International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 9; Issue 02 (A); February 2020; Page No.21163-21169
DOI: http://dx.doi.org/10.24327/ijcar.2020.21169.4151

Research Article

DEMOGRAPHIC AND CLINICAL PROFILE OF CHRONIC KIDNEY DISEASE IN TERTIARY CARE CENTER

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A R T I C L E I N F O

Article History:
Received 4th November, 2019
Received in revised form 25th December, 2019
Accepted 18th January, 2019
Published online 28th February, 2020

Key words:

Most common clinical presentation of CKD was volume overload followed by shortness of breath, oliguria, and gastritis.

A B S T R A C T

Background: Chronic kidney disease (CKD) is major public health problem in Nepal. Common causes of end-stage renal disease (ESRD) in Nepal are Diabetes Mellitus (DM), Chronic Glomerulonephritis and Hypertension (HTN). Common clinical features of CKD are volume overload, shortness of breath, oliguria, proteinuria and elevated blood pressure. So if we detect all these features early, we can extend the quality life of CKD patients. **Objectives:** Primary objective-To study demographic profile of chronic kidney disease in tertiary care center. Secondary objective. To study clinical presentations in different stages of CKD. **Methods:** This study was a prospective observational study, done in Tribhuvan University Teaching Hospital (TUTH) from September 2017 to September 2018. Patients attending medical OPDs or admitted in medical wards and other wards of TUTH during this period, who were more than 18 years and diagnosed as having Chronic Kidney disease of stage III to IV were enrolled in the study. Patient having Chronic Kidney disease of stage I to II, on maintenance haemodialysis and post- transplantation patients were excluded from the study. A written consent was taken from each patient as per the format of the Institution Review Board. Patients who did not give consent were excluded from the study. Creatinine clearance and stage of CKD for each patient was calculated using Cockcroft-Gault formula once patient`s creatinine level stabilized. Data analysis was done using Statistical Package for Social Sciences (SPSS) software version 25. **Results:** In our study, total number of patients included were 138. Mean age was 48±17.08 years; 69% were male and remaining 31% female; 96% were Hindu, 3% Muslim and 1.4%, Buddhist; 64% were residing in hilly area, 32 % from tarai and remaining 4% from mountains. Most of the cases were of CKD stage V (103, 74.6%), followed by stage IV (23, 16.7%), and stage III (12, 8.7%), respectively. Most common clinical presentation was volume overload (111, 80.43%), followed by shortness of breath (90, 65.2%), oliguria (85, 61.59 %), gastritis (60, 43.47%) and (10, 7.24%) were asymptomatic. In our study, complication encountered in 78, 56.52 % patients which includes metabolic acidosis (45, 57.69%), hyperkalaemia (15, 19.2%), pulmonary oedema (9, 11.53%), uremic encephalopathy (5, 6.4%), uremic pericarditis (4, 5.12%) which were mainly seen CKD stage V(75, 96.15%).Most common aetiology of CKD was CGN (68, 49.3%) followed by DM (38, 27.5%), hypertension (23, 16.7%),ADPKD (3, 2.17%), Obstructive uropathy (5, 3.6%), RAS (1, 0.72%).There was significant and graded association between the stages of CKD and haemoglobin, Calcium, phosphorus, and iPTH (p value <0.05). **Conclusion:** Most common clinical presentation of CKD was volume overload followed by shortness of breath, oliguria, and gastritis.So any patient with these features needed to be evaluated thoroughly to detect presence of renal disease as early as possible to prevent complications and to improve the quality of life. Most common aetiology being chronic glomerulonephritis followed by diabetes mellitus, hypertension, ADPKD, obstructive sssssssssssuropathy, and RAS in decreasing order respectively. Early diagnosis and proper management have important roles in prevention of CKD progression to end-stage renal disease (ESRD). For this purpose, determining the aetiology of CKD is helpful.

INTRODUCTION

Prevalence of CKD is estimated to be 8–16% worldwide.[1] Chronic kidney disease (CKD) is a major public health problem in Nepal. It is estimated that the prevalence of CKD is around 10.6% in urban areas of Nepal and most common causes of End Stage Renal Disease (ESRD) in Nepal are believed to be Diabetes Mellitus, Glomerulonephritis and Hypertension.[1] In a study done at Chittagong Medical College Hospital in Bangladesh in January 04 - December 05, Chronic Glomerulonephritis was the leading cause of CKD, found in 41.8%(48) of patients, followed by Diabetes Mellitus 26.1% (30), Hypertension 13% (15), Obstructive Uropathy 13% (15) and Others 6.1%.[2] It is estimated around 2.6 million Nepalese people suffer from kidney disease and kidney disease increasing in Nepal by more than 10000 people per year.[3] In Bangladesh there are about 20 million people suffer from CKD and about 20 thousand CKD patients are becoming ESRD per year.[2]Demographic status of the patients undergoing dialysis at national kidney center showed mean age of the patients to be 47 years with almost half of the patient (46%) from 41-60

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years age group.[4] Among the patients 65 % male, 85% married, 80% were literate, 57% were past smoker and 75% were drinker and 59 % were from Kathmandu valley.[4]The commonest clinical features were oedema (88.7%), proteinuria (86.7%), and elevated Blood Pressure (85.7%). About 68% had oliguria and pallor was present in 83.2 %.[5]

However, the burden is shown to be as high as 20 % in different studies.[4] Mortality rates in population with CKD remain above 20 percent per year even with the use of dialysis, with more than half of the deaths related to cardiovascular disease.[5] This study will elucidate the problem of so much significance with a huge impact on health & quality of life of people. Aim of our study is to find out demographic, clinical profile and aetiology of chronic kidney stage at our center.

Background

Chronic kidney disease (CKD) is a worldwide public health problem, with adverse outcomes of kidney failure, cardiovascular disease (CVD), and premature death.[6] Data from the United States suggest that for every patient with end-stage renal disease (ESRD), there are more than 200 with overt chronic kidney disease (Stage III or IV) and almost 5000 with covert disease (stage I or II). Unfortunately, this type of information is lacking for most other countries, so international comparisons are based on ESRD, rather than chronic kidney disease.[7] Prevalence of CKD is estimated to be 8–16% worldwide.[1] Evidence suggests that hypertension and diabetes are the two major causes of kidney disease worldwide[8, 9] with diabetes mellitus being the most common cause of chronic kidney disease the risk of which are highest in the poorest populations.[1] There is a wide variation among communities in the incidence of ESRD and this variation mirrors that of the prevalence of diabetes, obesity, and hypertension of the respective community.[10] This observation has worrisome implications for the future incidence of ESRD in the developing world, where the prevalence of diabetes is expected to double by 2030. It is estimated that by that year, more than 70 percent of patients with ESRD will be residents of developing countries.[7]

Status of CKD in developing countries and South Asia

High and increasing rates of risk factors, such as obesity, smoking, and inactivity, suggest that the prevalence of no communicable disease will grow most rapidly in low- and middle-income nations during the coming decades.[11, 12] multiple studies have shown primary glomerulonephritis to be the most common cause of CKD in the developing world. The incidence of various types of primary glomerulonephritis (GN) has been reported to vary between 0.2 and 2.5/100,000/year.[13] In most countries, the basis this data is the incidence on kidney biopsy performed within the period of evaluation in a given population. Diabetes causes 9.1 to 29.9 percent of the cases of ESRD in various developing countries, and hypertension leads to 13 to 21 percent of the cases. Other important causes include urolithiasis with subsequent obstruction and infection, long-term drug abuse, and possibly environmental pollution.[7] South Asia has a high incidence of chronic kidney disease.[14] However; the awareness of CKD in the general population is very low. Bogdan Ene-Iordache and colleagues (May, 2016) reported findings from 75,058 people from 12 countries, including three south Asian countries (Nepal, India and Bangladesh), in which only 6% of the general population and 10% of high-risk populations surveyed were aware of their CKD status.[15]

Current Chronic Kidney Disease (CKD) nomenclature used by KIDGO

The definition and classification for chronic kidney disease was proposed by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF- KDOQI) in 2002 and endorsed by the Kidney Disease: Improving Global Outcomes (KDIGO) in 2004.[9]

In 2002, the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) introduced a conceptual model for the definition and classification of chronic kidney disease.[16] In 2004, Kidney Disease: Improving Global Outcomes (KDIGO) endorsed this framework with minimal modifications6which defined CKD on the basis of presence of kidney damage or glomerular filtration rate (GFR <60 ml/min per 1.73 m2) for ≥3 months, irrespective of cause, and was classified into five stages based on the level of GFR. KDIGO in 2009 October initiated a collaborative meta-analysis and sponsored a Controversies Conference to examine the relationship of estimated glomerular filtration rate (GFR) and albuminuria to mortality and kidney outcomes. This meta-analysis found out that, in addition to previous belief, micro albuminuria at any level of eGFR is considered to represent CKD, and this micro albuminuria is thought to occur as the result of hyper filtration in the kidneys due to diabetes and hypertension- related changes in the glomeruli.[17]

On the basis of analyses[18] in 45 cohorts that included 1,555,332 participants from general, high-risk, and kidney disease populations, it was agreed to retain the current definition for chronic kidney disease of a GFR <60 ml/min per 1.73 m^2 or a urinary albumin-to-creatinine ratio >30 mg/g, and to modify the classification by: Adding albuminuria stage, Subdivision of Stage III and Emphasizing clinical diagnosis[19].According to KIDGO 2017 guideline, CKD is defined as abnormalities of kidney structure or function, present for > 3 months, with implications for health. CKD is classified based on cause, GFR category (G1–G5), and albuminuria category (A1–A3), abbreviated as CGA.[20]

Creatinine and eGFR

Creatinine is a breakdown product of creatinine phosphate in muscle, and is usually produced at a fairly constant rate by the body (depending on muscle mass) in liver. For the adult male, the normal range is 0.6-1.2 mg/dl (53-106 μmol/L) by the kinetic or enzymatic method OR 8 to 1.5 mg/dl (70-133 μmol/L) by the older manual Jaffé reaction. For the adult female, who generally have a lower muscle mass, the normal range is 0.5-1.1 mg/dl (44-97 μmol/L) by the enzymatic method.[21] Mild-to-moderate elevations in serum creatinine levels are associated with increased rates of death from any cause[23] and from cardiovascular causes[11], and elevated serum creatinine may be an independent predictor of all-cause and of cardiovascular disease mortality.[23] Because serum creatinine is a crude indicator of renal function, and often underestimates renal dysfunction in women and the elderly, calculated measures of eGFR by the Cockroft- Gault equation or by the Modification of Diet in Renal Disease equations, now available on personal digital assistants, are the preferred methods of estimating and reporting renal dysfunction.[24]

Renal Failure and End-Stage Renal Disease

Renal failure is defined as either GFR less than 15 ml/min per 1.73 m^2, which is accompanied in most cases by signs and symptoms of uraemia, or a need to start kidney replacement therapy (dialysis or transplantation). Kidney failure is not synonymous with end-stage renal disease (ESRD). End-stage renal disease is an administrative term in the United States and indicates that a patient is treated with dialysis or transplantation.[19] Following table shows the classification of stages of chronic kidney disease, the prevalence of each stage along with expected management, estimated by using data from NHANES III.[25] Stages I to III are considered to be "early-stage" CKD. People with early stages of the disease are typically asymptomatic, and the diagnosis is made by using laboratory tests or imaging.[26]

Table 1 Expected management by Stages of CKD.

Stage	Description	GFR	Prevalence,%	Action
_	At increased risk	> 60 (with CKD risk factors)	_	Screening; CKD risk reduction
I	Kidney damage with normal or increased GFR	> 90	3.3	Diagnosis and treatment; treatment of comorbid conditions; slowing progression &CVD risk reduction
II	Kidney damage with mild decreased GFR	60-89	3.0	Estimation progression
III	Moderately decreased GFR	30-59	4.3	Evaluating and treating complications
IV	Severely decreased GFR	15-29	0.2	Preparation for RRT
V	Kidney failure	<15 (or dialysis)	0.1	RRT(if features of uremia)

Cardiovascular events in CKD

The connections between chronic kidney disease and cardiovascular disease are numerous [27]. CKD per se is considered to be a coronary artery disease (CAD) equivalent, in fact persons with early stages of CKD are more likely to die of CVDs than progress to end-stage renal disease (ESRD) [28, 29] with mortality rates estimated to be 10–30 times higher in dialysis patients as compared to the healthy population[27, 29]. There are numerous studies to suggest that CKD is an independent risk factor for poor CVD outcomes.

Objectives

Primary Objectives: To study the demographic profile of chronic kidney disease in a tertiary care center. Secondary Objectives: To study the clinical presentations in different stages of CKD

MATERIAL AND METHODS

Study Design: It was a prospective, observational study.

Place of Study: The study was conducted in Maharajgunj Medical Campus, Tribhuvan University Teaching Hospital, Institute of Medicine, Kathmandu, Nepal. TUTH is a tertiary care center that provides comprehensive health care services to patients from all over the country including all social strata and demographic profiles. So data collection will be comprehensive and easier. Duration of Study: Study was done from September 2017 to September 2018. Inclusion Criteria: All adults greater than or equal to 18 years who are diagnosed as CKD stage III-V as per definition. Give written consent. Exclusion Criteria: Patient on maintenance hemodialysis. Post-transplant patient. Patients who did not gave written consent. CKD Stage I and II. Sampling Method: Non-probability sampling was used. Sample size: Considering 10% prevalence of CKD, ratio of End Stage Renal disease other stage of CKD 1:15, the total population to be studied is 20 lakhs. So taking 95% confidence interval and margin of error 5%. Methodology and statistical analysis: Patients attending medical OPDs or admitted in medical wards and other wards of TUTH during the period from September 2017 to September 2018, who were more than 18 years and diagnosed as having Chronic Kidney disease of stage III to V were enrolled in the study. Patient on maintenance haemodialysis and post- transplantation patients were excluded from the study. A written consent was taken from each patient as per the format of the Institution Review Board. Patients who did not give consent were excluded from the study.

Demographic profile of the patients were noted (Sex, age, religion caste occupation address, and contact number), risk factors (hypertension, diabetes,) and presence of other comorbidities (ischemic heart disease, stroke and heart failure) were collected at the start of the study period. Investigations including haemoglobin, creatinine, uric acid, iPTH, calcium, phosphorus, fasting lipid profile was obtained from each patients. Creatinine clearance and stage of CKD for each patient was calculated using Cockcroft-Gault formula once patient's creatinine level stabilized. Data analysis was done using Statistical Package for Social Sciences (SPSS) software version 25.0.

RESULTS

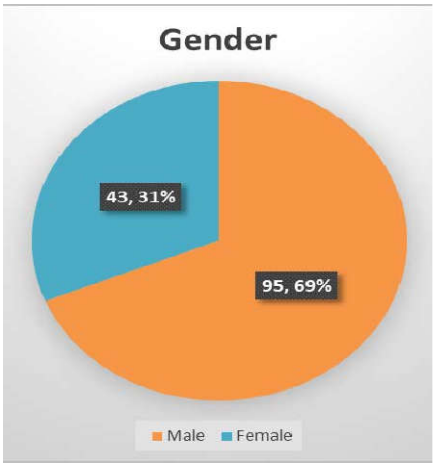
Age Distribution of study population

Mean age of the study population was 48.93 years ± 17.08 (Mean ± SD). The minimum age was 18 years and the maximum age was 84 years.

Table 2 Table showing distribution of age (n = 138)

Age group	Number of patients
18-40	49(35.5%)
41-60	55(39%)
>60	35(24%)

Sex distribution among study population



Of the total study population 95, (69 %) were male and remaining 43, (31 %) were female.
Of total study population 64 % belonged to Hilly area, remaining 32 % from Tarai and 4 % from Mountain.

Religion distribution of study population

Of total study population, 133 (96.4 %) were Hindu, 3 (2.2 %) were Muslim and remaining 2 (1.4 %) were Buddhist.

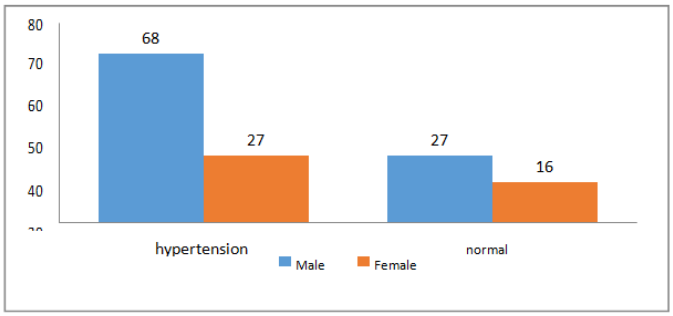
Table 3 Table showing distribution of religion (n = 138)

Religion	Number of patients (%)
Hindu	133 (96.4 %)
Muslim	3 (2.2 %)
Buddhist	2 (1.4 %)

CKD stage distribution among study population

Of total study population most of the cases were in Stage V (103, 74.6 %), rest were in Stage IV (23, 16.7%), and Stage III (12, 8.7%).

Hypertension

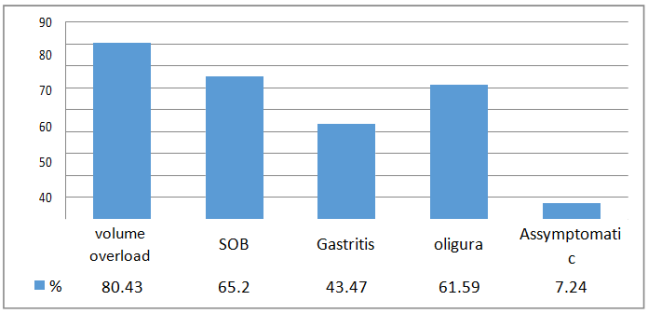


Prevalence of hypertension among study population was found to be 68.8 % (95) Hypertension was present in 71.5 % (68) among male and 28.42(27) of female patient.

Prevalence of hypertension in different stages of CKD

Clinical presentation in study population

Most common clinical presentation in study population were volume overload 111(80.43%), shortness of breath 90(65.2%), oliguria 85(61.59 %), gastritis 60(43.47%) and 10(7.24%) were asymptomatic.



Bar diagram showing clinical presentation in study population

Table 4 Table showing clinical presentation in different stages of CKD

Clinical feature	CKD III	CKD IV	CKD V
Volume overload	0	16	95
SOB	0	5	85
Oliguria	0	7	78
Gastritis	2	6	52
Asymptomatic	10	0	0

In CKD stage III most of the patients were asymptomatic 10 (83.33%) and were incidentally diagnosed and rest had gastritis 2 (16.66 %).

Complication in different stages of CKD on presentation

Of study population 78 (56.52%) patients had complication, out of which most common complication encounter were metabolic acidosis 45 (57.69%), hyperkalaemia 15 (19.2%), pulmonary oedema 9 (11.53%), uremic encephalopathy 5 (6.4%), uremic pericarditis 4 (5.12%).

Table 5 Showing complications in different Stage of CKD

Complication	CKD III	CKD IV	CKD V	Total
Metabolic acidosis	0	0	45	45
Hyperkalaemia	0	2	13	15
Pulmonary oedema	0	0	9	9
Uremic Encephalopathy	0	1	4	5
Uremic Pericarditis	0	0	4	4
Total	0	3	75	78

Of study population complications were encountered mainly in CKD stage V 75(96.15%), and rest were in CKD stage IV 3(3.84%) however CKD stage III none of the complication had been encountered.

Aetiology of CKD among study population

Among study population most common aetiology of CKD were CGN 68(49.3%) followed by DM 38 (27.5%), hypertension 23(16.7%), ADPKD 3 (2.17%), Obstructive uropathy 5 (3.6%), RAS 1(0.72%).

Table 6 Showing aetiology in different stages of CKD.

Aetiology	CKD III	CKD IV	CKD V	Total
CGN	7	5	56	68
DM	5	11	22	38
HTN	0	6	17	23
Obstructive uropathy	0	0	5	5
ADPKD	0	1	2	3
RAS	0	0	1	1
Total	12	23	103	138

Of study population in stage III total number of cases were 12 and most common aetiology was CGN 7(58.33%) followed by DM 5(41.66%). In CKD stage IV total number of cases were 23 and most common aetiology was DM 11(47.8%) followed by hypertension 6(26%), CGN 5(21.7%) and ADPKD 1(4.3%). Majority of the cases were in CKD stage V, 103, and most common aetiology of CKD was CGN 56(54.36 %), followed by DM 22 (21.35%), HTN 17 (16.5%), obstructive uropathy 5 (4.8%), ADPKD 2 (1.94%), and RAS 1 (0.97%).

Correlation of phosphorus level with CKD

Mean value of serum phosphorus for CKD Stage III, IV, V, were 3.8±0.57 mg/dl, 4.89 ± 1.16mg/dl, and 6.69 ± 2.1 mg/dl and statically significant (p=<0.001). i.e. as creatinine clearance decreases serum phosphorus level increases. Similar findings were found in number of other studies.

Table 7 Serum phosphorus level in different stages of CKD

	CKD III	CKD IV	CKD V	p-value
Phosphorus (mg/dl) Mean±SD	3.8± 0.57	4.89±1.16	6.69±2.19	<.001
Number of patients	12	23	103	

Creatinine level in different stages of CKD

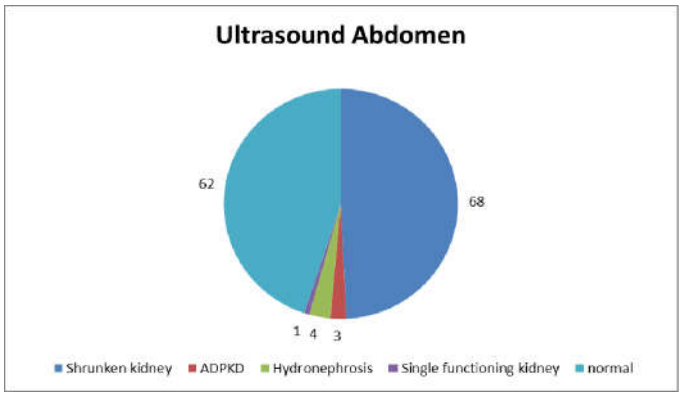
Mean value of s. creatinine for CKD Stage III, IV, V, were 233 ± 55.8mmol/l, 380±227.7mmol/l, and 919±417mmol/l and statically significant (p<0.001).

Table 8 Creatinine level in different stages of CKD

	CKD III	CKD IV	CKD V	p-value
Creatinine(mmol/dl) Mean±SD	233.0±55.8	380.6±227.4	919.2±417.5	<.001
Number of cases	12	23	103	

USG finding in study population

Most common finding were shrunken kidney 68 (49.2%), followed by normal sized kidney 62 (44.99%) ADPKD 3 (2.2 %), Hydro nephrosis 4 (2.8 %) and single functioning kidney in 1 (0.72 %).



Showing ultrasonography finding among study populations

DISCUSSION

This study was observational, prospective study, carried out among the 138 CKD patients with chronic kidney disease stage III to V not under maintenance hemodialysis presenting to medical OPD and medical ward of Tribhuvan University Teaching Hospital (TUTH) from September 2017 to September 2018. The patients who fulfilled the inclusion criteria were enrolled in study population. According to KIDGO 2017 guideline, CKD is defined as abnormalities of kidney structure or function, present for > 3 months, with implications for health. CKD is classified based on cause, GFR category (G1–G5), and albuminuria category (A1– A3), abbreviated as CGA.[20] A study done by PK Chhetriet, al, in Nepal Medical College Teaching Hospital On Chronic kidney disease V on hemodialysis which showed 57.0% were male and 43 were female average age of presentation was around 46 years majority of patients were less than 60 years Old. Which is comparable to our study, Mean age in our study population was 48.96 ±17 yrs. (Mean ± SD). The minimum age was 18 yrs. and the maximum age was 84 yrs. Of the total patients, 69% were male and remaining 31% were female, majority were less than 60 years (75%).[30] A study done by Mittal S et, al Chronic renal failure in India in 835 cases of CKD with a median age of 43 years, 67.8 % of them were men. Which is comparable to our study, Mean age in our study population was 48.96 ±17 yrs. (Mean ± SD), 69% were male and remaining 31% were female.[31] A study done by Afshar R *et al*, Epidemiology of chronic renal failure in Iran: a four year single- center experience, in 2007 of the 1200 patients, 61% were males and 39% females, Which is comparable to our study, Mean age in our study population was 48.96 ±17 yrs. (Mean ± SD), 69% were male and remaining 31% were female.[32] In our study 133 (96.4 %) were Hindu, 3 (2.2 %) were Muslim and remaining 2 (1.4%) were Buddhist, 64% were belongs to hilly area, remaining 32% from Tarai and 4% from Mountains. Occupation distribution in our study population, 75 (51 %) were Dependent,

26 (18.8 %) Farmer, 15 (10.9 %) Businessman, 12 (7.2 %), migrant worker and others 12 (8.7 %). Of the total 138 sample, 8.7% (12) in stage III, 16.7 % (23) were in stage IV and 74.6% (103) in stage V CKD i.e. more number of patients were in stage V then in earlier stages of CKD. This contradicts the global prevalence of CKD patients by stage, i.e. in multiple studies it is shown that there are more number of patients in early stage of CKD than late.32, 70 The reason behind this is that CKD is asymptomatic in its early stages (with hypertension found incidentally) and symptoms only start occurring after creatinine clearance starts decreasing from 60, first being the symptoms of anemia [33, 34].So since this study was a hospital based study, patients presenting with early stage of CKD were far less than those presenting with late stage CKD. A study done by Chen W*et al* on Treatment of Metabolic Acidosis in Patients with CKD in which, Metabolic acidosis was a common complication of advanced CKD[35], present in 30-50% of individuals with eGFR<30 ml/min/1.73 m2which in comparable with our study, metabolic acidosis was observed in 45 (57.69 %) out of all the complications 78 (56.52%), seen in CKD V. A study done by S Gilligan *et al*, the prevalence rates of hyperkalemia was (14%- 20%) in CKD severity increases as eGFR decreases, which is comparable to our study, hyperkalemia observed in 15 (19%) out of all complication, 2 cases were from CKD stage IV rest 13 from CKD stage V.[36]

In a study done by Prasad R *et al*, on clinical and biochemical spectrum of chronic kidney disease in tertiary care center at SIMS, Mangalore India, kidney size was decreased in 64% of the patients, normal sized kidneys were seen in 30% of the patients, which is attributable to the large number of diabetic nephropathy cases in which normal kidney size is a known entity. Which is comparable to our study as well, in our study most common Ultrasonographic finding were Shrunken kidney 66 (47.8 %), normal kidney 63 (45 %), ADPKD 3 (2.2 %), Hydro nephrosis 3 (2.2 %) and single functioning kidney in 3 (1.4 %)[37]. A study done by Chonchol Metal 80 on Prevalence of subclinical hypothyroidism in patients with chronic kidney disease, which shown prevalence of subclinical hypothyroidism was 17.9% at an estimated GFR <60 ml/min per 1.73 m2, which in comparable to our study, 14.5 % had subclinical hypothyroidism.

CONCLUSION

CKD is one of the important health problems in Nepal. Most common clinical presentation of CKD was volume overload followed by shortness of breath, oliguria, and gastritis. So any patient with these features; need to be evaluated thoroughly to detect presence of renal disease as early as possible to prevent complications and to improve quality of life. Most common complication of CKD was metabolic acidosis followed by hyperkalaemia, pulmonary oedema, uremic encephalopathy, and uremic pericarditis. Most common aetiology being chronic glomerulonephritis followed by diabetes mellitus, hypertension, ADPKD, Obstructive uropathy, and RAS in decreasing order respectively. Early diagnosis and proper

management have important roles in prevention of CKD progression to end-stage renal disease (ESRD). For this purpose, determining the etiology of CKD is helpful.

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How to cite this article:

Dr. Sourabh Singh Dudve and Dr. Shiwaanee Gupta (2020) 'Demographic and Clinical Profile of Chronic Kidney Disease in Tertiary Care Center', *International Journal of Current Advanced Research,* 09(02), pp. 21163-21169. DOI: http://dx.doi.org/10.24327/ijcar.2020. 21169.4151

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