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Burden and Predictors of Chronic Kidney Disease in Developing Country

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ABSTRACT

Chronic Kidney Disease (CKD) is being recognized as a global public health problem. It is a major non-communicable disease with the global prevalence varying between 10.5% and 13.1%. Diabetes and hypertension appear to be the leading causes of chronic kidney disease worldwide.

An institution based cross-sectional study was undertaken from Oct 20, 2018 to Nov 20, 2019 G.C. Data was collected using a pre-tested questionnaire designed to meet the study objective. After describing variables, logistic regression was conducted to identify independent associated factors of CKD. Statistical significance was declared at P<0.05.

Of the 450 studied patients, 260(57.8%) were males and more than half (54.2%) were between ages of 25 to 40 years. The prevalence of CKD among patients admitted to medical ward was 17.3% (95% CI 13 - 29.9) and 14.4% (95 % CI 6.2 – 12.3) by Cockcroft Gault and MDRD equations, respectively and majority (61.5%) of them were stage 5. Hypertension (AOR= 7.8 95%CI 4.1, 14.9), history of recurrent urinary tract infection (AOR= 3.5 95% CI 1.1, 7.3) and history of using nephrotoxic drugs (AOR=3.4 95% CI 2, 9.3) were significantly associated with CKD.

The burden of CKD among patients in a medical inpatient unit was high and majority of the patients present late. Hypertension, use of nephrotoxic agents and recurrent urinary tract infections were found to be important predictors.

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Abbreviations

ACSH: Ayder Comprehensive Specialized Hospital, **AKI:** Acute Kidney Injury, **BMI:** Body Mass Index, **BP:** Blood Pressure, **CKD:** Chronic Kidney Disease, **DM:** Diabetes Mellitus, **ESRD:** End Stage Renal Disease, **GFR:** Glomerular Filtration Rate, **HIV:** Human Immunodeficiency Virus, **MDRD:** Modification of Diet in Renal Disease, **UTI:** Urinary Tract Infection, **NSAID:** Non-Steroidal Anti-Inflammatory Drugs, **SPSS:** Statistical Package for Social Science

Background

Chronic Kidney Disease (CKD) is defined as the presence of markers of kidney damage for ≥ 3 months. These markers include structural or functional abnormalities of the kidney, pathological abnormalities or other kidney damages, including abnormalities in the composition of blood or urine, abnormalities in imaging tests, presence of Glomerular Filtration Rate(GFR)< 60 mL/min/1.73 m^2 [1]. The presence of kidney disease is usually evaluated by GFR, an important marker of kidney function, and using indicators of kidney damage like proteinuria, abnormal urinary sediment, abnormal imaging studies and presence of kidney transplant [2].

CKD is a continually growing problem worldwide with estimated prevalence of ranging 10.5-13.1 % and has a risk-multiplier effect on major non-communicable diseases, including cardiovascular diseases. Because of this CKD has become a major health problem globally, especially in developing countries with substantial effect in Sub-Saharan Africa [1,3]. The disease epidemiology is markedly different from other regions. Although middle-aged and elderly populations are predominantly affected in developed countries, in sub-Saharan Africa, CKD mainly affects economically productive young society between the ages of 20 to 50 years. Furthermore, it is may not be associated with major risk factors like Hypertensio¬n, diabetes and smoking [4,5]. Hence determining magnitude and associated factors of CKD will be paramount important in our set up.

In addition to GFR, proteinuria has a significant role in assessing risk of CKD, especially important since patients with stage 1-2 CKD and proteinuria have worse outcomes than people with stage 3 and no proteinuria. Furthermore, the risk of development

of ESRD and cardiovascular mortality is accurately predicted by proteinuria measurements than by GFR [6-8]. Chronic kidney disease is generally unrecognized in the early stages, as there are no particular symptoms. They could have nonspecific symptoms generally unwell feelings and decrease in appetite or indistinguishable symptoms like pallor, fatigue, gastrointestinal disorders like hiccups, nausea and vomiting or with symptoms of heart failure [9].

CKD is usually diagnosed during the evaluation of patients who have hypertension and diabetes due to high prevalence of asymptomatic patients. However, developing countries are highly affected with CKD that cannot be explained by diabetes or hypertension, around 43% of people with CKD do not have diabetes or hypertension [10-12]. Indeed in some places such as Sri Lanka and Nicaragua, the conventional risk factors were not associated with the disease prevalence [13,14]. But in Ethiopia there is scarcity of data on prevalence and factors associated with CKD, the only report that we have is from Southern Ethiopia done only in diabetes patients. In this study we aim to describe the prevalence and factors associated with CKD in patients admitted to medical ward in tertiary hospital, Northern Ethiopia.

Methods

An institution-based cross-sectional study was conducted in Ayder Comprehensive Specialized Hospital (ACSH) which is located in Mekelle, Tigray regional state, Northern Ethiopia. This hospital provides referral service to a 9 million population in its catchment areas of the Tigray, Afar, and Amhara Regional States. The hospital has a total of 500 inpatient beds and 108 beds are assigned to the medical ward for medical cases admission, with an average of 250-300 admissions monthly [15]. The study was conducted from October 20, 2018 to November 20, 2019 G.C.

Source and Study Population

The source population for this study was all admitted patients to Ayder comprehensive specialized hospital, whereas the study population of this study was patients attending their medical care in medical ward ACSH during the study period.

Sample Size Determination and Sampling Technique

The sample size was calculated by using a single population proportion formula with assumptions, p= 50%(as there was no previous study in Ethiopia on similar study population), 95% level of confidence and 5% margin of error, then sample size became 384.after adding 10% non-response rate, the minimum calculated sample was 424. Computer generated simple random sampling technique was used to select the study participants.

Eligibility Criteria

Patients above 18 years of age admitted to medical ward of ACSH were included after excluding patients who had clear risk for acute kidney injury and/or diagnosed with acute kidney injury.

Study Variable

Dependent Variable

Chronic Kidney Disease Status

Independent Variables

Age, Gender, Occupation, Income, Educational Status, Hypertension, Diabetes, Family history of CKD, History of smoking, Body Mass Index , Exposures to nephrotoxins (like NSAIDS, radio contrast media and others)

Data Collection Procedures

Total of 982 patients were admitted to medical ward during the study periods, from those 572 patients were enrolled by using systematic random sampling technique to collect data using questionnaires by interviewing study participants and check list were also used to collect secondary data. The questionnaire was designed to collect data related to socio demographic characteristic, history and physical examination, associated factors and investigation results like renal function test. The study groups were enrolled, after excluding those with feature of acute kidney injury such us recent rise in creatinine, sepsis, critically ill and shock patients as can be seen in Figure 1.

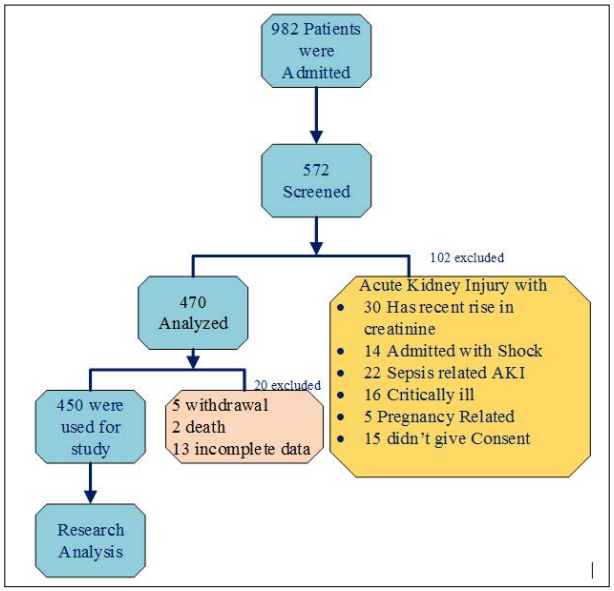

Figure 1: Data Collection Procedure Flow Chart

Physical Examinations

Height was measured using portable stadiometer and weight was determined using a weight scale, patient were dressed but without shoe by trained nurses. BMI was calculated as weight (in kilograms) divided by height in square meters. As per the WHO criteria, BMI was classified as normal/underweight BMI<25kg/m^2, overweight: BMI 25-29.9kg/m^2 and obese: BMI≥30kg/m^2 [26].

We identified coexisting illness using patient medication chart, laboratory results and self-report method. Participants were considered to have diabetes mellitus if previously they had been recognized by the doctor as having DM, two fasting glucose values of ≥126 mg/dl using fingertip blood (Accu-trend glucometer) or they reported taking anti diabetic drug. Blood pressure was measured two times using a calibrated sphygmomanometer at the heart level. Hypertension was defined as systolic BP ≥ 140mmHg or diastolic BP ≥ 90mmHg or use of medication for hypertension.

Sample Collection and Laboratory Analysis

A random urine sample of MSU (midstream urine) had been collected from each patient using a clean catch technique and sterile container. Urinary excretion of protein and sugar was detected using urinary strips 'ACCU-ANSWERR '. Serum creatinine was measured by alkaline picrate method (Jaffe kinetic assay). For estimated glomerular filtration rate (eGFR) determination, the abbreviated equations from the Modification of Diet in Renal Disease (MDRD) study and Cockcroft-Gault was used. Equation from the MDRD study: estimated GFR (mL/min per 1.73 m2) = 1.86 × (SCr) −1.154 × (age) −0.203, multiply by 0.742 for women

and by 1.21 for African ancestry and Cockcroft-Gault equation: Ccr (mL/ min) = (140-age) × Weight (Kg)/72 × SCr (mg/dL) × 0.85 if female.

Staging of kidney function was based on the national kidney foundation disease outcome quality initiative (NKF-KDOQI) classification [8]. An eGFR<60ml/min was used to define chronic kidney disease. KDIGO guideline recommended to use albumin-to –creatinine ratio (ACR) more than 30mg/g to define CKD but such test was not available in the study area [6]. Those with newly detected high creatinine and having patient with difficulty to differentiate acute kidney injury and chronic kidney disease were advised to start further work up and appointed at least after 3 months for follow-up investigation and treatment at the hospital and it was revised from Smart Care using their identification number.

Data Quality Control

Training was given for data collectors and supervisors about the aim of study, data collection procedures and ethical issues. Validity was checked by doing pretest on 30 patients at Mekelle hospital (out of the study area), the data collection tool was modified.

Data Analysis

Data entry and analysis were performed using Statistical Package for Social Science (SPSS) version 23. Categorical variables were described using frequencies and percentages. Continuous variables were also described using an appropriate combination of measure of central tendency and measure of dispersion. Odds ratio with its 95 % confidence interval and p-value were calculated by running logistic regression to identify factor associated with CKD. Variables with a p-value less than 0.05 during bivariate analysis were selected for multivariable analysis. Statistical significance was declared at p value < 0.05.

Results

Demographic and Clinical Characteristics of Participants

From four hundred seventy included patients, data of 450 patients was analyzed making response rate of 96.6%. The mean and SD of the age of the study participants was 45 ± 18 years and more than half (54.2%) of them were between 25 to 54 years of age. Table 1 shows, from the study, 260 (57.8 %) participants were males, with male to female ratio of 1.4:1. About 20.9% of the participants were not engaged in any formal education, and more than half of the participants were not employed in any work and live in rural area.

Table 1: Socio demographic characteristics of the study participants admitted to medical ward of ACSH, North Ethiopia, October 20, 2018 to November 20, 2019 (N=450)

Characteristics		Frequency (N=450)	Percentage	95% Confidence Interval	
				Lower	Upper
Sex	Male	260	57.8	53.6	61.8
	Female	190	42.2	38.2	46.4
Age in years	18-24 Years old	67	14.9	12.7	16.3
	25-54 Years old	244	54.2	53.2	57.8
	55-64 Years old	55	12.2	10.1	13.4
	65+ Years old	84	18.7	17.5	19.5
Residence	Rural	269	59.8	55.4	63.9
	urban	181	42.2	36.1	44.6
Educational status	Higher education	68	15.5	12	18.4
	Secondary school	131	29.1	24.9	33.3
	Primary school	65	14.4	11.1	18.0
	Able to read and write	92	20.4	16.9	24.2
	Unable to read & write	94	20.9	17.3	24.2
Occupational status	Farmer	165	36.7	32	41.1
	Merchant	90	20	16.6	23.5
	Government employe	74	16.7	13.3	19.8
	House wife	31	6.9	4.7	9.3
	Others	90	20	16.3	24

Laboratory Related Characteristics

In the present study, it has been revealed that the prevalence of abnormal urinary finding (dipstick proteinuria) was found in 24.4% (95% CI 20.9, 28.4) of the admitted patients. More than half of the patients have already small shrunken kidney size at presentation, showing most of them came with advanced kidney disease (Table 2).

Table 2: Laboratory related characteristics of the study participants admitted to medical ward of ACSH, North Ethiopia, October 20, 2018 to November 20, 2019 (N=450)

Characteristics	Frequency (N=450)	Percentage	95% Confidence Interval	
			Lower	Upper
Laboratory values				
Anemia (HGB<12mg/dl)	214	47.6	45.8	50.2
HBV infection	16	3.6	2.8	6.3
HCV infection	14	3.1	2.2	5.8
HIV infection	32	7.1	4.7	9.3
Urine dipstick proteinuria	110	24.4	20.9	28.4
Abdominal ultrasound findings				
Small shrunken kidney	60	13.3	10.4	16.2
Enlarged kidney	14	3.1	1.8	4.9
Normal sized kidney	344	76.4	72.4	80.4
Poly cystic kidney	18	4	2.2	5.7
Obstructive Uropathy	10	2.2	1.1	3.8
Others*	4	0.9	0.1	1.8

Prevalence of CKD

The prevalence of CKD was 17.3 % (CI 95% 13 - 29.9) and 14.4% (CI 95 % 6.2 –12.3) by Cockcroft Gault and MDRD equations respectively. When looking at the prevalence of CKD estimated by the MDRD equation versus by C-G equation, the MDRD tends to underestimate this prevalence in comparison with C-G, though the difference was not statistically significant. Table 3 demonstrates the prevalence of CKD classified by stages as per Cockcroft Gault equation according to national kidney foundation classification. There were 48 patients (61.5 %) stage 5, 12.8 % stage 1 and 15.3% stage 4 CKD patients by Cockcroft Gault equation.

Table 3: Prevalence of CKD according to the MDRD and Cockcroft-Gault equations (N =450)

Stages of CKD	eGFR ml/min/1.73 m2	Cockcroft- Gault N (%)	MDRD N (%)
1	≥90	2 (2.5)	4(6.1)
2	60 to 89	4(5.12)	2(3.03)
3a	45 to 59	4(5.12)	1(1.5)
3b	30 to 44	8(10.2)	6(9.2)
4	15 to 29	12(15.3)	14(21.5)
5	<15	48(61.5)	38(58.1)
Overall		78(100)	65(100)

Factors Associated with CKD

The univariate analysis showed significant association between CKD (eGFR <60 ml/min/1.73 m2) and the following variables, smoking, use of nephrotoxic drug, history of diabetes, history of hypertension, family history of kidney disease, elevated systolic blood pressure, obesity, high FBS. After incorporating all significant ($p<0.20$) variables in the univariate analysis, multivariate logistic regression was performed to identify risk factors independently associated with CKD (Table 4).

Table 4: Bivariate analysis of factors associated with chronic kidney disease among patients admitted to Medical ward, ACSH, North Ethiopia, October 20, 2018 to November 20, 2019

Variables		CKD (N=78)(%)	Non CKD (N=372) (%)	COR	95% CI	P-value	AOR	95% CI	P-value
Age	>65 years	14(17.9)	70(18.8)	1.1	0.5 ,1.9	0.84			
	≤65 years	64(82.1)	302(81.2)						
Gender	Male	52(66.7)	208(55.9)	0.63	0.38, -1	0.08			
	Female	26(33.3)	164(44.1)						
Smoking status	Yes	19(24.5)	40(10.8)	2.6	1.4 - 4.9	0.02*	1.8	0.83,4.2	0.129
	No	59(75.6)	332(89.2)						
Use of nephrotoxic drug	Yes	48(61.5)	32(8.6)	1.9	0.9 - 3.9	0.04*	3.4	2, 9.3	0.001
	No	30 (38.5)	340 (91.4)						
History of DM	Yes	13(16.7)	28(7.5)	3.03	1.4 – 6.3	0.003*			
	No	65(83.3)	344(92.5)						
History of HTN	Yes	27(34.6)	55(14.8)	3.05	1.7 – 5.2	0.012*			
	No	51(65.4)	317(85.2)						
History of recurrent UTI	Yes	53(67.9)	77(20.7)	8.1	4.7-13.9	0.005*	3.5	1.1,7.3	0.017
	No	25(32.1)	295(79.3)						
Family history of kidney disease	Yes	6(7.7)	4(1.1)	7.6	2.1-27.8	0.02*	1.2	1.0 , 6.3	0.161
	No	72(92.3)	368(98.9)						
Obesity (BMI >30kg/m^2)	≥30	3(3.8)	3(0.8)	4.9	0.9-24.8	0.054			
	<30	75(96.2)	369 (99.)						
HIV infection	Yes	20(25.6)	107(28.7)	0.8	0.5 - 1.5	0.578			
	No	58(74.8)	265(71.2)						
FBS	≥126	13(16.7)	28(7.6)	2.4	1.2 - 4.9	0.013*	2.5	0.8,7.5	0.08
	<126	65(83.3)	344(92.4)	1					
SBP	≥140	47(60.2)	59(15.8)	8	4.7-13.6	0.007*	7.8	4.1,14.	0.000
	<140	31(39.8)	313(84.2)	1					

COR crude odds ratio, *AOR* adjusted odds ratio, *CI* confidence interval, *DM* diabetes mellitus, *N* number
1 = references .CKD chronic kidney disease,* significant

A binary logistic regression as shown in Table 5 was conducted to identify significant associated factors of CKD in admitted patients. Systolic hypertension, history of recurrent UTI and history of use nephrotoxic drugs were found to have a significant association with CKD. Accordingly, the odds of CKD were higher in patients with hypertension (AOR=7.8 95% CI: 4.1- 14.9, p=0.000), history of recurrent UTI (AOR=3.5, 95% CI: 1.1 - 7.3, p=0.017) and history of using nephrotoxic drugs (AOR=3.4, 95% CI: 2 - 9.3, p=0.001).

Table 5: Factors associated with CKD in patients admitted to medical ward according to a multivariable analysis, ACSH, North Ethiopia, October 20, 2018 to March 20, 2019

Variable	AOR	95% Confidence Interval		p-value
		Lower	Upper	
History of recurrent UTI	3.5	1.1	7.3	0.017
History of nephrotoxic drugs use	3.4	2.0	9.3	0.001
Systolic BP	7.88	4.1	14.9	0.000

Discussion

This study was carried out to determine prevalence and associated risk factors of CKD in medical hospitalized patients. Chronic kidney disease was found in 17.3% (95% CI 13 - 29.9) of all patients in medical ward admitted for different reasons. This is similar to the study done in Uganda that found 18 % among hospitalized patients [17]. The participants in the Uganda study were critically ill and hence the slight increase in total number of renal dysfunction cases. But studies in Germany and Haiti showed higher prevalence of 24% and 27% respectively [18,19]. This might be due to the involvement of only elderly patients and used ACR to calculate proteinuria which can pick earlier CKD. Another study done in Switzerland and United States showed lower prevalence, that is, 13.8 and 10%, respectively [20,21]. This could be partly explained by they have conducted population based study with distributed risks and , might be due to our hospital being only referral hospital where patient's with complication requiring renal replacement therapy are also admitted.

Majority of patients in this study present with stage 5 CKD (ESRD) in contrast to other studies done in US and Swiss where the prevalence of CKD stage 3 to 5 was only 4.7% and 4.5 % respectively [18,21]. The reason why patients present in ESRD in this study may be due to our center being a referral hospital and only center in the region providing dialysis where patients with complications requiring RRT are admitted. This is consistent with many of African countries study like, Uganda and Botswana [17,22].

Worldwide hypertension is recognized as one of the leading causes of CKD [23]. This study revealed that patients with systolic hypertension were 7.8 times more likely to develop CKD than the non-hypertensive patients. Studies done in Uganda, Haiti and DRC also found correlation between hypertension and CKD [5,17,18]. The use of nephrotoxic agents has been associated with CKD as demonstrated in Burundi [24]. Similarly, in the present study the association of nephrotoxic drugs with CKD was 3.4 times than non-users. However, in Uganda, it was not found to be associated, this can be due to they have only assessed NSAID use unlike this study that include other nephrotoxic agent including contrast media [17].

While diabetes in most studies is mentioned as an independent predictor for CKD, in this study the prevalence of diabetes in the participants was 9.1 % (95 % CI 6.4-12.0), however in the multivariate regression model it was not significantly associated with CKD. A probable explanation for this might be the recent development of diabetes (78% of them <5 years) in the study participants. This is similar to study done in Haiti and Iran [18,16, 26-28].

Limitation of the Study

This study was done in a tertiary hospital with a high risk profile. But stage 1 and 2 were under estimated because this study didn't use Urinary Albumin-to-Creatinine ratio. As this is a cross-sectional study design makes it may be impossible to infer a causal relationship between CKD and the risk factors.

Conclusion and Recommendation

In conclusion, we found a high prevalence of CKD among adult patient admitted to medical ward of Ayder Hospital and majority of them were CKD stage 5 (ESRD). In this study significant association was demonstrated between CKD and elevated systolic blood pressure, history of using nephrotoxic drugs and history of recurrent urinary tract infection which are easily preventable. The study recommends further investigations at community level to find out the point prevalence of CKD and the data have to be noted by the health authorities in the country to integrate CKD in public health planning for early detection. High risk patients need to be screened and advised on the use of nephrotoxic drugs.

Declarations

Ethical Approval and Consent to Participant

Ethical clearance waived from Mekelle University, College of Health Sciences, and Institutional Review Board (IRB) with ethical clearance number ERC: 1405/2018. Permission received from the medical director of the hospital before the commencement of the study and informed written consent was also obtained from all eligible participants. The study adhered to relevant guidelines and regulations.

Consent for Publication: Not applicable for this manuscript

Availability of Data and Materials: The data set generated and analyzed during this study is available and can be shared from the corresponding author upon on reasonable request.

Computing Interest: The authors declare that they have no computing interest.

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Author's contribution

MKW selected the topic, planned the study protocol, oversaw the study, entered the data, and reviewed the literature. MKW, MGW, EB and MG conducted the analysis and interpreted the results. MKW, MKW and EB drafted the final manuscript. All the author(s) reviewed and approved the final manuscript

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