Original Article

Chronic Kidney Disease in a Tertiary Care Hospital in Nepal

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Abstract

Introduction: Chronic kidney disease (CKD) is an increasingly recognized major public health problem globally and in Nepal. It has a high prevalence in the population and is associated with high morbidity, mortality and health care costs. Here, we aimed to study the socio-demographic profiles, etiologies of CKD and associated co-morbidities in patients attending a referral hospital.

Methods: We conducted a hospital based, descriptive, observational, cross-sectional study among adult patients with CKD attending Tribhuvan University Teaching Hospital (TUTH), Kathmandu. Patients younger than 16 years and renal allograft recipients were excluded from the study. A diagnosis of CKD was established by the treating nephrologist based on KDIGO 2012 clinical practice guideline. Prior informed consent was taken. Data was collected on clinical features, socio-demographic profiles, major co-morbidities, presumed etiology of CKD and hematological and biochemical parameters of the patients. SPSS version 24 (Chicago, IL, USA) was used for the analysis of data. The study protocol was approved by the Institutional Review Board (IRB) of Institute of Medicine (IOM).

Results: A total of 401 patients with CKD were included in the study. The mean age of the patient was 50.92 years (SD=17.98), male to female ratio was 1.8:1. Among these patients, 86% were Hindu, 24.4% were farmers, 57% were from the Hilly region of Nepal, 51% were active smokers, and 51.6% were alcohol consumers. Chronic glomerulonephritis (CGN) (36.2%; n= 145), diabetes mellitus (31.9%; n= 128) and hypertension (21.7%; n=87) were the three most common identified causes of CKD. Among the biopsy proven CGN patients, IgA nephropathy was the most common cause. In a large proportion of patients (68.3%) cause of CGN was not known. Most of the patients were in CKD stage 5 (27%), and stage 5D (55.8%). Coronary artery disease (CAD) (in 7% patients), heart failure (in 2.7%) and stroke (in 2.2%) were the most common comorbidities. Anemia was prevalent in CKD from stage 3 onwards, the severity increased with increasing stage ($p < 0.001$). Hemodialysis was the predominant mode of renal replacement therapy (RRT) used by 98.2% of CKD 5D patients.

Conclusion: Nepalese patients of CKD are younger; males are more affected than females. CGN, diabetes and hypertension are three most common causes of CKD; IgA nephropathy is the most common cause of biopsy proven CGN leading to CKD. Anemia is common from CKD stage 3 onwards. The most common associated co-morbidity is CAD.

Key words: Chronic kidney disease, CKD; Chronic glomerulonephritis, CGN; Diabetes mellitus, DM; Hypertension; Nepal

Introduction

The term chronic kidney disease (CKD) refers to any disorder that affects the structure and or function of kidney, has been present for at least three months and has implications for health.[1,2] CKD is a major public health problem worldwide and is associated with considerable morbidity and mortality.[3] CKD is a newly recognized public health problem in Nepal as well. [4] The estimated prevalence of CKD is around 10.6% in urban areas of Nepal.[5] A study by International Society of Nephrology's Kidney Disease Data Center (ISN-KDDC) in 12 low and middle income countries reported yet higher prevalence of CKD in the cohorts from Nepal.[6] The overall prevalence of CKD was 20.1 %, the prevalence of estimated glomerular filtration rate

(eGFR) < 60 ml/min/1.73 m^2 was 16.2% and that of albumin creatinine ratio (ACR) > 30 mg/gm was 5.8%. The awareness level was also low in both general and high risk populations (6 % versus 10%).[6] In another study, the number needed to screen to detect a new case with eGFR < 60ml/min/1.73 m^2 was 2.6.[7]

The epidemiology of CKD is expected to differ between developed and developing countries. In addition to non-communicable diseases, communicable diseases especially infections and toxic exposures are thought to be common causes of CKD in developing countries.[8] In Nepal, data on different aspects of CKD are still few and inadequate. Information about the population affected, their causes / risk factors and co-morbidities should considerably help the health care providers, planners, and policy makers to identify key strategies for prevention and management of CKD. In the present study, we aimed to study the epidemiology, socio-demographic profiles, etiology, and associated co-morbidities of CKD patients at a tertiary care hospital in Nepal.

Methods

This study was a hospital based observational, descriptive, cross-sectional study, conducted at Tribhuwan University Teaching Hospital (TUTH) in Nepal over a period of 12 months from June 2017 to May 2018. TUTH is a 700 bedded tertiary care hospital located in Kathmandu and provides multi-specialty health care services to patients from all 77 districts of Nepal. A prior approval was obtained from the Institutional review board (IRB) of Institute of Medicine (IOM). Written informed consent was taken from all the participants (or their primary caretakers wherever applicable).

CKD was defined based on KDIGO 2012 clinical practice guideline [2] for the evaluation and management of chronic kidney disease as either of the following present for ≥ three months: (a) Markers of kidney damage (one or more): albuminuria (AER >30 mg/24 hours; ACR >30 mg/g [>3 mg/mmol]), urine sediment abnormalities, electrolyte and other abnormalities due to tubular disorders, abnormalities detected by histology, structural abnormalities detected by imaging, history of kidney transplantation or (b) Decreased GFR <60 ml/min/1.73 m^2 (GFR categories G3a–G5). Consecutive patients attending the nephrology outpatient department or admitted to the Nephrology or Internal Medicine wards of TUTH who met the criteria for CKD were considered for enrollment. Glomerular filtration rate (GFR) was calculated using CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation for eGFR,[9] then categorized into different stages. We included a total of 401 patients aged 16 years and above, with CKD stages 3, 4, 5, and 5D (patients under dialysis) by a method of non-probability sampling. Patients were excluded if they denied consent, were younger than 16 years or were renal transplant recipients. Data were collected on the socio-demographic profiles, presumed etiology of CKD, major associated co-morbidities, and hematological and biochemical parameters and filled in the predesigned proforma. In the data analysis, continuous variables were expressed as mean ± standard deviation (SD) and categorical variables were expressed as frequency and percentage. Analysis of normal variance (ANOVA) test was employed to compare the mean laboratory parameters amongst different stages of CKD. A p-value < 0.05 was considered statistically significant. The data entry and all statistical analysis were performed using SPSS version 24 (Chicago, IL, USA).

Results

Demographic characteristics of the patients

A total of 401 patients were included in the study. The demographic characteristic of the study population is presented in Table 1. The mean age of the patient in the study was 50.92 years (SD=17.98). On subgroup analysis based on stages of CKD, it was observed that the mean age of patient in CKD stage 3, 4, 5, and 5D were 51 years, 58 years, 58 years, and 46 years respectively. There were 260 (64.8%) male and 141 (35.2%) female patients; the male to female ratio being 1.8:1. Gender distribution of patients in different stages of CKD were, CKD stage 3 (n=18): male 67% and female 33%; CKD stage 4 (n=51): male 63% and female 37%; CKD stage 5 (n=108): male 56 % and female 44 %; and CKD stage 5D (n=224): male 69 % and female 31 %. Gender distribution of patient in different stages of CKD is represented in Figure 1.

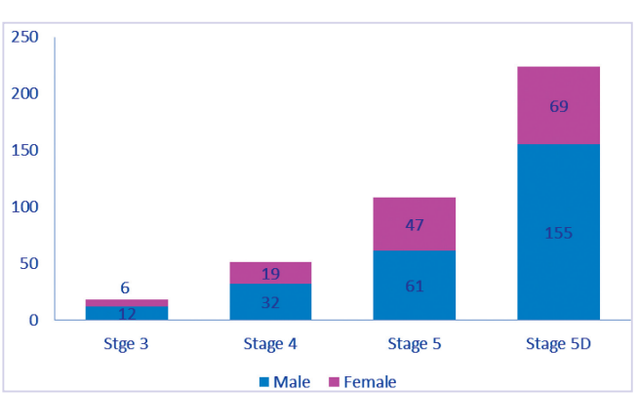

Figure 1: Gender of patients in different stages of CKD (n=401)

Among 401 patients, 86% were Hindu, 24.4% were farmers, 57.1% were from Hilly region of Nepal, 35% were illiterate, 51% were current smoker, and 51.6% were consuming alcohol, and 81% were married. Most of the patients (39.6%) were Brahmin or Chhetri caste under the traditional caste system. Annual family income was less than 500,000 NPR (1 $ is equivalent to around 110 NPR) in the majority of the patients (72.5%).

Table 1: Demographic characteristics of the study population (n=401)

Characteristics		Frequency	Percentage
Sex	Male	260	64.8
	Female	141	35.2
Religion	Hindu	345	86
	Buddhist	48	12
	Muslim	4	1
	Christian	4	1
Occupation	Farmer	98	24.4
	Housewife	89	22.2
	Businessman	45	11.2
	Government employee	28	7
	Dependent	81	20.2
	Migrant worker	26	6.5
	Carpenter	6	1.5
	Student	20	5
	Driver	7	1.7
	Teacher	1	0.2
Address	Terai	130	32.4
	Hilly	229	57.1
	Himalayan	42	10.5
Ethnicity	Brahmin and Chhetri	159	39.6
	Madhesi	40	10
	Dalit	30	7.5
	Newar	70	17.5
	Janjati	102	25.4
Education	Illiterate	140	35
	Primary level	129	30
	Secondary level	100	25
	Higher secondary or university	40	10
Family income per annum	Less than 1 lakh	120	30
	1 to 5 lakh	171	42.5
	5 to 10 lakh	60	15
	More than 10 lakh	50	12.5
Marital status	Married	325	81
	Unmarried	48	12
	Divorced	16	4
	Widow or widower	12	3
Smoking	Yes	204	51
	No	197	49
Alcohol consumption	Yes	207	51.6
	No	194	48.4

Etiology of CKD

We found that the three most common causes of CKD in the studied population were chronic glomerulonephritis (36.2%), diabetes mellitus (31.9%), and hypertension (21.7%) followed by other causes (Table 2).

Table 2: Etiology of CKD in study population (n=401)

Etiology	Frequency	Percentage
Chronic glomerulonephritis	145	36.2
Diabetes mellitus	128	31.9
Hypertension	87	21.7
Obstructive nephropathy	23	5.7
NSAIDS	3	0.7
Renal amyloidosis	2	0.5
ADPKD	8	2
Multiple myeloma	1	0.2
Recurrent UTI	1	0.2
Others	3	0.7
Total	**401**	**100**

NSAIDS, Non-steroidal anti-inflammatory drugs; ADPKD, Autosomal dominant polycystic kidney disease; UTI, Urinary tract infection

Only 31.7% patients with presumed diagnosis of chronic glomerulonephritis (CGN) had biopsy proven diagnosis. In the majority of patients with presumed diagnosis of CGN (68.3%), the original disease that led to CKD was not known. Among the biopsy proven CGN patients, IgA nephropathy was the most common cause, followed by ANCA (anti neutrophil cytoplasmic antibody) associated vasculitis and lupus nephritis (Table 3).

Table 3: Etiology of chronic glomerulonephritis (CGN) in study population (n=145)

Etiology	Frequency	Percentage
Unknown	99	68.3
IgA nephropathy	19	13.1
Lupus nephritis	8	5.5
Focal segmental glomerulosclerosis (FSGS)	2	1.4
Membranoproliferative glomerulonephritis (MPGN)	1	0.7
Minimal change disease (MCD)	1	0.7
Anti GBM disease	2	1.4
ANCA associated vasculitis	9	6.2
Non proliferative glomerulonephritis	1	0.7
Systemic sclerosis	1	0.7
Membranous nephropathy	2	1.4
Total	**145**	**100.0**

Migrant workers and CKD

We observed that, out of 401 CKD patients, 26 (6.5%) patients were migrant workers who had been to foreign countries for work and returned home, the foreign countries were mostly Gulf countries. Most of the patients were male (male, 96.2%; female, 3.8%). The mean age in this group of patients was 36.5 years (SD=12). Out of 26 patients, 18 (69.2%) had presumed diagnosis of CGN as the cause of CKD; however, only 27.8 % of the presumed CGN cases (8 out of 26) had biopsy proven diagnosis, in which IgA nephropathy was the most common (3 out of 8). The etiology of CKD in migrant worker is shown in Table 4.

Table 4: Etiology of CKD in migrant worker (n=26)

Etiology	Frequency	Percentage
Chronic glomerulonephritis	18	69.2
Hypertension	5	19.2
Diabetes	2	7.7
ADPKD	1	3.8
Total	**26**	**100**

ADPKD, Autosomal dominant polycystic kidney disease

Distribution of patients based on stages of CKD

Table 5 shows the distribution of patients based on stages of CKD. Most of the patients were in CKD stage 5 (108, 27%), and stage 5D (224, 55.8%). Amongst the patients under maintenance dialysis, 98.2% (n=220) were under maintenance hemodialysis (MHD) and 1.8% (n=4) were under peritoneal dialysis (PD). Among the patients who were under MHD, 78.8% (n=172) patients were under MHD for less than 6 month, 10.5% (n=23) patients were under MHD for 6 to 12 month and 11.4% (n=25) patients were under MHD for more than 12 month. For these patients (n=220), 94.1% (n=207), 4.5% (n=10) and 1.4% (n=3) were under MHD two, three and one session per week respectively.

Table 5: Distribution of patients based on stages of CKD (n=401)

CKD stage	Frequency	Percentage
Stage 3	18	4.5
Stage 4	51	12.7
Stage 5	108	27
Stage 5D	224	55.8
Total	**401**	**100**

CKD and co-morbidities

The various co-morbidities associated with CKD were coronary artery disease (CAD) in 28 patients (7%), heart failure in 11 (2.7%), stroke in 9 (2.2%), chronic obstructive pulmonary disease in 8 (2%) and chronic liver disease in 5 patients (1.2%).

Analysis of laboratory parameters

We noted that anemia was present throughout CKD stages 3, 4, 5, and 5D. The severity of anemia increased significantly ($p < 0.05$) with increasing CKD stage. We also observed that, intact parathyroid hormone (iPTH) and phosphorus increased significantly ($p < 0.05$) with increasing CKD stage. Though corrected calcium, and vitamin D levels decreased with increasing CKD stage, the difference did not reach statistical significance ($p > 0.05$). The mean vitamin D value was in insufficient range in CKD stages 4, 5 and 5 D (Table 6).

Table 6: Comparison of laboratory parameters of the study population (n=401)

Parameters	CKD stage	Mean	SD	p-value
Hemoglobin	Stage 3	9.98	2.00	< 0.001
	Stage 4	8.97	2.24	
	Stage 5	8.79	2.10	
	Stage 5D	8.23	1.72	
iPTH	Stage 3	98.47	63.68	0.002
	Stage 4	223.05	355.42	
	Stage 5	330.61	372.36	
	Stage 5D	356.98	324.81	
Albumin	Stage 3	29.55	7.58	0.005
	Stage 4	31.56	7.07	
	Stage 5	33.70	5.73	
	Stage 5D	33.61	5.33	
Corrected calcium	Stage 3	2.00	0.23	0.358
	Stage 4	1.98	0.21	
	Stage 5	1.92	0.30	
	Stage 5D	1.90	0.29	
Phosphorus	Stage 3	3.14	0.77	< 0.001
	Stage 4	3.82	1.39	
	Stage 5	4.89	1.82	
	Stage 5D	4.82	1.96	
Vitamin D	Stage 3	30.98	14.85	0.876
	Stage 4	27.41	12.79	
	Stage 5	27.83	16.74	
	Stage 5D	27.86	16.83	

Discussion

CKD, with its associated morbidity and mortality, has now been recognized as a major public health problem globally.[3] However, the demography and causes of CKD differ between different countries.[8] We found that the affected population was young (mean age, 50.9 years; SD, 17.98 years). Similar results were found in studies from Africa[10], India[11,12], and Saudi Arabia.[13] However, studies from developed countries showed patients of CKD were relatively older and the average age was above 60 years.[14] The discrepancy could be explained by the fact that in Western countries there is greater access to health care, preventive means, early detection & management of patients at risk of developing CKD and better longevity. It is likely that diseases like diabetes and hypertension are earlier detected and better managed in the West along with timely detection and treatment of diseases like glomerulonephritis. We observed that male were affected more compared to female irrespective of stages of CKD (Table 1), the overall male to female ratio being 1.8:1, and this finding was consistent with other studies.[11,14] It was surprising that the difference in male versus female was more marked in CKD 3 and CKD 5D; we hypothesize that this difference is due to paternalistic and male dominated Nepalese society where female patients seek health care relatively later and significantly fewer female patients have access to renal replacement therapy.[15] We observed that more than 50% of the patients were coming from the Hilly regions of Nepal and only 10% were Madhesis. This underrepresentation of Nepalese Madhesis could be because of their poor access to health care as well as the vicinity to Northern India where many of them traditionally seek health care.

In the present study, we found that 51% of the individuals were current smoker, and 51.6% of the individuals were consuming alcohol on regular basis. This finding of the study is collaborated by study of Haroun et al.[16], who reported that current cigarette smoking was significantly associated with risk of CKD in both men and women (hazard ratio in women 2.9 [1.7 to 5.0] and in men 2.4 [1.5 to 4.0]). Menon et al.[17] illustrated that 52% of CKD patients had history of excessive alcohol consumption, which is consistent with our study. Campaigns on smoking cessation and promotion of healthy lifestyles could help in curbing the increasing epidemics of non communicable diseases including CKD.

We observed that the majority of the patients were involved in agriculture (24.4%), were housewives (22.2%) or dependent (20.2%); only a quarter of the studied patients were in some active professions. This is reflective of employment pattern in contemporary Nepalese society. We also discovered that 6.5% of CKD patients had been migrant workers in foreign countries. This group of patients was relatively young (mean age, 36.5 years; SD, 12 years), and in the vast majority of them the cause of CKD was presumed chronic glomerulonephritis (69.2%). This could be because the migrant workers have poor access to the health care services in foreign country, lack health related awareness, and have repeated chronic untreated infections; the role of yet unidentified environmental factors leading to CKD in workers in the Gulf countries remains to be investigated.

Data regarding the financial impact of CKD on patients in Nepal are limited. In a study done at National Kidney Center (NKC), Nepal, it was shown that about 37% of CKD stage 5 patients had to sell their property for the treatment.[18] On an average, one patient spent Rs. 2,40,000 per year (1 $ = 110 NPR) in dialysis. Similarly, medication cost was Rs.1,80,000 per annum and the cost of transplantation was Rs.5,00,000 to 10,00,000.[18] However, recently, the dialysis service has been provided free of cost by Government of Nepal in the government recognized health care institutions across the country.[19] In our study we found that, the majority of the patients (72.5%) had annual family income less than 500,000 NPR (1 $ is equivalent to around 108 NPR), and 35% were illiterate. This highlights the challenges and economic burden imposed by CKD to the patients, society and nation as a whole. Poverty, lack of regular health check up, and health awareness could be contributing factors for CKD.[11]

In our study, we discovered that the most common etiology of CKD was CGN (36.2%). Only 31.7% patients with presumed diagnosis of CGN had biopsy proven diagnosis. Among the biopsy proven CGN patients, IgA nephropathy appeared to be most common, present in 13.1% patients. In a large proportion of patient (68.3%) cause of CGN was not known. This finding is in contrast with study conducted in developed nations where diabetes mellitus is the commonest cause of CKD. [20] The high prevalence of CKD secondary to CGN in developing countries could be explained by repeated infections leading to chronic inflammation. The health seeking behavior of Nepalese patients, poor socioeconomic status, absence of health insurance and poor access to reliable health care could have all led to late presentation of treatable diseases and missed window of opportunity to prevent CKD. Diabetes mellitus and hypertension were the second and third most common causes of CKD in our study population, this reflects the increasing impact of these non communicable diseases in developing country like Nepal as well.

Most of the patients were in CKD stage 5 (27%), and stage 5D (55.8%). Out of 224 patients who were under maintenance dialysis, 98.2% (n=220) were under Maintenance Hemodialysis (MHD) and 1.8% (n=4) were under peritoneal dialysis (PD). This limited use of PD as the modality of renal replacement therapy could be multi-factorial, namely inadequate time given by health professionals in counseling on PD, emergency start of HD and continuation of the same, poor hygienic practices of many patients, lack of home support for PD, poor access to clean water, the additional costs of PD fluid (though this is provided free of cost of late) etc.[21,22] If PD could be made more popular,this could address the issue to need to travel long distances or migrate just to get HD.

End-stage kidney disease substantially increases the risks of death, and cardiovascular disease.[23] In our study, we found out of 401 patients, 28 patients (7%) had CAD, and 11 patients (2.7%) had heart failure. This relatively lower prevalence of cardiovascular co-morbidities could be explained by younger age of the patients and CGN being the most common cause rather than diabetes mellitus.

Early stages of CKD are usually asymptomatic and symptoms are observed in late stages due to complications of decreased kidney function. Major complications are related to cardiovascular disease, anemia, infections, neuropathy and abnormalities of mineral and bone metabolism.[24] We found that anemia was universal to CKD stage 3, 4, 5, and 5D. The severity of anemia increased significantly ($p < 0.05$) with increasing CKD stage. Presence of anemia in CKD stage 3 could be reflective of the population prevalence of anemia in Nepal and the poor nutrition of Nepalese in general,[25-27] rather than any CKD specific factors. We also observed that, iPTH and phosphorus increased significantly ($p < 0.05$) with increasing CKD stage (Table 6).This finding is consistent with several other observations and is explained by CKD physiology.[28] Though corrected calcium, and vitamin D decreased

with increasing CKD stage, these parameters didn't reach statistical significance.

We recognize that being a relatively small, observational, cross sectional hospital based study, our findings may not be generalizable to the whole CKD patients from Nepal. However, we believe that the inferences drawn from meticulous interpretation of data from this nationally representative cohort in a referral hospital would partially fill the gaps in data on CKD in Nepal and help health care providers and policy makers in identifying priority intervention areas. The findings of this study need to be validated from large scale multi-center and population based studies.

Conclusion

The mean age of the Nepalese patients with CKD is younger compared to their Western counterparts. Males are almost twice as affected as females, at least in hospital based study. CGN is still the most common cause of CKD in Nepal, followed by diabetes and hypertension. IgA nephropathy is the most common biopsy proven cause of CGN leading to CKD. Anemia is more common in Nepalese CKD patients and is prevalent from stage 3 onwards. Hemodialyis is the predominant mode of renal replacement therapy for end stage kidney disease in Nepal.

Conflict of interest: None declared.

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