

Discussion

CKD is a worldwide public health threat, but the dimension of this problem in Bangladesh is probably not fully appreciated. Since patients in the early stages of CKD are largely asymptomatic (8), they often do not take any measures to treat which eventually progressed over time to ESRD. This prevented finding out the actual prevalence of CKD in the poor country. This study, for the first time, aimed to screen of CKD patients in their early stages, to avoid adverse outcomes of CKD through early detection and intervention. Here, we found that the overall prevalence of likely CKD was 18.2% among the undiagnosed asymptomatic Bangladeshi subjects, where most of them were in stage 1 (82% of CKD subjects). Among the associated risk factors, we had identified diabetes, hypertension, obesity, and smoking that significantly affected CKD.

Stages 1 and stage 2 of CKD appear to be very common as reported in the National Kidney Foundation (NKF) K/DOQI guidelines (25). Our study showed 82% of likely CKD subjects were in stage 1, and 18% were in stage 2. These findings supported earlier study that reported prevalence of CKD in stage 2 was around 12% (8). Our study showed an overall prevalence of CKD around 18.2% which also correlated with previous reports showing overall prevalence of CKD among Bangladeshi population (around 14% to 19.5%) (5, 8). Since the symptomatic participants avoided takeing part in screening, our study did not find any subjects in CKD stage 3, 4 and 5. This is more alarming since large proportion of asymptomatic individuals in our study had found with CKD. Thus, this study surely showed the effectiveness of identifying a large number of individuals in the early stages of CKD, which is alarming for a developing country like Bangladesh.

Table 4. Adjsuted odds ratio for CKD risk factors

Variables	Category of Characteristics	Adjusted OR (95% CI)	*P* value
Age	30-40 years (Ref.)	1	
	41-50 years	1.43 (0.60-3.42)	0.42
	51-59 years	1.77 (0.72-4.37)	0.21
	>60 years	3.39 (1.30-8.80)	0.01*
Gender	Male (Reference)	1	
	Female	1.35 (0.52-3.50)	0.53
BMI	Normal weight (Ref.)	1	
	Underweight	0.43 (0.16-1.10)	0.07
	Overweight	3.78 (1.85-8.53)	0.00*
	Obesity	3.98 (1.33-10.71)	0.00*
Smoking habit	Never (Ref.)	1	
	Yes	2.36	0.02*
Diabetes	No (Ref.)	1	
	Yes	7.46 (3.39-16.38)	0.00*
Hypertension	No (Ref.)	1	
	Yes	1.16 (0.58-2.38)	0.66
WHR	Control (Ref.)	1	
	Low risk	0.52 (0.18-1.54)	0.52
	High risk	0.94 (0.36-2.42)	0.93
Alcohol consumption	No	1	
	Yes	0.61 (0.19-1.94)	0.40

*Statistically significant.

In our study, the association between proteinuria with CKD were investigated. Prevalence of proteinuria was significantly (P = 0.0001) higher among previously documented CKD patients. Overall, 10.75% of the participants in our study showed +1 (30-100 mg/dL) positive dipstick proteinuria. This value was lower than the 15% found in Congo (28) and 11% found in Bolivia (29). It had been reported that proteinuria accounts for 4-1% of the population in Japan (30), 7%-9% in Taiwan (31) and 0%-5% in China (32). This discrepancy between studies may be partly due to various definitions (microalbuminuria versus dipstick proteinuria) and the criteria of selection (random versus without random sample and/ or high-risk population versus whole population) applied in each survey. As it is a key prognostic finding and it has a significant beneficial role for early diagnosis of CKD, screening of urine for proteinuria using the dipstick test is being used successfully (33).

According to previous studies, CKD is strongly associated with age since ageing is associated with gradual loss of total glomeruli (34). Our study also found that most of the subjects with likely CKD were in the age group of above 60 years (30.1%). Nevertheless, our study showed that younger age group (30-40 years) accounted for 16% of total likely CKD, which supported earlier study that reported a significant proportion of middle-aged people developed CKD in Bangladesh (10). When we adjusted our data, we found that age above 60 years increased the chance of developing CKD by 3.39 folds (ORs: 3.39) than the younger age group (30-40 years).

Iseki et al reported that the prevalence of CKD was lower among people who were married (35). In this study, we saw that among the CKD patients, 95.9% were married. This might be because the mean age for marriage among the rural Bangladeshi people was 18.3 for women and 25.7 for men according to Bangladesh Bureau of Statistics-2018 (36), and most of the subjects in our study after 30 got married which prevented us to get enough unmarried subjects. Furthermore, the positive association between education and health is well established (37). In the present study, we observed that 60% of the study population had completed primary level education, so health related awareness was very poor. Furthermore, individuals with higher occupational status are less likely to develop a poor health outcome than those with a lower occupational status (38). In addition, job related stress has a negative impact on the health outcome of an individual although its impact appears to vary across the occupational classes (39). These findings are also reflected in our study also, in our study, we saw that most of our study subjects were domestic helpers (53%) and day labour (24.4%).

Diabetes, hypertension, obesity, and smoking are previously considered as risk factors for developing CKD (4,8,10). Our study, like previous studies, also found a strong association between CKD and diabetic group (P <0.01), between CKD and obese group (P=0.00), CKD and hypertension group (P=0.009), and CKD and smoking habit group (P=0.03). Although unlike other studies (5), the association between hypertension and CKD after adjustments were not found significant, our adjusted data revealed that diabetes, smoking, obesity and hypertension increased the chance of developing CKD by 7.46, 2.36, 3.98 and 1.16 folds, respectively. Among the other confounding risk factors, our study did not find any significant association between CKD and alcohol consumption, between CKD and gender, and CKD and WHR.

Conclusion

In conclusion, we suggested that early screening for CKD among the general population was utmost important since around 18.2% subjects with CKD were found asymptomatic in our study. This early screening could be used to identify the people with risk of CKD and developing the disease. It will ultimately save more expenses and reduce burden of disease. Early detection of CKD should lead to treatment that prevents or delays the occurrence of significant morbidity and mortality. A country like Bangladesh with meagre number of nephrologists and limited resources, early prevention through screening can be the most valuable and effective strategy.

Limitations of the study

This investigation was conducted in a limited area, therefore large studies on this subject are suggested.

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Authors' contribution

ZZ, KF and LA were responsible for designing the study. Besides, ZZ and AFS contributed to data analysis, and drafted the initial manuscript. ZZ, RZ, and LA reviewed, revised the manuscript and approved the final manuscript. ZZ and FK were responsible for data collection.

Conflicts of interest

There was no competing interest to declare.

Ethical considerations

Ethical issues have been completely observed by the authors.

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