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Chronic Kidney Disease and Associated Risk Factors Assessment among Diabetes Mellitus Patients at A Tertiary Hospital, Northwest Ethiopia

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ABSTRACT

BACKGROUND: *The prevalence of chronic kidney disease, particularly in diabetic patients, is increasing rapidly throughout the world. Nowadays, many individuals in developing nations are suffering from diabetes which is one of the primary risk factors of chronic kidney disease.*
METHODS: *Institution based cross-sectional study was conducted at the University of Gondar Hospital from February to April 2016. A total of 229 study participants were selected using systematic random sampling technique. Urine sample was collected for albumin determination by dipstick. The Simplified Modification of Diet in Renal Disease study equation was used to estimate glomerular filtration rate. Binary logistic regression model was used to identify risk factors.*
RESULTS: *Of the total 229 study participants, 50.2% were females and the mean age was 47±15.7 years. Among study participants, the prevalence of chronic kidney disease (CKD) was found to be 21.8% (95% CI: 16% - 27%). Of all study participants, 9(3.9%) had renal impairment (eGFR < 60 ml/min/ 1.73 m^2) and 46 (20.1%) had albuminuria. Older age (AOR: 5.239, 95% CI: 2.255-12.175), systolic blood pressure ≥140mmHg (AOR: 3.633, 95% CI: 1.597-8.265), type 2 diabetes mellitus (AOR: 3.751, 95% CI: 1.507-9.336) and longer duration of diabetes (AOR: 3.380, 95% CI: 1.393-8.197) were independent risk factors of CKD.*
CONCLUSIONS: *The study identified high prevalence (21.8%) of CKD among diabetic adults. CKD was significantly associated with older age, systolic blood pressure, type 2 DM and longer duration of DM. Thus, DM patients should be diagnosed for chronic kidney disease and then managed accordingly.*
KEYWORDS: *Chronic kidney disease, Diabetes mellitus, Glomerular filtration rate, Risk factors*

INTRODUCTION

Chronic kidney disease (CKD) is a progressive loss in renal function over a period of three months or years. Kidneys can get damaged from a physical injury or a disease like diabetes mellitus (DM) or high blood pressure. Once kidneys are damaged, they cannot filter

blood or perform other activities. This is usually associated with a reduction in glomerular filtration rate (GFR) and proteinuria (1,2).

CKD is a worldwide public health problem, both for the number of patients and cost of treatment involved. It was a cause of 409,000 and 956,000 deaths in 1990 and 2013, respectively. Of those deaths, 46,000 (1990) and 173,000 (2013) were caused by CKD due to DM (3). Globally, diseases of the kidney and urinary tract together are the 12th cause of death and the 17th cause of disability (4). CKD affects around 10–13% of the general population (5). It has been estimated that more than 500 million individuals globally have CKD, regardless of the cause (6). In sub-Saharan Africa, CKD is a considerable health burden. CKD is at least 3-4 times more frequent in Africa than in developed world (7).

CKD is associated with adverse outcomes of kidney failure, cardiovascular disease (CVD), and premature death (5,8). The risk of cardiovascular mortality, kidney failure, kidney-disease progression, acute kidney injury, cognitive decline, anaemia, mineral and bone disorders, fractures and hospitalizations are higher among patients with CKD than those with normal renal function (9,10). Many of the complications of CKD can be prevented or delayed by early detection and treatment (11).

Major risk factors for the development and progression of CKD are diabetes and hypertension. CKD due to diabetes and hypertension affects nearly 5-7% of the world population and is more common in developing countries and disadvantaged and minority populations (12). Diabetes causes 9.1-29.9% of the cases of end stage renal disease (ESRD) in various developing countries, and hypertension leads to 13-21% of the cases (13). Hypertension affects almost 25% of the adult population in Africa and is the cause of chronic kidney failure in 21% of patients on renal replacement therapy in South Africa. The prevalence of diabetic nephropathy is estimated to be 23.8% in Zambia, 14%-16% in South Africa, 12.4% in Egypt, 9% in Sudan, and 6.1% in Ethiopia (7).

CKD is an important cause of death and disability worldwide, but awareness of the disorder remains low in many communities and among many healthcare providers (10). The prevalence of DM is increasing alarmingly in developing countries like Ethiopia (14). In parallel, CKD will increase even if studies did not show the exact magnitude particularly in the study area, Gondar. Therefore, this study was aimed to assess the prevalence of CKD and associated risk factors among DM patients attending at University of Gondar Hospital, Northwest Ethiopia.

MATERIALS AND METHODS

Population and study design: The study was conducted at the University of Gondar Hospital Chronic Illness Clinic, Gondar, Northwest Ethiopia. Adult (≥18 years) DM patients who volunteered to give informed written consent were included in the study. Pregnant, hospitalized, non-fasting, febrile patients, and patients with HIV and CVD were excluded. Institution based cross-sectional study was conducted from February to April 2016.

Data collection: The sample size was calculated using single population proportion formula considering 18.2% CKD prevalence in Southern Ethiopia (15) and assumptions of 5% margin of error, 10% non-response rate and 95% level of confidence. Even though, 252 study participants were assumed to be included, only 229 volunteered to give informed written consent to participate in the study. Study participants were selected by systematic random sampling technique.

Socio-demographic, clinical and anthropometric data were collected by nurses after the participants agreed to sign written consent. Height was measured using standiometer, and weight was recorded using a balace with patients being bare-footed and wearing light clothes. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). Underweight, normal weight, overweight and obese were

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classified as BMI <18.5, 18.5- 24.9, 25-29.9 and ≥30, respectively.

Blood pressure was measured by nurses using an analogue sphygmomanometer and stethoscope. Measurements were taken from the upper arm while placing the hand at the heart level after the patients had been sitting for more than 5 minutes. Systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg or current uses of blood pressure-lowering medication were used to define hypertension (16). Considering their current fasting blood glucose (FBG) level, participants were classified as with good glycemic control (FBG <150 mg/dl) and poor glycemic control (FBG ≥150 mg/dl) (15).

Laboratory technologists collected blood and urine samples, and performed biochemical tests. Five milliliters of fasting venous blood sample was collected with standard venipuncture technique to separate serum. Mindray BS-200 (Shenzen Mindray Bio-Medical electronics Co. Ltd, China) analyzer was used for biochemical analysis. Serum glucose, creatinine and urea level were measured using the enzymatic glucose oxidase, kinetic alkaline picrate and enzymatic glutamate-dehydrogenase (GLDH) methods, respectively. Ten milliliters of freshly voided urine was collected by clean and dry container. Then, urine albumin was determined by using dipsticks (COMBINA 11S, Human). Presence of albumin in the urine (from +1 to +4) was defined as albuminuria.

The glomerular filtration rate (GFR) was estimated using Modification of Diet in Renal Disease (MDRD) study equation as follow: $186 \times [\text{serum creatinine } (\frac{mg}{dl})]^{-1.154} \times (age)^{-0.203} \times$ (0.742 if female) x (1.212, if black) (17). CKD was defined incorporating both eGFR and albuminuria. Patients having CKD were classified into five stages according to the Kidney Disease: Improving Global Outcomes (KDIGO) classification system as follows: stage 1: albuminuria with eGFR of ≥90 ml/min/1.73 m^2, stage 2: albuminuria with eGFR of 60-89 ml/min/1.73 m^2, stage 3: eGFR of 30-59 ml/min/1.73 m^2, stage 4: eGFR of 15-29 ml/min/1.73 m^2 and stage 5 (kidney failure): eGFR of <15ml/min/1.73 m^2. Stage 3 was further classified into 3A (eGFR of 45–59.9 ml/min/1.73 m^2) and 3B (eGFR of 30–44.9ml/min/1.73 m^2) (1).

Data analysis: Data were checked, sorted, categorized and coded manually. Then, data were entered into EPI info version 3.5.3 and then transferred to SPSS version 20 for analysis. Bivariate and multivariate logistic regression models were used to assess associated risk factors. Variables with a p-value of ≤0.2 in the bivariate analysis were remained in the multivariate logistic regression model to control the effect of confounding variables and to identify independent risk factors of CKD. Both crude and adjusted odds ratios with their 95% confidence intervals (CI) were computed to measure the strengths of associations between variables. A p-value of <0.05 was considered as statistically significant.

Ethics approval: Ethical clearance was obtained from Research and Ethical Review Committee of School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar. Permission letter was also taken from the clinical dDirector of the hospital and head of the DM clinic. To ensure confidentiality of the study participants' information, anonymous typing was applied so that the name of the participants and any identifier was not written on the questionnaire. Data were collected after full written consent had been obtained from each participant. Patients with abnormal test results were consulted to consult physicians for further diagnosis and treatment accordingly.

RESULTS

Socio-demographic and clinical characteristics: The mean age of the study participants was 47±15.7 years. The majority, 184(80.3%), of the participants were ≤60 years old, 182(79.5%) were urban dwellers, 202(88.2%) were Orthodox Christianity followers and 130(56.8%) were married (Table 1).

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Table 1: Socio-demographic characteristics

Characteristics		Number	Percent
Age (year)	≤60	184	80.3
	>60	45	19.7
Sex	Male	114	49.8
	Female	115	50.2
Religion	Orthodox	202	88.2
	Muslim	23	10.0
	Protestant	4	1.8
Residence	Urban	182	79.5
	Rural	47	20.5
Marital status	Single	35	15.3
	Married	130	56.8
	Widowed	43	18.8
	Divorced	21	9.2
Educational status	No education	95	41.5
	Primary school	64	27.9
	Secondary school	38	16.6
	Higher education and above	32	14.0
Occupation	Merchant	18	7.9
	Housewife	61	26.6
	Government employed	69	30.1
	Self-employed	22	9.6
	Farmer	42	18.3
	Others	17	7.4
Income (Ethiopian birr)	<1001	124	54.1
	1001-2000	47	20.5
	2001-3000	26	11.4
	3001-4000	11	4.8
	>4000	21	9.2

Among the study participants, 119(52%) had type 2 DM and 101(44.1%) had hypertension. Family history of CKD was found in 30(13.1%) participants. The majority of the participants, 133(58.1%), were classified as normal weight, 216(94.3%) never smoked and 168(73.4%) had no alcohol consumption habit (Table 2).

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Table 2: Clinical and behavioral characteristics

Characteristics		Number	Percent
Body mass index	Underweight (< 18.5)	22	9.6
	Normal weight (18.5-24.9)	133	58.1
	Overweight (25-29.9)	54	23.6
	Obese (≥30)	20	8.7
Systolic blood pressure	<140 mmHg	163	71.2
	≥140 mmHg	66	28.8
Diastolic blood pressure	<90 mmHg	209	91.3
	≥90 mmHg	20	8.7
Hypertension	Present	101	44.1
	Absent	128	55.9
Waist circumference	Low risk	155	67.7
	High risk	74	32.3
Types of diabetes	Type 1	110	48.0
	Type 2	119	52.0
Duration of diabetes	<10 years	179	79.2
	≥10 years	50	21.8
Family history of kidney disease	Yes	30	13.1
	No	199	86.9
Smoking habit	Never smoked	216	94.3
	Smoker	4	1.7
	ex-smoker	9	3.9
Alcohol consumption habit	Yes	61	26.6
	No	168	73.4
Fasting blood sugar	<150mg/dl	102	45.5
	≥150mg/dl	127	55.5
Urea level	Normal (≤40 mg/dl)	215	93.9
	High (> 40mg/dl)	14	6.1
Urine albumin	Negative	183	79.9
	Positive	46	20.1
Chronic kidney disease	Present	50	21.8
	Absent	179	78.2

Prevalence of CKD: The estimated prevalence of CKD was 21.8% (95% CI: 16% - 27%). Of all the study participants, 9(3.9%) had renal impairment (eGFR < 60 mL/min/1.73m^2) and 46 (20.1%) had albuminuria (Table 2). All of the participants who had renal impairment and the majority of the participants with albminuria (37/46, 80%) were type 2 DM patients (Table 3).

Table 3: Prevalence and stages of CKD

Stage	Description	eGFR (ml/min/1.73m^2)	N (%)
1	Normal eGFR with albuminuria	≥90	9(3.9)
2	Slightly decreased eGFR with albuminuria	60-89.9	32(14.0)
3	Moderately decreased eGFR	30-59.9	8(3.5)
3A	Mildly to moderately decreased eGFR	45-59.9	5(2.2)
3B	Moderately to severely decreased eGFR	30-44.9	3(1.3)
4	Severely decreased eGFR	15-29.9	0(0)
5	Kidney failure	<15	1(0.4)
	Total		50(21.8)

eGFR: estimated glomerular filtration rate, N: number, %: percent

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Associated risk factors of CKD: In the bivariate analysis, older age, obesity, elevated systolic blood pressure (SBP), hypertension, increased waist circumference (WC), type 2 DM, longer duration of diabetes and family history of kidney disease were found to be significantly associated with CKD.

The multivariable logistic regression analysis showed that older age, elevated SBP, increased WC, type 2 DM, and longer duration of diabetes were independently associated with CKD. The odds of CKD was 5.239 (AOR: 5.239, 95% CI: 2.255-12.175) times higher among DM patients aged >60 years compared with DM patients ≤60 years of age. Patients having SBP ≥140mmHg were 3.633 (AOR: 3.633, 95% CI: 1.597-8.265) times more likely to develop CKD than having SBP <140mmHg. Furthermore, patients with type 2 DM and longer duration of diabetes were 3.751 (AOR: 3.751, 95% CI: 1.507-9.336) and 3.380 (AOR: 3.380, 95% CI: 1.393-8.197) times more likely to be affected by CKD than counterparts, respectively (Table 4).

Table 4: Factors associated with CKD

Variables		CKD		COR (95% CI)	P-value	AOR (95% CI)	P-value
		Yes N (%)	**No** N (%)				
Age	≤60years	23(10)	161(70.3)	1.00		1.00	
	>60years	27(11.8)	18(7.9)	10.5(5.013-21.992)	0.000	5.239(2.255-12.175)	0.000
Sex	Male	20(8.7)	94(41)	1.00			
	Female	30(13.1)	85(37.1)	1.659(0.877-3.138)	0.120		
BMI	≤24.9	32(14)	123(53.7)	1.00		1.00	
	25-29.9	9(3.9)	45(19.7)	0.769(0.340-1.736)	0.527	0.226(0.067-0.758)	0.016
	≥30	9(3.9)	11(4.8)	3.145(1.201-8.238)	0.02	0.992(0.255-3.860)	0.991
Systolic BP	<140mmHg	23(10)	140(61.1)	1.00		1.00	
	≥140mmHg	27(11.8)	39(17)	4.214(2.179-8.151)	0.000	3.633(1.597-8.265)	0.002
Diastolic BP	<90 mmHg	44(19.2)	165(72.1)	1.00			
	≥90 mmHg	6(2.6)	14(6.1)	1.607(0.584-4.424)	0.358		
Hypertension	Present	36(15.7)	65(28.4)	4.51(2.266-8.977)	0.000		
	Absent	14(6.1)	114(49.8)	1.00			
WC	Low risk	24(10.5)	131(52.7)	1.00			
	High risk	26(11.4)	48(21)	2.957(1.550-5.640)	0.001	3.430(1.212-9.704)	0.020
Types of DM	Type1	9(3.9)	101(44.1)	1.00		1.00	
	Type2	41(17.9)	78(34.1)	5.899(2.705-12.863)	0.000	3.751(1.507-9.336)	0.004
Duration of DM	<10years	30(13.1)	149(65.1)	1.00		1.00	
	≥10years	20(8.7)	30(13.1)	3.311(1.663-6.591)	0.001	3.380(1.393-8.197)	0.007
FBS	<150mg/dl	17(7.4)	85(37.1)	1.00			
	≥150mg/dl	33(14.4)	94(41)	1.755(0.912-3.378)	0.092		
FH-KD	Yes	11(4.8)	19(8.3)	2.375(1.045-5.398)	0.039		
	No	39(17)	160(69.9)	1.00			
Alcohol consumption	Yes	9(3.9)	52(22.7)	0.536(0.243-1.182)	0.122		
	No	41(17.9)	127(55.5)	1.00			

AOR: Adjusted odds ratio, BMI: Body mass index, BP: Blood pressure, CKD: Chronic kidney disease, COR: Crude odds ratio, DM: Diabetes mellitus, FBS: Fasting blood sugar, FH-KD: Family history of kidney disease, N: Number, P: P-value, WC: Waist circumference, %: percent, 1.00: Reference group.

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DISCUSSION

This study has assessed the prevalence and risk factors of CKD among diabetic adults at University of Gondar Hospital using an estimated glomerular filtration rate (eGFR) and urine albumin according to KDIGO guideline (1). The prevalence of CKD was 21.8% (95% CI: 16% - 27%). Of all our study participants, 9(3.9%) had renal impairment (eGFR < 60 mL/min/1.73m^2) and 46 (20.1%) had albuminuria (Table 2). All of the participants who had renal impairment and of the with albminuria (37/46, 80%) were type 2 DM patients. Nine (3.9%), 32(14.0%), 8(3.5%), and 1(0.4%) DM patients had an estimated GFR of ≥90 ml/min/1.73m^2 (stage 1), 60–89.9 ml/min/1.73m^2 (stage 2), 30-59.9 ml/min/1.73m^2 (stage 3) and <15 ml/min/1.73 m^2 (stage 5), respectively (Table 3).

Our estimate prevalence of CKD was lower than reports from Spain (27.9%) (18), Netherlands (28%) (19), UK (31%) (20), Mediterranean area (34.1%) (21), USA (39.6%) (22) and Japan (42.3%) (23). This difference in CKD prevalence might be because of the differences in case-mix (some of the studies included both type 1 and type 2 DM patients but others included only type 2 DM patients), creatinine and albumin assays, sample size and ethnic variations.

This study found a significant association between CKD and older age (AOR: 5.239, 95% CI: 2.255-12.175). This result is consistent with other studies' outputs in various areas (18, 22, 24-26). As age increases, there is progressive loss of nephrons and decreased renal blood flow, which leads to CKD (27). It is reported that findings of renal insufficiency (eGFR <60 mL/min/1.73 m^2) and albuminuria become more prevalent in older age (28). Similarly, another study reported that individuals aged ≥65 years had 101.5 and 2.5 times greater chance of developing renal insufficiency and proteinuria compared to their counterparts, respectively (29). Thus, screening of CKD in old age group is an important strategy to take an appropriate intervention.

CKD was independently associated with type 2 DM (AOR: 3.751, 95% CI: 1.507-9.336) and longer duration of DM (AOR: 3.380, 95% CI: 1.393-8.197) in our study subjects. This corresponds with the findings of several studies which reported that the likelihood of developing CKD was greater among patients with longer duration of diabetes (24,30,31). CKD is estimated to affect ~50% patients with type 2 DM. Improvement in cardiovascular survival in patient with type 2 DM has contributed to patient surviving longer, allowing sufficient time to develop renal disease (32). However, CKD was not independently associated with type 2 DM in Japanese study (23).

According to our study, elevated SBP (AOR: 3.633, 95% CI: 1.597-8.265) was a risk factor for CKD. This was in agreement with other related studies, in which elevated SBP was independently associated with CKD (18, 33). The beneficial effects of controlling blood pressure (BP) and using antihypertensive agents for kidney function in diabetics has been described in current guidelines, which points out that control of BP reduce the rate of progression of renal disease in diabetes (34,35).

Obesity was not independently associated with CKD in our study. However, it was associated by bivariate analysis (COR: 3.145, 95% CI: 1.201-8.238). In addition, increased WC (AOR: 3.430, 95% CI: 1.212-9.704) was independently associated with CKD in this study. Other similar studies reported as obesity was independent risk factor of CKD (36,37). This variation might be due to differences in lifestyles such as dietary habit, sedentary way of life and physical activities. In addition, our few sample size may affect the statistical tool to show the association between obesity and CKD. Obesity is associated with renal damage leading to albuminuria and poor outcomes of chronic kidney disease, pointing to the need for prevention (38,39).

Single evaluation of eGFR and urine albumin may inflate the prevalence of CKD because of acute kidney infection and creatinine variability. We used dipstick method to measure urine albumin, and we were unable to calculate urine albumin-to-creatinine ratio to determine albuminuria. In addition, our sample size was relatively small and associations between

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different severity levels of CKD with risk factors have not been confirmed. Despite these, the results of this study are important in raising awareness of the community regarding CKD among DM patients at the study setting.

In conclusion, the present study identified high prevalence of chronic kidney disease among diabetic adults. Older age, elevated systolic blood pressure, increased waist circumference, type 2 diabetes mellitus, and longer duration of diabetes were independently associated with chronic kidney disease. Estimated glomerular filtration rate and albuminuria should be determined for diabetes mellitus patients at a regular interval of time for earlier diagnosis of chronic kidney disease to take an appropriate intervention.

ABBREVIATIONS

BMI: Body Mass Index; BP: Blood Pressure; CKD: Chronic Kidney Disease; CVD: Cardiovascular Disease; DBP: Diastolic Blood Pressure; DM: Diabetes Mellitus; eGFR: estimated Glomerular Filtration Rate; ESRD: End-Stage Renal Disease; GFR: Glomerular Filtration Rate; KDIGO: Kidney Disease Improving Global Outcome; MDRD: Modification of Diet in Renal Disease; SBP: Systolic Blood Pressure.

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