Prevalence of Chronic Kidney Disease (CKD) and Identification of Associated Risk Factors among Rural Population by Mass Screening

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ABSTRACT:
The prevalence of Chronic Kidney Disease (CKD) is rapidly increasing worldwide. Population-based studies on the prevalence of kidney damage are limited in developing countries. The present work relates to a population-based screening study in a rural population. Objectives: The study was performed to investigate the prevalence of chronic kidney disease (CKD) in rural residents and find out the association of the associated risk factors and variables. Methods: This is a descriptive cross sectional study. The demographic variables included were age, sex, marital status, religion, occupation, socioeconomic status, monthly income. The clinical variable was hypertension. The risk factors under the study were Body Mass Index (BMI), smoking habit, hypertension, and diabetes mellitus. Data pertaining to biochemical investigations were urine for albumin, serum creatinine and random serum glucose. CKD suspected patients were subjected to repeat serum creatinine and urinary albumin testing three months after the initial testing to confirm diagnosis of true CKD. Results: 1240 patients of which 650 were males and 590 females, aged between 18 and 65 years were entered into this study. The result evidenced over-all CKD prevalence 19 % determined by Cockcroft-Gault and 19.5 % MDRD equations. Stage 3 CKD was found to be predominant in both Cockcroft-Gault (12.8%) and MDRD equations (13.2%). The risk factors were thought to be associated with CKD which demonstrated association with hypertension (19.3%), diabetes (4.9%) and others (1.3%). A total of 206(88%) patients determined by Cockcroft-Gault and 210 (89.4%) by MDRD equations were diagnosed as having CKD in 2nd follow up visit (3 months after the 1st visit). Conclusion: It appears from this study that one out of three people in this population at risk remained undiagnosed as CKD and with poorly controlled CKD risk factors. This is a growing problem and a challenge to this country. On priority basis CKD needs to be addressed through the development of multidisciplinary health teams and establishment of improved communication between traditional health care givers and nephrology services.

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Introduction

Chronic kidney disease (CKD) is a major public health problem worldwide due to a change of its underlying aetiopathogenesis[1]. Although kidney disease infectionse now considered less important in the western world[2], but currently hypertension and diabetes are evidenced as the two major determinants of kidney disease[3,4]. CKD patients are at high risk for progression to the end stage renal disease (ESRD) – a condition requiring dialysis or kidney transplantation to maintain patients long-term survival with high cost for maintenance of therapy requiring between US $70 and $75 billion worldwide excluding kidney transplantation. Presently the predicted number of ESRD patients is estimated to be over 2 million[5]. CKD has a complicated interrelationship with other diseases 6. Recent studies revealed that CKD is as an independent risk factor for cardiovascular disease (CVD)[7,8,9]. Progress to kidney failure or other adverse outcomes could be prevented or delayed through early detection and treatment of CKD[10,11]. National Kidney Foundation (NKF) developed a practice guideline for CKD or glomerular filtration rate (GFR) below 60 ml/min/1.73 m2 for three or more months with or without evidence of kidney damage, irrespective of the cause[12,13]. GFR is estimated by serum creatinine based on equations, such as Cockcroft-Gault (CG) equation and the Modification of Diet in Renal Disease Study (MDRD) equation[14,15,16].

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Leaving aside hypertension and diabetes, age is pinpointed as a key predictor of CKD and 11% of individuals older than 85 years without hypertension or diabetes had stage-3 or worse CKD[16]. Regarding sex factor males of African-Americans, Europe, Asia, and Australia as well as in developing regions such as China, India and Africa with pre-existing hypertension or diabetes and CKD are at much higher risk for ESRD[17]. The precise nationwide prevalence of CKD in Bangladesh is still unknown. However one study undertaken in slums of Dhaka revealed 16% prevalence. Nearly 1.3% was found to belong to stages-I, 3.4% stage II, 11% stage III, 0.3% stage IV and only 0.1% stage V diseases[18]. In another investigation conducted in Savar, Dhaka showed that prevalence rate of CKD in rural population was 17.4%. The distribution stages recorded were 1.7% stage- I ,2.1% stage II 2, 13.1 % stage III, 0.3% stage IV and 0.2% stage V[19]. Since dialysis and kidney transplants are too costly for a large number of people, early detection and intervention are the only cost-effective strategies for CKD treatment. In this viewpoint public health programs with active participation of the public is indispensable[20]. The detection of CKD is increasing world-wide due to more awareness, improving logistic facilities, easy access to Renal Replacement Therapy (RRT), more early referral and progressively rising incidence of DM and HTN[21]. In Bangladesh the available informative data is very meager. The present study is therefore undertaken to find out CKD patients particularly asymptomatic CKD patients prevalent in a particular community representing a cohort section of the whole population in Bangladesh.

Methods

The present study was a prospective study conducted in the Department of Nephrology, Mymensingh Medical College Hospital over a period 1 year from April 2009 to March 2010. Adult populations having age ranging from 18 – 65 years of either sex residing in the study area for at least 6 months were eligible. Persons with age <18 years or >65 years,, febrile illness, severe cardiac or respiratory failure, previously known kidney disease, urinary tract infection, pregnant women, menstruating women, persons declining consent were excluded.

The sample size was determined using the formula: n = (Z2 ′ p ′ q)/d2, where Z is Standard normal deviate 1.96; p = Prevalence of CKD in community, 18% as per Kidney Foundation of Bangladesh; q = (1-p), 0.82, and d = allowable error (here 10% of 'p'). The calculated sample size obtained is1750. In this study 1240 cases were feasible to be included. The sampling procedure followed was a 3-stage study. The demographic variables studied were age, sex, marital status, religion, occupation, socioeconomic status, monthly income. The clinical variable was hypertension. The risk factors were Body Mass Index (BMI), smoking habit, hypertension, and diabetes mellitus.

The biochemical investigations conducted were urine for albumin, serum creatinine and random serum glucose. Subjects with suspected of CKD had to undergo repeat serum creatinine and urinary albumin testing three months after initial diagnosis. eGFR (Corrected CCr) < 60 ml/min/1.73 m2 or eGFR (corrected CCr) ≥ 60 with albuminuria was screened as CKD. Measurement of GFR was done as per formula of Cock Croft- Gault and MDRD (modification of diet in renal disease) equation.

The laboratory techniques applied was estimation of Random serum glucose using glucose oxidase method and serum creatinine was estimated using kinetic method. Hospitex Screen Master, Techno-168 (ISE, SRL-Italy) was employed for estimation of serum creatinine and serum glucose. Serum creatinine was estimated by Hospitex Screen Master, Techno-168 (ISE SRL, Italy) and Blood glucose was estimated by Hospitex Screen Master, Techno-168(ISE SRL, Italy). A structured data collection form was used containing all the variables. The history and physical findings with investigation findings were recorded. All data were collected in individual case record form. Data processing and analysis were done with the help of computer using SPSS (Statistical Package for Social Science version 12). The test statistics used to analyze the data were Chi square Test and Student's t test. The level of significance was set at 0.05 and $p < 0.05$ was considered significant. The summarized data are presented in the form of tables and charts.

Result

One thousand two hundred forty residents (650 males and 590 females, aged between 18 and 65 years) were enrolled into this study. It is evidenced from the data sheet processing result that 40% of patients were within age range of 30 to 40 years, followed by 27.4% at 30 years or below, 20% between 41 to 50 years, 8.7% between 51 to 60 years and rest 3.9% above 60 years. The mean age of patients was 37.1 ± 10.9 years. Over half (52%) of the patients was male and the remaining 48% was female that is male to female ratio is approximately 1:1. With regard to occupation and monthly income of patients about 39% patients were housewife followed by 15.2% day laborer, 13.1% farmer, 12.1% businessman, 11% service holder, 5.8% student, 2.9% rickshaw puller and 0.9% unemployed. About 64% of patients had monthly income below Taka 5 thousand, 14.3% earned between Taka 5 – 10 thousand, 20.4% between Taka 10 – 20 thousand and only 1.4% taka 20 or > 20 thousand. The median monthly income was Taka 4300 and the lowest and highest monthly incomes were Taka 1500 and 30000 respectively. The analysis of distribution of risk factors revealed that over three-quarter (77.7%) of the patients was within normal body weight in terms of BMI. Eighty patients (6.5%) were underweight and 197(15.8%) were overweight and obese. The behavioral risk factor smoking was predominant among the study population (39%). Hypertension and diabetes comprised of 19.3% and 4.9% of the patients respectivel

All patients were subjected to dipstick test for albuminuria. Of them 1037(83.6%) did not exhibit albuminuria,139(11.2%) had '+', 54(4.4%) had '++' and 10(0.8%) had '+++' albuminuria. Thirty three (5.1%) of 650 males had serum creatinine > 1.5 mg/dl and 20(3.4%) of 590 females had serum creatinine > 1.3 mg/dl. About 6% of patients had RBS > 180 mg/dl. The comparison of renal function in different age groups showed that the mean serum creatinine was significantly higher in those who were more than 60 years of age compared to those were at 60 years or less than 60 years (1.4 ± 0.6 vs. 1.0 ± 0.7 mg/dl, p<0.001). CCr was found two-times higher in patients aged ≤60 years than who were >60 years (83.5 ± 31.7 vs. 46.3 ± 16.1 ml/min/1.73m2, p < 0.001).On the other hand the mean serum creatinine was almost similar in diabetic and hypertensive patients (1.5 ± 0.5 and 1.5 ± 0.2 mg/dl respectively). However, mean CCr was higher in diabetic patients than that in hypertensive patients (46.2 ± 15.8 and 42.4 ± 7.1 ml/min/1.73m2 respectively). Figure 1 below shows the correlation between eGFR and age of the study subjects and demonstrates that with the increase of age the mean eGFR decreases insidiously (r = -0.448, < 0.001).

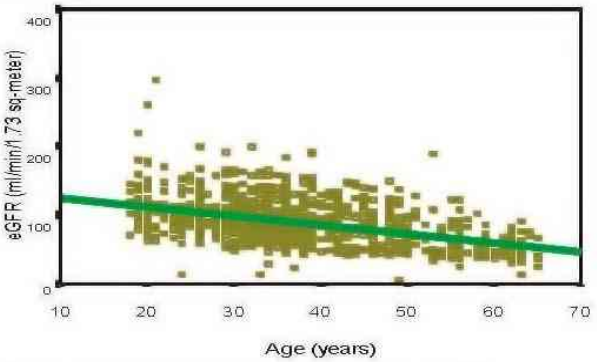

Fig.1: Correlation between age and eGFR

The result presented in Table 1 shows that stage 3 CKD was determined to be predominant by both Cockcroft-Gault (12.8%) and MDRD equation (13.2%). Using Cockcroft-Gault equation, 1.9%, 3.6%, 0.6% and 0.1% patients were screened as stage 1, stage 2, stage 4 and stage 5 CKD, respectively. While by MDRD equation, the prevalence of stage 1, stage 2, stage 4 and stage 5 CKDs were found 2%, 3.6%, 0.5% and 0.2%, respectively.

Table 2 further evidences that the patients with CKD were significantly older than those without CKD (47.4 ± 10.9 vs. 34.7 ± 9.3 years, p < 0.001). Males are significantly prone to develop CKD than their female counterparts (61.2% vs.38.8%, p = 0.002). Family history of hypertension and diabetes mellitus were more frequently present among participants with CKD. Table 3 indicates association of CKD with risk factors. It is remarkable that about 20% of the patients screened as CKD were found overweight and obese compared to 14.3% of the who did not have CKD (p = 0.020). Smoking habit was comparatively higher in CKD group than the normal population (47.2% vs. 37.1%). The prevalences of DM, HTN and combined DM & HTN were significantly higher among CKD patients.

Table1. CKD staging by different equations variables in 1 st follow up (n = 1240)

Staging of CKD	Equation	
	Cockcroft - Gault (Ccr)	MDRD (eGFR)
Stage 1	24 (1.9)	25 (2.0)
Stage 2	45(3.6)	45 (3.6)
Stage 3	158 (12.8)	164 (13.2)
Stage 4	7 (0.6)	6 (0.5)
Stage 5	1 (0.1)	2 (0.2)
Normal	1005 (81.0)	998 (80.5)

Numbers in the parentheses denote corresponding

Table 2. Association between demographic by MDRD equations

Demographic variables	Group		p-value
	CKD (n = 242)	Normal (n = 998)	
Age (years)#	47.4 ± 10.9	34.7 ± 9.3	<0.001
Sex* Male Female	148(61.2) 94(38.8)	502(50.3) 496(49.7)	0.002
Family H/O hypertension*	57(23.6)	28(2.8)	<0.001
Family H/O Diabetes Mellitus *	47(19.4)	7(0.7)	<0.036

Data were analyzed using Chi-square (χ^2) test
Student's t Test was employed to analyze the data

Table 3. Association between risk factors and CKD

Modified marker	Group		p-value
	CKD (n = 235)	Normal (n = 998)	
Overweight and Obese (?25 kg/m2)	48 (20.4)	144 (14.3)	0.020
Smoking	111 (47.2)	373 (37.1)	0.004
DM (self-reported + RBS ≥ 11.1 mg/dl)	60 (25.0)	20 (2.0)	<0.001
HTN (self-reported + newly diagnosed)	148 (63.0)	91(9.1)	<0.001
Combined DM and HTN	43 (18.3)	6 (0.6)	<0.001

Data were analyzed using Chi-squared (χ^2) Test.

Fig.2 depicts data analysis of CKD in 2nd visit 3 months after the first check up date evidenced that patients who were screened as suspected CKD in 1st visit were subjected to examination of their serum for creatinine estimation and urine for albumin. A total of (88%) of patients in Cockcroft-Gault and 210 (89.4%) in MDRD equation were diagnosed as having CKD in 2nd follow up visit.

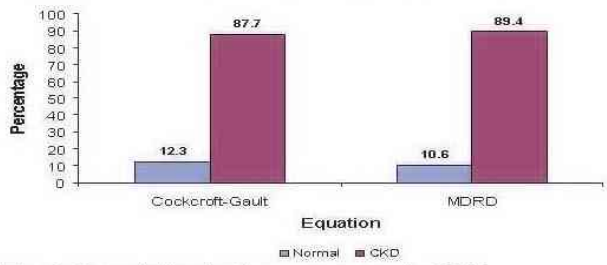

Fig.1: Correlation between age and eGFR

Table 4 reveals that Stage 3 CKD was most dominant in the both Cockcroft-Gault (67.2%) and MDRD (69.8%) equation 3 months after the 1st visit.

Table 4. CKD staging by different equations in 2nd follow up (n = 235)

Staging of CKD	Equation	
	Cockcroft-Gault (Ccr)	MDRD(eGFR)
Stage 1	8 (3.4)	8 (3.4)
Stage 2	34 (14.5)	26 (11.1)
Stage 3	**158 (67.2)**	**164 (69.8)**
Stage 4	5 (2.1)	11(4.7)
Stage 5	1 (0.4)	1(0.4)
Normal	29(12.3)	25(10.6)

Figures in the parentheses denote percentage.

Discussion

In the present demographical investigation the mean age of patients was 37.1 ± 10.9 years covering 52% male and 48% female having 1:1 male-female ratio. The median monthly income of patients was Taka 4300. The lowest and highest incomes were Taka 1500 and 30000 respectively. About 77.7% of the patients possessed normal weight in terms of BMI, 6.5% underweight and 15.8% overweight and obese. Reports published by other investigators indicated more or less similar findings. Chen et al[22] found mean age 58.4 ± 15.3 years ranging between 18 and 104 years and female- male ratio was 1.8:1. Rahim et al [23] observed 48% of patients with normal BMI, 46% underweight and 15% obese. This finding is not in agreement with our findings which might be thought to be due to non homogenicity of population. In another study, Ingsathit et al[24] observed 63.8% underweight, 27.3% normal and 8.9% over weight and obese which was nearly consistent with this study.

The present study revealed the fact that smoking was predominant among the populations under investigation (39%) and other risk factors such as hypertension (19.3%) followed by family history of hypertension (7%), diabetes (4.9%) and other diseases (1.3%). Only a negligible proportion of people informed about their close relationship with kidney diseases (0.005%). Analogously Haroun et al [25] opined that BP, cigarette smoking, gender, and diabetes status play role as risk factors of CKD. Brown et al[26] and Satko[27] pointed out in their study that family history of kidney disease significantly was associated with renal impairment. This underscores the influence of genetic factors in CKD. The researchers evaluating risk of developing CKD in relatives of these "high risk" groups supported the notion of clustering of CKD in families.

It is interesting to note that the majority (83.6%) of the patients did not exhibit albuminuria, 139(11.2%) had '+', 54(4.4%) had '++' and 10(0.8%) had '+++' albuminuria. Studies in America and the Dutch study revealed the prevalence of albuminuria 9.3% and 7.2%, respectively[21]. In Japan, the episode was 4.7% and 3.5% for males and females, respectively [27]. Keane and Eknoyan[28] stressed the need of examining albuminuria in the routine analysis, not only as a relatively simple, non-invasive and cost effective measure to give the qualitative and quantitative assessment of the early stage of CKD, but also to reveal those at high risk of developing CKD, and is very much informative in the prediction of hypertension, diabetes and cardiovascular disease. In the total population under study by Iseki et al[29]patients found to have proteinuria by dipstick on screening examination were reported to incur a 14-fold relative risk of end-stage renal failure during 10 year of follow-up. It was evidenced that for those with established renal disease, proteinuria could be an important predictor of the risk of progression and mortality[30]. Thirty three (5.1%) of 650 males had serum creatinine > 1.5 mg/dl and 20(3.4%) of 590 females had serum creatinine > 1.3 mg/dl. Diabetes, hypertension, older age, male sex was found associated with increased likelihood of elevated serum Creatinine levels[31]. This finding was consistent with our findings. About 6% of participants had random blood sugar > 11.1 mmol/l. Chadban et al[32] observed in AusDiab kidney study the prevalence of reduced GFR <60 ml/min/1.73 m2, but this was 3 fold higher in those with diabetes compared with those without diabetes . However our study is not consistent with this study because most of our CKD population belonged to GN rather than DM and their livelihood is spent in poor hygienic conditions.

In order to measure the renal function in this study, we used the MDRD modified glomerular filtration rate estimating equation with CKD because this formula was provided especially suitable for the Asian population[33]. MDRD has been reported to be more accurate in provide more acceptable estimation of GFR than Cockcroft-Gault equation in patients with GFR < 60 min/1.73 m2[34]. Coresh et al 21 observed in their study on prevalence of CKD and decrease kidney function in the adult population that 11% population had CKD and most of the populations were in stage-3 which is consistent with our finding. Ingsathit et al 28 found that 17.5% of a representative cross-section of the Thai population to acquire CKD. Huda[35] reported that nearly 1.3% had stage-I, 3.4% stage-2, 11% had stage-3, 0.3% stage-4 and only 0.1% stage -5 diseases. Another study conducted by Muqueet 19 in Savar, Dhaka showed that prevalence of CKD in rural population was 17.4%. Among them 1.7% had stage I ,2.1% stage 2, 13.1 % stage3, 0.3% stage 4 and 0.2% stage 5. Nan Chen et al[36] showed that the prevalence of CKD was 11.8% among the community population in Shanghai. It was 2.4%, 3.6%, 5.5%, 0.3% and 0.04% in stages 1–5, respectively. A total of 235(97.1%) attended the second visit complying with the advice.

A total of 206(88%) of patients determined by Cockcroft-Gault and 210(89.4%) MDRD equations were diagnosed as having CKD in 2nd follow up visit (3 months after the 1st visit). Stage 3 CKD was most dominant in the both Cockcroft-Gault (67.2%) and MDRD (69.8%) equation 3 months after the 1st visit. Remaining patients showed normal renal function after 2nd visit three months later possibly because they previously suffered from either acute renal failure or transient proteinuria. This study found a significant association between increasing age and CKD. The patients with CKD were significantly older than those without CKD (47.4 ± 10.9 vs. 34.7 ± 9.3 years, $p < 0.001$). This finding ascribes to other researchers..Mulder et al[37] found a substantial reduction in kidney function with ageing.

The prevalence of CKD among older people was significantly higher, predominantly in male. Family history of hypertension and kidney disease was also recorded to be more frequently encountered in the CKD group than that of the normal group as determined by MDRD and Cockcroft-Gault equation. Coresh and his associates[21] reported that age dependence seems to be even stronger when assessing kidney function using the Cockcroft-Gault formula. The prevalance of CKD was found higher in male (54.2%) than female counterpart which demonstrated that male (58.1%) was significantly prone to develop CKD. There is a strong relationship occurrence between hypertension and CKD which has been seen prospectively in men. Klagg et al[38,39] investigated at over 330,000 men and found that higher BP is associated with a higher incidence of end-stage renal disease.

In the risk factors over weight and obese, smoking, diabetes, hypertension and combined diabetes and hypertension were significantly higher in CKD patients than those without CKD as determined in both MDRD (20.7% vs. 14.2%, $p = 0.013$, 46.7% vs. 37.2%, $p = 0.006$, 24.8% vs. 2%, $p < 0.001$, 62.4% vs. 8.8%, $p < 0.001$ & 17.4% vs. 0.7%, $p < 0.001$, respectively) and Cockcroft-Gault (20.4% vs. 14.3%, $p = 0.020$, 47.2% vs. 37.1%, $p = 0.004$, 25% vs. 2%, $p < 0.001$, 63% vs. 9.1%, $p < 0.001$ & 18.3% vs. 0.6%, $p < 0.001$, respectively) equations. These data evidenced a greater prevalence of moderate or severe CKD among hypertensive and diabetic individuals. Klein et al, (1999) identified smoking as a potential risk factor for CKD[40].

Conclusion

Total of 235 and 242 participants were screened as suspected CKD in 1st visit which evidenced an overall CKD prevalence of 19% and 19.5% as determined by Cockcroft-Gault and MDRD equations respectively. Stage 3 CKD was found to be predominant in both Cockcroft-Gault (12.8%) and MDRD equation (13.2%). Using Cockcroft-Gault equation, 1.9%, 3.6%, 0.6% and 0.1% participants were screened as stage 1, stage 2, stage 4 and stage 5 CKD, respectively.

It is apprehended that one out of three patients in this at-risk population has remained as undiagnosed CKD and poorly controlled CKD risk factors. This growing problem poses clear challenges to our country. With this viewpoint, CKD should be addressed through the development of multidisciplinary teams and improved communication between traditional health care givers and nephrology services. Attentions to CKD risk factors are indispensable and must be given become a priority.

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