

Original Article

Stratification and Assessment of Risk Factors of Chronic Kidney Disease in Hospitalized Patients

*Hasan MK¹, Ali MH², Rahman MA³, Mille M⁴, Rahman A⁵, Jafri MH⁶**Abstract:**

Chronic kidney disease (CKD) has become a global public health concern. The adverse outcome of CKD are high in number in developing countries due to scarcity of facilities for renal replacement therapy and high cost of services for management of ESRD. It is one of the leading cause of hospital deaths. CKD is strongly associated with diabetes, hypertension, glomerulonephritis and elevated lipids. Therefore, identifying the preventable risk factors, pathophysiological mechanisms and stratification of CKD helps in decreasing and slowing its progression. This study was conducted for the staging of chronic kidney disease (CKD) and assessment of the risk factors with CKD in hospitalized patients of Dhaka Medical College Hospital in collaboration with Medicine and Nephrology department. This was a cross sectional observational study where 125 patients having chronic kidney diseases (CKD) were diagnosed on the basis of history, clinical examinations and investigations, who had fulfill the inclusion and exclusion criteria admitted in the department of medicine and department of nephrology from January to December 2016. Sampling method was purposive sampling. A specifically designed questionnaire were used to get the personal and medical history data. Blood and urine samples were collected and data was analyzed using SPSS (22.00). Out of 125 patients, no Stage-1 patient was found, remaining were Stage- 2 CKD 7.2%, Stage- 3 CKD 63.2%, Stage- 4 CKD

was 25.6%, and Stage- 5 CKD was 4%. Among 125 participants, 52.0% had glomerulonephritis (GN), 31.2% had diabetes mellitus (DM) and 9.6% had hypertension (HTN). Mean age was 48.41 (± 13.99) years, mean body weight was 50.61 (± 10.73) Kg, mean BMI was 22.9 (± 1.69), male female ratio was 3.6:1. Age group 51 to 60 years were suffering more. The association between CKD and other risk factors including obesity and overweight, use of tobacco, diabetes and hypertension were highly significant. The commonest risk factors for CKD like DM and HTN are also alarmingly high and obviously adding to the existing burden of CKD. Early detection of the risk factors of CKD, early referral to nephrologist, appropriate treatment of hypertension, DM, GN and other risk factors, life style modification with specific emphasis on reduction in salt intake, physical exercise, and abstinence from smoking would retard progression of kidney disease to an advanced stage.

Keywords: CKD, DM, HTN, ESRD, Mean

INTRODUCTION

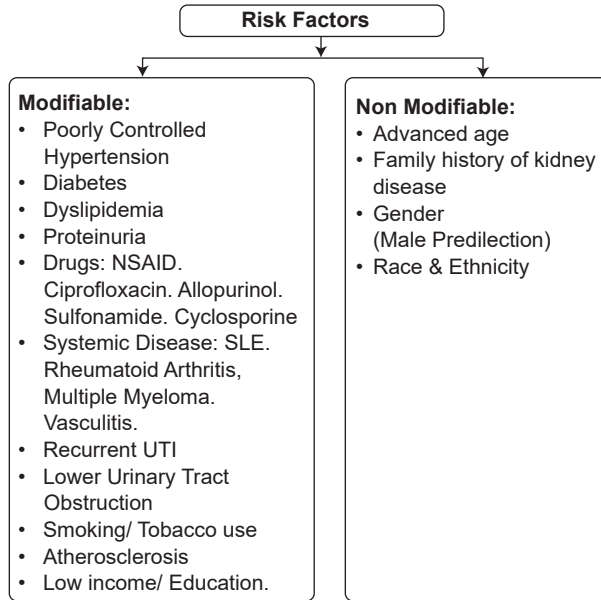
CKD can be defined by kidney damage of more than 3 months as defined by the structural or functional abnormalities of the kidney, with or without decreased GFR, manifested by either pathological abnormalities or markers of kidney damage in blood or urine or imaging; or decrease GFR of less than 60ml/min/1.73m² for not less than 3 months with or without evidence of kidney damage.¹ It is a complex progressive condition that develops slowly in some individuals, but rapidly in others. It is one of the major non-communicable public health problems affecting approximately 10% of global population. In addition to the underlying cause of renal failure, the rate of disease progression may be dictated by the presence of CKD risk factors. The principal outcome of CKD includes progressive loss of kidney function leading to end-stage renal disease (ESRD) and the development and progression of cardiovascular disease (CVD)^{2,3}. Globally, CKD is the 12th cause of death and the 17th cause of disability respectively.⁴ Unfortunately CKD is under-diagnosed and undetected resulting in lost opportunities for improving its clinical outcome.⁵ Notably, the incidence and prevalence of CKD have shown a

1. *Dr. Mohammad Kamrul Hasan, MD (Medicine), Assistant Registrar, Dept. of Medicine, Dhaka Medical College and Hospital (DMCH), Dhaka. Email: dr.kamrul78@yahoo.com
2. Dr. Md. Haidar Ali, FCPS (Medicine), IMO, Dept. of Medicine, DMCH, Dhaka.
3. Dr. Md. Ashikur Rahman, MD (Medicine), Junior Consultant, Dept of Medicine, SBMCH.
4. Dr. Mariam Mille, MBBS, HMO, Dept. of Medicine, DMCH, Dhaka.
5. Dr. Ashiqur Rahman, MBBS, HMO, Dept. of Medicine, DMCH, Dhaka.
6. Dr. Mohammad Hasan Jafri, MBBS, Intern, Dept. of DMCH, Dhaka.

*For Correspondence

dramatic increase over the past two decades. It was recently estimated that 11% of adults in the US alone have early CKD that may progress to ESRD and require renal replacement therapy (RRT), such as dialysis or transplantation. In developing nations including Bangladesh, 95% of ESRD patients die without having renal replacement therapy (RRT). In earlier studies it was shown that, in Bangladesh, each year about 30,000 CKD ultimately enter into RRT^{6,7} The staging of CKD is useful because it endorses a model in which primary physician and specialist both share responsibility for the care of CKD patients. But only for kidney specialist will be tough to provide the care of whole CKD population in a densely populated region like Bangladesh. Besides, classification of CKD also offer specific clinical action plan for each stage which will help both patients and practitioners involved in the treatment of CKD. So, if we identify earlier stage of CKD, will be able to institute corrective strategies to decrease complications and also the progression to ESRD. Because, if we delay the progression of CKD in earlier stage, it is not only prevents progression of ESRD but also help measures to prevent cardiovascular complications.⁸ Furthermore, if we arrange an elective vascular access at stage IV, we can avoid temporary vascular access through central venous catheter which increases later morbidity and mortality. The population of Bangladesh is 168 million and population density is over 1033/km². So, naturally the incidence of infectious disease causing post infectious glomerulonephritis is high. Moreover, the incidence of non-infectious disease like diabetes, hypertension the two most important systemic disease responsible for producing chronic kidney disease leading to end stage renal disease is also going up. According to WHO, the total number and projected number of people in Bangladesh suffering from diabetes mellitus is 3,196,000 and 11,140,000 in 2000 and 2030 respectively. So, glomerulonephritis, diabetes and hypertension are responsible for 85% ESRD in Bangladesh.⁸ Improving outcome for people with CKD requires a coordinated worldwide approach to prevention of adverse outcomes through defining the disease and its outcomes, estimating disease frequency, identifying early stage of disease and antecedent risk factors and detection and treatment for population at increased risk for adverse outcome.¹ The number of CKD patients are continuously increasing all over the world including Bangladesh. Almost one quarter of world's population resides in South Asia-India, Pakistan, Bangladesh, Sri Lanka & Nepal. The commonest risk factors for CKD like DM and hypertension are also alarmingly high and obviously

adding to existing burden of CKD^{8,9} The association between CKD and other risk factors like age, obesity, use of tobacco, DM, HTN was also highly significant. When more than one risk factor is present the chance of developing CKD is extensively eminent. The present studies therefore proposes that a nationwide survey is inevitable and suggests to be conducted encompassing the entire cross section of population to find out the stratification of CKD and assessment of its associated risk factors, so that a preventive strategy or an entire defensive framework could be adopted or planned to reduce the disease in community. Besides large portion of Bangladeshi people live with extreme poverty and are alienated from the light of education. Hence their concern about disease is not sufficient and most of them are not capable of bearing the expenditure of treatment.⁹ the relationship between kidney and hypertension is interesting because the kidney can be affected hypertensive process, or it can also cause hypertension. 80-90% of patients with chronic kidney disease experience hypertension during the course of their disease. Uncontrolled hypertension accelerates the rate of the prevalence of hypertension in urban adult population of Asia varies between 15-35%.⁸ There is no nationwide survey to show prevalence of hypertension in adult population of Bangladesh. In a small community based study showed that in native Bangladesh overall prevalence rate of systolic hypertension is 14.4% and diastolic hypertension is 9.1%¹⁰ The observation that small reductions in the decline in renal function early in the disease process can provide marked benefits later, in terms of delaying progression to RRT, suggests that substantial benefits can be gained from the early identification and treatment of individuals at risk. In order to develop effective strategies to identify such individuals and delay or prevent disease progression, a comprehensive understanding of the complex interplay between risk factors influencing the disease process is required. The present study implies that the urgent need to develop comprehensive strategies targeted reducing CKD burden and may lead to a better understanding of risk factors of CKD. However, little attention has been paid to the stratification of CKD and its risk factors assessment among the population of Bangladesh. With increasing number of CKD patients, CKD related excess CVD, ESRD and consequent financial burden of renal replacement therapy, the importance of CKD and its risk factor has to be realized. Nevertheless, it is true that adopting interventions at early stage of CKD can save a family and the entire nation as well from an intense catastrophe.



Classification	Definition of risk factors
Category I	Factors for which interventions have been proven to lower risk
Category II	Factors for which interventions are likely to lower risk
Category III	Factors for which modification may lower risk
Category IV	Factors for which modification is not possible

MATERIALS AND METHODS

This cross-sectional study was carried out at indoor department of medicine and department of nephrology, Dhaka Medical College Hospital during January 2016 to December 2016. A total of 125 subjects were included having chronic kidney diseases (CKD), diagnosed on the basis of history, clinical examinations and investigations. Inclusion criteria covered both male and female patients with CKD with age > 18 years. Patients with fever and unstable hemodynamic condition, having nephrotoxic drugs in the previous two weeks and patient undergone IV contrast X-ray were excluded from the study. After taking consent from the patient detailed clinical history and relevant data were collected in a preformed data sheet for each patient and different samples were sent to Bio-Chemistry, Microbiology, pathology and Radiology laboratories of Dhaka Medical College Hospital for relevant investigations. Participants were categorized by BMI as per WHO criteria into normal (BMI 18.5-24.9), underweight (>18.5), over weight (25.0-29.9), obese (30-39.9), and morbid obese (≥40.00). Participants were considered to have diabetes mellitus if previously they had been recognized by the doctor as having DM or any documents in favor of DM or they reported taking insulin or oral ant

diabetic drug or random plasma glucose ≥ 11.1 mmol/L with symptom. Hypertension was defined as systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg or use of medication for hypertension irrespective of the blood pressure¹³. A random urine sample of MSU (midstream urine) had been collected from each participant using a clean catch technique and sterile container. Urinary excretion of protein and sugar was detected by multisticks named “Uripath 5” made in the UK¹³. Serum creatinine was measured by alkaline picrate method (Jaffe kinetic assay), which was not standardized by IDMS. Serum creatinine was determined as μmol/L and converted to mg/dl by conversion factor 88.4. CCR (creatinine clearance rate) and estimated GFR (glomerular filtration rate) were calculated from serum creatinine (mg/dL) by using Cockcroft-Gault and MDRD (modification of diet in renal disease) equations¹³. Age, occupation, marital status and address were recorded as per statement of the participants at the time of interview. Weight was taken with light cloths without shoes by an appropriately calibrated weight measuring scale placed on a flat surface. Height was measured without shoes in erect posture on a flat surface placing the heels, buttock, scapulae and occiput touching the wall on the back while extending great toes and gazing horizontally forward to a point on the opposite wall. Blood pressure (B.P.) was measured after 5 minutes rest, being relaxed in chair with a support on the back keeping bared arm on a table at a heart level. A conventional sphygmomanometer was used ensuring 80% of the arm covered by bladder. Systolic BP was based on 1st Korotkoff sound and diastolic BP based on 5th Korotkoff sound. The averages of the two readings separated by 2 minutes were taken for analysis according to the criteria mentioned.

Staging of CKD as per K/DOQI guideline

Stage	Description	GFR (ml/min/1.73m ²)
1	Kidney damage with normal or increased GFR	≥90
2	Kidney damage with slightly decreased GFR	60-89
3	Moderate decreased GFR	30-59
4	Severely decreased GFR	15-29
5	Kidney failure	<15 [or dialysis]

RESULTS

Table-I. Shows that among the participants 84 (67.2%) had family history of hypertension and 41 (32.8%) had not. Patients with CKD had higher family history of hypertension.

Table I. Distribution of participants by family history of hypertension

F/H of Hypertension	Frequency n%	Percentage n%
Yes	84	67.20
No	41	32.80
Total	125	100

Table-II. Shows that it was to be found that male and female participants suffered more in between 51 to 60 years of age. Male and female suffered more or less equally before 30 years of age

Table II: Age and sex distribution of the participants

Age group	Male n%	Female n%	Total n%
< 30 years	2 (2.04)	01 (3.70)	03 (2.40)
31 - 40 years	09 (9.18)	02 (7.41)	11 (8.80)
41 - 50 years	27 (27.55)	06 (22.22)	33 (26.4)
51 - 60 years	41 (41.83)	13 (48.15)	54 (43.20)
> 60 years	19 (19.39)	05 (18.52)	24 (19.2)
Total	98 (100)	27 (100)	125 (100)

Table-III Shows that in all age group, male suffered more than female. Among 125 participants, CKD was due to glomerulonephritis in 44 (44.89%) participants in male and 11 (40.74%) in female. CKD was due to DM in 31 (31.63%) male participants & 9 (33.33%) female participants. CKD was due to HTN in 13 (13.26%) male participants and 3 (11.11%) female participants. CKD was due to Drugs in 4 (4.08%) male participants and 2 (7.4%)

female participants CKD was due to PKD in 3 (3.06%) male participants and 1 (3.7%) female participants

Table III: History of CKD patients (n=125)

Causes of CKD	Male		Female	
	Frequency n %	Percentage n %	Frequency n %	Percentage n %
GN	44	44.89	11	40.74
DM	31	31.63	9	33.33
HTN	13	13.26	3	11.11
Drugs	4	4.08	2	7.40
PKD	3	3.06	1	3.7
Others	3	3.06	1	3.7
Total	98	100	27	100

Table-IV. Shows tht among the study population, male participants suffered more than female in all age groups Out of 125 study population, creatinine clearance rate of 63.2% subjects were between 30-59.9 ml/min, 25.6% subjects were between 15-29.9 ml/min, 7.2% subjects were between 60-89.9 ml/min and 4% <15 ml/min.

Table IV: Stages of CKD of the study population (n=125)

Ccr (ml/min)	CKD stage	Frequency	Percentage
15	5	5	4
15 - 29.9	4	32	25.6
30 - 59.9	3	79	63.2
60 - 89.9	2	9	7.2
> 90	1	0	0

Table-V Shows that majority of the participants (63.2%) were in stage 3, followed by stage 4 (25.6%). 7 (7.2%) patients were in stage 2 and 5 (4%) were stage 5. No patient was in stage 1

Table V: Comorbidities of study population

Stages of CKD	Age (Years) Mean (±SD)	RBS (mg/dl) Mean (±SD)	Creatinine (mg/dl) Mean (±SD)	Ccr (ml/min) Mean (±SD)
Stage- 2 (n=9)	39.78±14.01	102.91±18.29	1.98 ± 0.22	64.78 ± 4.32
Stage- 3 (n=79)	49.44± 9.35	103.21±13.13	2.22 ± 0.52	40.31 ± 6.5
Stage- 4 (n=32)	50.28±11.02	123.99±49.15	4.79 ± 1.01	23.74 ± 2.74
Stage- 5 (n=5)	53.2±24.37	119.39±39.21	8.66 ± 1.47	10.63 ± 2.51

DISCUSSION

The present study, cross sectional in design, was done to observe various risk factors like age, gender, and socio-economic status, family history of kidney disease, hypertension and diabetes in chronic kidney disease subjects. Related medical history & clinical information of the subjects were taken by questionnaires from all the individuals included in this study. Gender was also confirmed as a key predictor of CKD in a similarly large meta-analysis of 68 studies involving 11,345 patients with non-diabetic CKD. This analysis found that men experienced a more rapid decline in renal function and worse outcomes than women. As we live in developing country like Bangladesh, most of the people are within low socioeconomic status and their GDP is 1284 US Dollar/year (Bangladesh Bureau of Statistics, 2015). Bangladesh Bureau of Statistics (2015) stated that monthly income <7000 TK. considered to be low socioeconomic status, 7000-12000 TK. considered to be middle socioeconomic status and > 12,000 Tk. considered to be upper socioeconomic status. In our study, most of participants (73.8%) were in poor socioeconomic status. Khan MIH (2006) showed that 54.2% of sufferer were from low socioeconomic condition. This finding is consistent with our finding. Regarding the underlying causes of CKD, diabetes mellitus (DM) is the most common cause followed by glomerulonephritis (GN) and hypertension (HTN) in developed countries (Simon, et al., 2006) But in our country glomerulonephritis (GN) is the most common cause of CKD (40%) followed by diabetes mellitus (DM) and hypertension (HTN) (Rashid, HU, 2007). Glomerulonephritis was diagnosed by history of swelling of the body, history of abnormalities of urine volume and or colour (e.g. Haematuria) and abnormal finding in urine routine examination (Proteinuria, RBC, WBC casts). Diabetic Kidney Disease (DKD) - was diagnosed by history of long duration diabetes (>10-15years), presence of other target organ damage e.g. diabetic retinopathy, peripheral neuropathy and proteinuria.¹¹ CKD due to hypertensive nephropathy- was diagnosed by history of long duration (>10 years) of uncontrolled hypertension or previous history of accelerated hypertension, onset of hypertension before proteinuria and presence of other target organ damage e.g. hypertensive retinopathy, LVH, proteinuria.¹¹ In our study, GN was also the cause of CKD in majority patients (44%). Other causes of CKD among the study population was DM (32%), HTN (12.8%), Drugs (4.8%), PKD (2.4%) and others (2.4%). In our study population,

stratification of CKD was done by measured estimated GFR (e-GFR) by Cock Croft -Gault formula based on serum creatinine. Mean creatinine clearance was 35.09 (± 12.4) ml/min, which was calculated by Cock Croft-Gault formula. Among 125 participants of CKD, most of the participants were in stage-3 which was about 63.2%, 7.2% were in stage-2, 25.6% were in stage-4 and 4% were stage-5. In Bangladesh, Huda, was conducted a study in slum areas of Dhaka to find out incidence of CKD which about 16% and most of them were in stage-3 which was about 11%.¹² Another study conducted by Muqueet, in Savar, Dhaka showed that prevalence rate of CKD in rural population was 17.4% and most of thm were in stage-3 which was about 13.1%.¹³ Coresh et al. showed in their study on prevalence of CKD and decrease kidney function in the adult population that 11% population had CKD and most of the population was in stage-3 which is similar to our finding.¹⁴ In our study we looked for assessment of risk factors like smoking, socioeconomic status, hypertension, drug induced nephropathy and diabetes mellitus with CKD. Type 2 diabetes is one of the fastest growing epidemics worldwide. The no. of individuals diagnosed with type 2 diabetes was estimated at 124 million in 1997, a number expected to reach 221 million in 2010. Significantly the presence of DM has a considerable impact on the progression of CKD. Nephropathy, a major complication of DM associated with poor glycemic control occurs in approximately one third of type 2 diabetic patients and is the single most important cause of ESRD in both the US and Europe. For example, approximately 24% of all patients in Europe beginning dialysis had diabetes in 1999. However, there is little awareness of the risk of CKD development and progression associated with DM. Smoking, a well-known risk factor for many diseases, was recently proven to play an important role in renal disease. Studies showed that, cigarette smoking is a risk factor for the development and progression of CKD. Many studies indicate that, the deleterious effects of smoking on renal function is not merely restricted to essential hypertension and diabetic nephropathy. Some of those studies found that, smoking is an independent predictor of micro albuminuria in healthy patients with primary hypertension. It is well known that, urinary albumin is a sensitive marker of glomerular injury. The fact that, there is a relationship between smoking and albuminuria indicates direct or indirect renal damage induced by smoking. The kidneys susceptible to damage by drugs because it is the root of excretion of many water soluble compounds including drugs and their metabolites. Some may reach

high concentrations in the renal cortex as a result of proximal tubular transport mechanisms. Others are concentrated in the medulla by the operation of the counter current system. Impairment of renal function may develop in patients on NSAID since prostaglandin play an important role in regulation renal blood flow. ACE inhibitors abolish the compensatory angiotensin-II mediated vasoconstriction of the glomerular efferent arteriole. In our study, out of 125 participants CKD due to drug induced nephropathy was 4.8% where male 4.08% & female 7.40%. Most of the participants suffered from kidney disease due to prolonged use of NSAIDs. In our study, 86.4% participants had hypertension among 125 participants of CKD. CKD was due to hypertension in 13 (13.26%) male participants and 3 (11.11%) female participants. The relationship between the kidney disease and hypertension is interesting because the kidney can be affected by the hypertensive process or it can also cause hypertension. Eighty to ninety percent of patients with chronic kidney disease (CKD) experience hypertension during the course of their disease

CONCLUSIONS

The association between CKD and other risk factors like age, obese and overweight, use of tobacco, diabetes and hypertension was also highly significant. The commonest risk factors for CKD like DM & HTN are also alarmingly high and obviously adding to the existing burden of CKD. Early detection of the risk factors of CKD, early referral to nephrologist, appropriate treatment of hypertension, DM, GN and other risk factors, life style modification with specific emphasis on reduction in salt intake, physical exercise, and abstinence from smoking will retard progression of kidney disease to an advanced stage.

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