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Detection of Chronic Kidney Disease in Adult Rural Population

Md. Abdul Muqueet[1], Prof. Harunur Rashid[2], Sakina Anwar[3]

Abstract:
Context: To find out the exact prevalence of CKD in rural area this study was done on the background of CKD is a major public health problem worldwide and a significant cause of morbidity and mortality. **Methods:** A multistage sampling following simple random sampling procedure was done to choose the study area and a total 1265 adult population ranging from 15-65 years of both sexes were studied. Height, weight of the subjects was measured and body surface area was calculated. Multistik test of urine was done for proteinurea and serum creatinine was estimated. **Results:** The study revealed 60.1% participants were young and middle aged (15-40 years). The mean age was 35.57 $\pm$ 12.98 years. The majority of the participants were female (63%). Multisticks test for urine demonstrated a total 76(6.0%) participants were proteinuric and among this 2.5% had isolated proteinuria. Proteinuria and MDRD equation depicted 238 (18.8%) were having CKD of them 1.7% in stage-1, 2.4% in stage-2, 14.0% in stage-3, 0.5% in stage-4 and 0.2% in stage-5. On the other hand, C-G equation revealed 226 (17.9%) having CKD. Of them 1.7% in stage-1, 2.1% in stage-2, 13.6% in stage-3, 0.3% in stage-4 and 0.2% were in stage-5. Ccr from Cockcroft-Gault equation was corrected for body surface area. Results from both equations were not significantly different. The compliance for follow up after 3 months was 72 (32%). Of them 57(79%) were confirmed as having CKD. **Conclusions:** The survey data revealed that CKD is not less common (18%) among the rural subjects. So, a nationwide screening programme is necessary to develop awareness of entire population and to find exact prevalence of CKD so that a cost effective preventive strategy could be adopted.

Indexing words: Chronic kidney disease, Body mass index, MDRD equation, C-G equation, Cockcroft-Gault equation

Introduction:

Chronic kidney disease (CKD) by definition and classification is new working tool to label the functional status of kidney in spite of its variable causes. This makes easy to diagnose kidney disease at an earlier stages and point out the potential scope for proper intervention to slow the progression of deterioration of renal function and reduce the morbidity and mortality due to late diagnosis and/or referral.

Patients with CKD most often present with nonspecific complaints or are asymptomatic and are referred to a nephrologist because of abnormal blood or urine findings. Late nephrology referral and evaluation of patients with CKD are associated with greater morbidity and mortality. For this reason, referral of patients earlier has been suggested[1].

The Kidney Disease Outcome Quality Initiative (K/DOQI) clinical practice guidelines for CKD evaluation, classification and stratification published by National Kidney Foundation provide a framework designed to address the growing burden of CKD in the United States. Staging of CKD is based on estimation of renal function by GFR. GFR is calculated from serum Creatinine by Cockcroft-Gault and MDRD (Modification of Diet in Renal Disease) equation. Some study showed that there were significant number of patients with normal serum Creatinine level had abnormal GFR with Cockcroft-Gault values <50 mi/mm^2. This group of patients may remain unrecognized by primary care physician who rely on serum creatinine abnormality to identify renal insufficiency. As a result these patients are becoming burden for themselves and for the whole family. In most of the cases the affected

1. Assistant Professor, Department of Nephrology, Pabna Medical College
2. Ex. Chairman, Department of Nephrology, BSMMU
3. Senior Consultant, Department of Medicine, Manikganj Sadar Hospital

family bears the financial burden years after years even after the death of the patient.

Proper intervention in early stage of CKD would slow the progression and reduce the rate of ESRD. So, in country like us it is very important to know the prevalence of CKD which emphasis the early detection and prevention. So, the study was aimed at to find out the prevalence of Chronic Kidney Disease (CKD) in adult rural population and association of some risk factors among them.

Methods

This cross sectional study was carried out in Nephrology department, Bangabandhu Seikh Mujib Medical University and Kidney Foundation. The study area was selected named Bongaon Union, a rural area of Savar thana 30 k.m. away from centre of Dhaka city. A total fifteen thousand population of both sexes, age between 15 and 65 years were included in the study. Persons having fever at the time of screening, recent history of fluid loss such as diarrhea, vomiting, trauma and pregnant women were excluded from the study. A total of twelve hundred sixty five population was screened from July 2003 to June 2005 A multistaged clustered sampling design was utilized by following simple random sampling procedure. First of all a Thana of Dhaka district was selected named Savar. This thana comprises with 12 Unions. Out of these 12 Union Bongaon Union was selected. According to local Union porishod authority there were about 15 thousand adult population who met the inclusion criteria. Among them 1265 participated in the study within mentioned period.

Local authority, Public leaders, Imam, Social workers motivated people to participate in this program. Leaflet distribution, miking, postering was done to create awareness about this program regularly.

Data were collected from all participants by direct interview and using structured questionnaire. Informed consent was obtained from all participants.

Data and samples were collected from a fixed centre in every Friday from 9:00 AM to 2:00PM.

Age, occupation, marital status, addresses were recorded as per statement of the participants at the time of interview.

Height, weight was measured following standard procedure and BMI was calculated.

Multisticks test of urine was demonstrated for proteinurea. Spot urine sample was collected in test tubes labeled with individuals registration no. for each participants and dipstick test was done on the spot using uripath seris reagent strips (plasmatec laboratory products, UK) for detection of urinary protein and sugar. Positive test was lebelled as + (30mg/dl), ++ (100mg/dl), +++ (300mg/dl), ++++ (1000mg/dl) depending on amount of proteinuria.

The serum creatinine was estimated by biochemistry auto analyzer.

Kidney Function:

Kidney function was stratified according to current national kidney foundation (NKF) guidelines on the evaluation, classification and stratification of chronic kidney disease[3].

Definition of CKD:

1. Kidney damage for ≥ 3 month, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by either:
   - Pathological abnormalities or
   - Markers of kidney damage, including abnormalities in the composition of the blood or urine or abnormalities in imaging tests.
2. GFR < 60ml/min/1.73m^2 for ≥3 month, with or without kidney damage.

CKD stage:

Stage-I : eGFR ≥ 90ml/min/1.73m^2 and positive proteinuria.
Stage-II : eGFR 60-89 ml/min/1.73m^2 and positive proteinuria.
Stage-III : eGFR 30–59 ml/min/1.73m^2 .
Stage-IV : eGFR 15–29 ml/min/1.73m^2 .
Stage-V : eGFR <15 ml/min/1.73m^2 or on dialysis.

Creatinine clearance (Ccr) and glomerular filtration rate (GFR) was estimated from serum creatinine level by using prediction equations. Cockcroft-Gault equation provides useful estimates of Ccr in adults. Normalization of Ccr for body surface area allows more accurate evaluation of renal function. MDRD equation also provides estimated GFR which compared with Cockroft-Gault Ccr after correction of body surface area.

Body surface area:

Body surface area (BSA) can be determined from height and weight using a nomogram found in standard references.

$$\text{BSA } (m^2) = \sqrt{\frac{Weight(kg)XHeight(cm)}{3600}}$$

Cockcroft-Gault equation:

$$\text{Ccr(ml/min)} = \frac{(140 - Age)XWeightinKg}{72XSerumCreatinine(mg/dl)} \text{ X (0.85 if female)}$$

$$\text{Corrected Ccr (ml/min/1.73m}^2\text{)} = \frac{Ccr(ml/\min)X1.73}{BSA(m^2)}$$

MDRD equation:

Abbreviated Modification of diet in renal disease (MDRD) study equation provides useful estimates of GFR in adults.

GFR ((ml/min/1.73m^2) = 186.3X (Scr)$^{-1.154}$ X (Age)$^{-0.203}$ X (0.742 if female)

Data processing and analysis:

Data were analyzed through SPSS program. Continuous data were presented as mean and standard deviation from the mean. Chi-square, fishers exact test, Students t- test and Spearman s correlation test was used for statistical analysis. Results were presented in tabulated form, charts and diagrams along with statistical interpretation**.**

Observations & results

The findings derived from analysis of the collected data are furnished below:

Distribution of proteinuria:

Out of 1265 participants 21(1.66%) had DM with proteinuria, 33(2.6%) had HTN with proteinuria, while 3192.5%) had isolated proteinuria. A total of 76(6%) were proteinuric (Fig. 1).

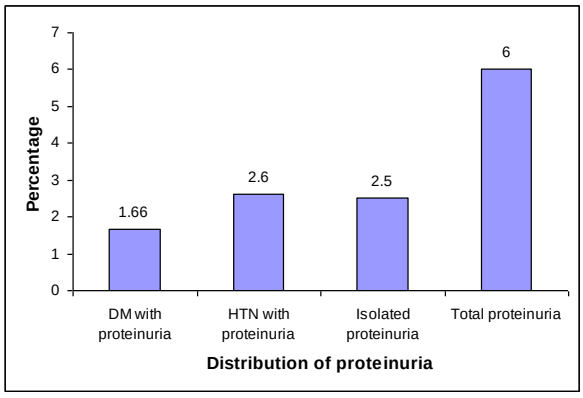


Fig. 1: Distribution of proteinuria among participants (n = 1265)

CKD staging using uncorrected Ccr:

CKD staging done by C-G equation using uncorrected Ccr, a citable proportion of the participants (34.2%) fell under CKD population (Table 2)

Table 1: CKD staging by C-G equation using uncorrected CCr (n = 1265)

Staging	No	%
Total CKD	**432**	**34.2**
Stage 1	10	0.8
Stage 2	35	2.8
Stage 3	362	28.6
Stage 4	23	1.8
Stage 5	02	0.2
Normal	**833**	**65.8**

CKD staging by different equation:

No wide variation in staging of CKD by different equations was observed. The stage 3 occupied the highest position (Table 2).

Table 2: CKD staging by different equations (n = 1265)

Staging of CKD	Equation	
	Cockcroft-Gault	MDRD
Total CKD	**226(17.9)***	**238(18.8)**
Stage 1	22(1.7)	21(1.7)
Stage 2	26(2.1)	31(2.4)
Stage 3	172(13.6)	178(14.0)
Stage 4	4(0.3)	6(0.5)
Stage 5	2(0.2)	2(0.2)
Normal	**1039(82.1)**	**1027(81.2)**

*Figures in the parentheses denote corresponding **%**.

Distribution of CKD:

Comparison was made of the distribution of CKD between Cockcroft-Gault and MDRD equations for detecting CKD. The proportion of CKD detected by Cockcroft and MDRD equations were 17.9% and 18.8% respectively and no significant difference was observed between two equations in terms of CKD detection (p > 0.05) (Fig. 2).

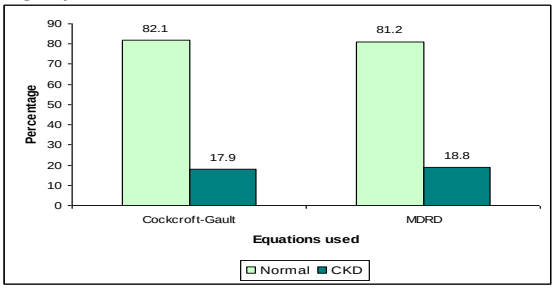


Fig. 2: Distribution of CKD among participants (n = 1265)

Comparison of risk factors between CKD (C-G) and CKD (MDRD)

The distribution pattern BMI and certain systemic diseases like HTN and DM in CKD population are almost similar whether CKD (C-G) or CKD (MDRD) equations are used for staging of CKD ($p > 0.05$) (Table 6).

Compliance of participants:

The compliance of the participants detected as having CKD in the first screening test. All the CKDs detected in the 1st round were instructed to attend at the 2nd follow up visit 3 months after 1st check up to have their serum checked for creatinine and urine for albumin. Of the 226 CKDs only 72 attended giving a compliance rate of 32% (Fig. 3).

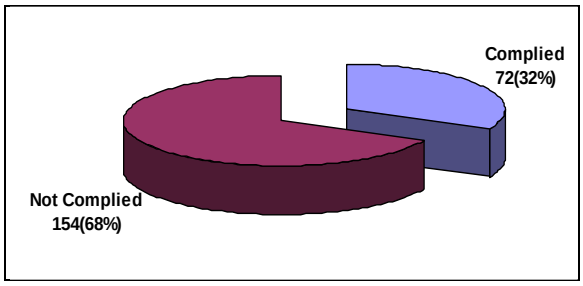


Fig. 3: Showing compliance of the participants (n = 226)

CKD status 3 months after 1st detection:

Out of 72 participants, 57 fulfilled the criteria of CKD giving rise a 79% of confirmed CKD (Fig. 4).

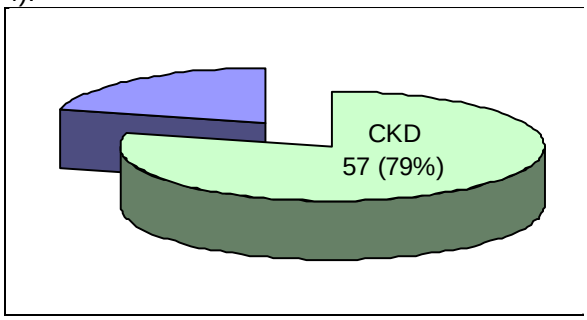


Fig. 4: CKD status 3 months after 1st detection (n = 72)

Discussion:

Among adults in rural population of Bangladesh the present study was done to examine the prevalence of chronic kidney disease (based on proteinuria and/or low GFR, estimated GFR was calculated from Cockcroft-Gault and MDRD equation.

Proteinuria is the cardinal manifestation of glomerulonephritis. Out of 1265 participants urine protein analysis using multisticks demonstrated that a total 76(6%) participants were proteinuric in the present study.

Glomerular filtration rate (GFR) is the singlemost best predictor of renal function in health and disease. Measuring GFR is expensive and cumbersome. Various methods of calculating estimated GFR (eGFR) from serum creatinine concentration have been studied, including Cockcroft-Gault and equation derived from the MDRD study population[4,5]. Both the equation are corrected for body surface area (BSA). Like our study several populations based study with the use of these equations found a surprisingly high prevalence of CKD. (a) The Third National Health and Nutritional Examination Survey (NHANES III)[6] for prevalence of low GFR in non diabetic Americans. (b) Prevalence of CKD and decreased kidney function in adult US population: NHANES III[7]. (c) Prevalence of CKD in Australian adults: The AusDiab kidney study[8]. (d) Prevalence study of CKD among Iceland adults[9]. High prevalence of CKD of all these study leading some authors to doubt the usefulness of these equation in epidemiological studies.[10,11,12]

In Iceland study a correction factor 0.84 is used in Cockcroft-Gault equation to estimate GFR form Ccr. But in the context of our study population the correction factor is yet to be determined. Other population based study did not use such correction factor. In the present study mean body surface area of the studied population was $1.49m^2 \pm 0.17m^2$ which was much lower than standard body surface area $1.73m^2$. To calculate estimated GFR (eGFR) from Cockcroft-Gault (C-G) equation, C-G Ccr (ml/min) was corrected for body surface area in every case. Detection of CKD using uncorrected Ccr (ml/min) from C-G equation without standardization of body surface area give rise inappropriately high prevalence (34.2%) of CKD. According to NKF: K/DOQI guideline unit of estimated GFR (eGFR) from prediction equation is ml/min/$1.73m^2$. So to detect CKD, Ccr from C-G equation should be corrected for body surface area. After correction, CKD prevalence was 17.9% which was comparable with CKD prevalence from MDRD equation (18.8%). MDRD equation calculates directly estimated GFR (eGFR).

Kunitoshi *et al*.,(2003) showed that proteinuria was a strong independent risk factor for developing ESRD[13]. Two community based screening program the Framinghum study[14] and the Okenowa study[15] demonstrated an approximately 10% prevalence of dipstick positive proteinuria in adults. The prevalence was higher in older than in younger and higher in woman than in man. In Hongkong a screening program on asymptomatic renal population found that prevalence of positive (> 1+) urine dipstick for protein is 3.2%[16].

NKF-K/DOQI guideline advocated using albumin-specific dipstick or albumin-to creatinine ratio in spot urine. But in our study we used dipstick for proteinuria and urine microscopy was not performed. Urinary tract infection was not evaluated for exclusion of proteinuria. In AusDiab kidney study[8] proteinuria was detected by protein to creatinine ratio and found that 2.4% was proteinuric. In Framingham cohort it is evident that proteinuria, even in casual urine specimens, carries substantial risk with the mortality rate increased threefold. In Bolivia a survey showed that 11% of apparently healthy subjects were proteinuric with dipsticks test.

Prevalence of CKD in our survey was 238 (18.8%) when MDRD equation was used. Out of which stage 1 (Proteinuria +GFR ≥90 ml/min) was 21(1.7%), stage 2 (proteinuria + GFR 60-89 ml/min) was 31(2.4%), stage 3 (GFR 30-59 ml/min) was 178(14.0%) stage 4(GFR 15-29 ml/min) was 6(0.5%) stage 5 (GFR <15 ml/min) was 2(0.2%).

Prevalence of CKD using MDRD in US adult population was 11%, out of which stage 1 was 3.3%, stage 2 (3%), stage 3 (4.3%), stage 4 (0.2%) and stage 5 (0.2%)[7]. In this NHANES III use of estimated GFR and Ccr equation, strengthened by appropriate calibration of serum creatinine level to the laboratory in which these GFR equations were developed. But in the study such calibration was not used.

Prevalence of CKD in this survey was 226 (17.9%) as Cockcroft-Gault equation was used. Out of which stage 1 was 22(1.7%), stage 2 was 26(2.1%), and stage 3 was 172 (13.6%) stage 4 was 4 (0.3%), stage 5 was 2 (0.2%). Prevalence of CKD using C-G equation in AusDiab kidney study was also 16%. According to NKF-K/DOQI CKD staging evidence of stage-I was 0.9%, stage-II was 2.0%, stage-III was 10.9%, stage-IV was 0.3% and stage-v was 0.3%[8].

In the present study the prevalence of individuals whose Ccr < 60ml/min/1.73m^2 by C-G equation was 14.1% and MDRD was 14.7% which was not different. But NHANES III showed the prevalence of individuals with CCR < 60 ml/min/1.73 m^2 (using C-G equation) was greater than those of estimated GFR < 60 ml/min/l.73m^2 using MDRD equation (7% versus 4.5%)[7]. This may be due to calibration of serum creatinine. In Iceland study eGFR < 60ml/min/1.73m^2 using MDRD equation the crude prevalence was 7.24%.

In the present study the prevalence of CKD with using both the formula revealed significantly high but the prevalence for both the formula was not different. A study of Bostom *et al.,*(2002) specifically evaluated the predictive performance of several GFR prediction equations in subject with CKD and normal serum creatinine[10]. They found that most accurate results were obtained with the Cockcroft-Gault equation, where as the most precise equation albeit biased, was the MDRD study equation. In the present study it was found that 12.1% of male and 12.6% of female with normal serum creatinine were detected as having CKD. In AusDiab kidney study Cockcroft-Gault estimates of creatinine clearance, when corrected for body surface area have been found to correlate well with gold standard measures of GFR[8]. From the above evidences use of both formula to find out the prevalence of CKD is justified.

In this study 11.9% of the CKD population were overweight and obese compare to 16.5% without CKD, although the difference between the two groups did not reach the level of significance (P=0.091) when using C-G equation. Also 15.1% of the CKD population were detected as overweight and obese compared to 15.8% of those without CKD and show no difference between the two groups (P=0.804) when using MDRD equation.

The AusDiab kidney study demonstrated hypertension (odds ratio: 5.4, 95% CI: 4.3, 6.9) were strongly predictive of proteinuria on univariate analysis and hypertension also predictive of renal impairment. The prevalence of reduced GFR <60ml/min/l.73 m^2 was fivefold more prevalent in those with hypertension compared to those without (P<0.00l).

According to NKF: K/DOQI guideline[3] CKD should be labeled if kidney damage with or without decreased GFR persist ≥ 3 months. In the follow up programme out of 226 CKD patient only 72 (32%) attended and complying to the advise. Out of these 72 person 57 (79%) met the CKD criteria after reevaluation. In other studies 18% of the participants showed compliance in KEEP study[17].

Conclusion:

The survey data revealed that CKD is not less common (18%) in the rural population. A similar survey conducted recently in the urban disadvantageous population also demonstrated a significant percentage of CKD. So to prevent or slow the progression of CKD, early detection and therapeutic intervention is the best way.

So, a nationwide screening programme is necessary to develop awareness of entire population and to find exact prevalence of CKD. As a result a cost effective preventive strategy could be adopted.

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