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Prevalence of chronic kidney disease and associated risk factors among diabetic patients in southern Ethiopia

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Abstract: Background: Chronic kidney disease (CKD) in diabetes is associated with an increased risk of premature mortality, kidney failure and cardiovascular disease. No studies are available on the prevalence of CKD among diabetics in Ethiopia. The aim of this study was to determine the prevalence of CKD and its associated risk factors among diabetic adults attending Butajira hospital of Southern Ethiopia based on estimated glomerular filtration rate (GFR). Methods: A facility based cross sectional study was conducted in Butajira hospital, southern Ethiopia among 214 randomly selected diabetic adults. Demographic, clinical, and laboratory data were collected from September 1, 2013 to October 31, 2013. The simplified Modification of Diet in Renal Disease (MDRD) and Cockroft-Gault (CG) equations were used to estimate GFR (eGFR) from serum creatinine value. SPSS 20.0 Software was used for data analysis. Results: 39 (18.2%) and 51 (23.8%) of the study participants were found to have CKD, as defined by eGFR < 60 ml/min/1.73 m^2, according to the MDRD and Cockroft-Gault equations, respectively. Of these; 17.3 and 22.9% have stage 3 CKD, and 0.9% have stage 4 CKD, respectively. Significant risk factors for CKD in the study subjects when using either the MDRD or C-G equation were older age, longer duration of diabetes, family history of kidney disease, and poor glucose control ($P < 0.05$). Additionally, female sex ($P < 0.008$) and obesity ($P < 0.038$) were independent risk factors for CKD when defined by the MDRD, and type 2 diabetes was when defined by C–G ($P < 0.03$). Conclusion: CKD was present in not less than 18.2% diabetic adults attending the follow up clinic at Butajira hospital, in southern Ethiopia. Risk factors for CKD were similar to those reported in developed country studies. Using the MDRD equation led to a lower prevalence of CKD and a better risk categorization than did by C-G equation, thus contributing to better management of clinical outcomes in diabetic care.

Keywords: Chronic Kidney Disease, Diabetes, Risk Factors, Estimated Glomerular Filtration Rate

1. Introduction

Chronic kidney disease (CKD) is a world-wide public health problem associated with adverse outcomes of kidney failure, cardiovascular disease (CVD), and premature death [1]. It has been estimated that more than 500 million individuals globally have CKD, defined by either kidney damage or glomerular filtration rate (GFR) < 60 ml/min/1.73 m^2 for ≥ 3 months, regardless of the cause [2,3]. Diabetes is a major public health problem around the world, estimated to affect more than 371 million people in 2012, and is the leading cause of end stage renal disease (ESRD) in both developed and emerging nations [4,5].

The risk of all cause and cardiovascular mortality, kidney failure, cardiovascular disease and hospitalizations is higher among diabetic patients with CKD, as defined by estimated GFR (eGFR) < 60 ml/min/1.73 m^2, than among those with normal renal function [6–8]. Additionally, affected patients have an increased risk of complications, such as hypertension, anemia, malnutrition, bone and mineral disorders, retinopathy and neuropathy, and thus suffer extra morbidity and mortality [9,10]. There is also an even higher prevalence of hypoglycemia due to decreased clearance of antidiabetic agents or impaired renal gluconeogenesis, and progressive renal dysfunction reduces drug elimination and prolongs exposure to higher drug levels [11].

Routine screening for CKD based on estimated GFR (eGFR) derived from serum creatinine measurements is recommended for diabetes care [12], as reduced eGFR is an independent predictor of cardiovascular and renal events and mortality in people with diabetes [6,8]. Furthermore, given that CKD (defined as eGFR < 60 ml/min/1.73 m^2) is often not detected until it is advanced, targeted screening of diabetes based on eGFR is cost effective and has potential benefits, such as early identification and treatment of affected patients [13].

Although estimating the prevalence of CKD combined with identification and treatment of risk factors is central to disease management and prevention planning, there are virtually no published studies on the prevalence and risk factors of CKD among diabetic patients in Ethiopia. Thus, the aim of this study was to estimate the prevalence of CKD among diabetic adults attending Butajira hospital of Southern Ethiopia, and to identify the associated risk factors based on eGFR derived from the MDRD Study and Cockcroft-Gault equations.

2. Materials and Methods

A facility based across sectional study was conducted in Butajira hospital of Southern Ethiopia over a period of two months (September 2013 to October 2013). The hospital is located in Butajira town, 130 km mid-south of the capital of Ethiopia, Addis Ababa. The hospital registers and treats all diagnosed diabetic patients and provides primary diabetes patient care.

The study was conducted among two hundred fourteen randomly selected diabetic patients who were registered at the follow up clinic of Butajira hospital. Participants, who were included in this study after being screened and counseled by their clinicians, were adults (≥18 years) and attending the hospital for follow up. Exclusion criteria were pregnancy, hospitalization, acute illnesses (fever), and none fasting. Patients found to have eGFR > 200 ml/min/1.73 m^2 or those receiving dialysis were also excluded.

The study participants underwent interview for collecting demographic and risk factor variables using a structured questionnaire designed by the investigators. Physical examinations, including measurement of height, weight and blood pressure were performed. Weight (kg) and height (meters) were assessed in light clothing without shoes and body mass index (BMI) was calculated as weight divided by height squared (kg/ m^2). Obesity was defined as a BMI ≥30 kg/m^2. Blood pressure was measured three times using a standard mercury sphygmomanometer after 5 min of rest in sitting position and then averaged. Systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg or current use of blood pressure-lowering medication was used to define hypertension.

2.1. Laboratory Measurements and Definitions

A fasting blood sample was collected from each participant using standard venipuncture techniques and biochemical analysis were performed using HumaStar 80 analyzer (Human Diagnostics, Germany). Serum glucose levels were measured using the enzymatic GOD-PAP method (Human Diagnostics, Germany). Serum creatinine was measured by kinetic alkaline picrate method (Human Diagnostics, Germany) with calibration traceable to reference material NIST SRM 909B level 2.

The GFR was estimated using the Modification of Diet in Renal Disease (MDRD) Study equation [14]: 186 × [serum creatinine (mg/dl)]$^{-1.154}$ × (age)$^{-0.203}$ × (0.742 if female) x (1.210,if African American), and Cockcroft-Gault formula[15] (normalized for the body surface area [BSA]): (140 - age [years]) x weight (kg) x (0.86, if female) x 1.73/72 x serum creatinine (mg/dl) x BSA (m^2).

All the participants with eGFR values of < 60 ml/min/1.73 m^2 screened at the 1st visit were advised to have their serum checked for creatinine two weeks after the first check-up. The CKD stages were categorized based on the classification system established by the National Kidney Foundation - Kidney Disease Outcomes Quality Initiative (K/DOQI) classification. For the purposes of this study, CKD was defined as K/DOQI CKD stages 3–5 (eGFR<60 ml/min/1.73 m^2): with eGFR 30–59, 15–29 and <15 ml/min/1.73 m^2, respectively. Stage 3 was further classified into 3A (45–59.9) and 3B (30–44.9)[3,16].

2.2. Statistical Analysis

The data was entered in to "EpiInfo version 3.1" and was analyzed using SPSS version 20.0 statistical software. Normally distributed variables are summarized by their means and SDs, median and range are used for skewed data. Chi-square (x^2) analysis was used for between-group comparisons of CKD proportions. Multivariate stepwise logistic regression was performed by including variables that were significant at P value < 0.02. Adjusted odds ratio (AOR) and their corresponding 95% confidence intervals (CI) were expressed to describe the association of risk factors with CKD (dependent variable). For all statistical analyses P value < 0.05 were considered significant.

2.3. Ethical Consideration

The ethical issue of this study was approved by the Ethical Committee of the college of Public Health and Medical Sciences, Jimma University. All participants were given detail information about the objective and purpose of the study and verbal consent was obtained from each participant.

3. Results

3.1. Demographic and Clinical Characteristics of Participants

For the included two hundred fourteen eligible diabetic participants, demographic, clinical, and laboratory data were collected between September 1, 2013 and October 31, 2013. The mean age of participants was 45 ± 14.5 years. Of

the total participants, 81.3% were less than 60 years old; 57.5% were males and 56.3% had type 2 diabetics. Mean body mass index (BMI) was 25.26 ± 4.35Kg/m^2. Mean values for systolic and diastolic BP were 121 ± 17 and 79 ± 10 mmHg, respectively. Mean fasting serum glucose was 172.85 ± 84.94 mg/dl. Mean serum creatinine was 1.07 ± 0.33 mg/dl. The mean GFR values estimated according to the MDRD and C-G equations were 96.70 ± 35.68 and 83.61 ± 29.73ml/min/1.73m^2, respectively.

3.2. Prevalence of CKD

Of the total participants, the estimated prevalence of CKD, defined by eGFR <60 ml/min/1.73 m^2, in this study was 18.2% (CI 95% = 12.3% - 23.2%) and 23.8% (CI 95% = 17.5% - 29.9%) when defined by according to the MDRD and C-G equations, respectively. By stages, the prevalence was; 17.3% with stage 3 CKD (14.0% stage 3A and 3.3% stage 3B), and 0.9% with stage 4 CKD by MDRD; whereas 22.9% with stage 3 (15.0% stage 3A and 7.9% stage 3B) and 0.9% with stage 4 by C-G (Table 1).

Table 1. *Prevalence of CKD according to the MDRD and Cockcroft-Gault equations (n =214).*

Stage	Description	eGFR (ml/min/1.73m^2)	MDRD N (%)	Cockcroft-Gault N (%)
0-2	CKD absent	≥60	175 (81.8)	163 (76.2)
3-5	CKD present	<60	39 (18.2)	51 (23.8)
3	Moderate ↓ GFR	30-59.9	37 (17.3)	49 (22.9)
3A	Mild to moderate GFR	45-59.9	30 (14.0)	32 (15.0)
3B	Moderate to severe ↓ GFR	30-44.9	7 (3.3)	17 (7.9)
4	Severe ↓ GFR	15-29.9	2 (0.9)	2 (0.9)

By age group, CKD prevalence was significantly higher among participants >60 years old than ≤ 60 years old: 42.9% vs. 14.5% (p < 0.001) and 64.3% vs. 17.7% (p < 0.001) according to the MDRD and C-G equations, respectively. CKD prevalence was higher in females than males: 28.6% vs. 10.6% by MDRD (P = 0.001), and 31.9% vs. 7.0% by C-G (P = 0.018). The prevalence was also significantly higher among type 2 diabetic participants than type 1: 28.1% vs. 17.9% by MDRD (P < 0.001), and 37.7% vs. 8.0% by C-G (P < 0.001) (Table 2).

Longer duration of diabetes, defined as duration more than 10 years, was reported in 31.8% of the participants and was associated with a high prevalence of CKD (32.4% and 39.7%) compared to shorter duration: 32.4% vs. 11.6% by MDRD (P < 0.001), and 39.7% vs. 16.4% by C-G (P < 0.001). CKD prevalence was significantly higher among participants with low monthly income <500ETB than those with ≥500ETB: 36.1% vs. 12.6% by MDRD (P = 0.005), and 35.4% vs. 17.0% by C-G (P = 0.002). However, there were no significant differences in CKD prevalence among participants with and without current smokers, and among those with less than high school and high school or higher education levels (Table 2).

Family history of kidney disease (FH-KD), present in 18.7% of participants, was associated with a higher prevalence of CKD than its absence: 42.5% vs. 12.6% by MDRD (P<0.001), and 55.0% vs. 16.7% by C-G (P<0.001). Furthermore, obesity that was reported in 14.5% of participants was associated with a high prevalence of CKD compared with lack of obesity: 45.2% vs. 13.7% by MDRD (P < 0.001), and 45.2% vs. 20.2% by C-G (P = 0.003) (Table 2).

Hypertension, reported in 58.2% of the total participants, was not associated with a high proportion of CKD; however, elevated systolic blood pressure (≥140mmHg) was associated with a higher prevalence of CKD: 30.0% vs. 15.5% by MDRD (P = 0.032), and 42.5% vs. 19.5% by C-G (P = 0.002). Uncontrolled diabetes associated with high fasting serum glucose (FSG), defined as FSG level ≥150 mg/dl, was found in 60.3% of participants and was associated with higher prevalence of CKD (24.0% and 31.0%) compared with controlled diabetes: 24.0% vs. 9.4% by MDRD (P=0.007), and 31.0% vs. 12.9% by C-G (P =0.002) (Table 2).

Table 2. *Distribution of CKD by characteristics of study participants using the MDRD and Cockcroft-Gault equations (n = 214).*

Variables	N	MDRD		Cockcroft-Gault	
		%CKD	*P*	%CKD	*P*
Age			*<0.001*		*<0.001*
>60 Year	40	42.9		64.3	
≤60 Years	174	14.5		17.7	
Sex			*0.001*		*0.018*
Male	123	10.6		17.9	
Female	91	28.6		31.9	
Types of diabetes			*<0.001*		*<0.001*
Type 1	100	7.0		8.0	
Type 2	114	28.1		37.7	
Duration of diabetes			*<0.001*		*<0.001*
≥10 years	68	32.4		39.7	
<10 years	146	11.6		16.4	
Education			*0.164*		*0.283*
< High School	169	20.1		25.4	
≥ High School	45	11.1		17.8	
Income			*0.005*		*0.002*
< 500ETB	79	27.8		35.4	
≥ 500ETB	135	12.6		17.0	
Family history of KD			*<0.001*		*<0.001*
Present	40	42.5		55.0	
Absent	174	12.6		16.7	
Smoking status			*0.310*		*0.461*
Current Smokers	13	7.7		15.4	
Non Smokers	201	18.9		24.4	
Obesity			*<0.001*		*0.003*
Present	31	45.2		45.2	

Variables	N	MDRD		Cockcroft-Gault	
		%CKD	*P*	%CKD	*P*
Absent	183	13.7		20.2	
Hypertension			*0.833*		*0.731*
Present	113	17.7		24.5	
Absent	101	18.8		22.8	
Systolic blood pressure			*0.032*		*0.002*
≥140 mmHg	40	30.0		42.5	
<140 mmHg	174	15.5		19.5	
Diastolic blood pressure			*0.434*		*0.092*
≥90 mmHg	45	22.2		33.3	
<90 mmHg	169	17.2		21.3	
Fasting Serum Glucose			*0.007*		*0.002*
≥150mg/dl	129	24.0		31.0	
<150mg/dl	85	9.4		12.9	

3.3. Risk Factors Associated with CKD

The univariate analysis showed significant association between CKD (eGFR <60 ml/min/1.73 m^2) and the following variables; older age (>60 years), female gender, type 2 diabetes, low monthly income, longer duration of diabetes, family history of kidney disease, elevated systolic blood pressure, obesity, high FSG. 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.

In multivariate analysis, older age (adjusted OR = 5.30, CI 1.81-15.56), female sex (adjusted OR= 3.34, CI 1.38-8.10), longer duration of diabetes (adjusted OR = 4.08, CI 1.70-9.77), family history of kidney disease (adjusted OR = 3.16, CI 1.29-7.77), obesity (adjusted OR = 2.75, CI 1.01-7.51) and poor glucose control (high FSG) (adjusted OR = 4.65, CI 1.69-12.76) were independently associated with CKD when defined by the MDRD equation. All the above variables, except sex and obesity, were independently associated with CKD when renal function was defined by C-G. Additionally, type 2 diabetes (adjusted OR = 2.86, CI 1.11-7.39) was found to be independently associated with CKD when C-G equation was used (Table 3).

Table 3. *Risk factors associated with CKD according to the MDRD and Cockcroft-Gault equations (n = 214).*

Risk Factors		MDRD equation		Cockcroft-Gault equation	
		Adjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Age	≤60 years	1.00		1.00	
	>60 years	5.30 (1.81-15.56)	*0.002*	11.40 (3.97-32.78)	*<0.001*
Sex	Males	1.00		1.00	
	Females	3.34 (1.38-8.10)	*0.008*	2.28 (0.97-5.37)	*0.058*
Types of diabetes	Type 1	1.00		1.00	
	Type 2	0.46(0.16-1.23)	*0.141*	2.86 (1.11-7.39)	*0.030*
Duration of diabetes	<10 years	1.00		1.00	
	≥10 years	4.08 (1.70-9.77)	*0.002*	3.57 (1.51-8.41)	*0.004*
FH-KD	Absent	1.00		1.00	
	Present	3.16 (1.29-7.77)	*0.012*	4.12 (1.79-10.88)	*0.001*
Obesity	No	1.00		1.00	
	Yes	2.75 (1.01-7.51)	*0.038*	1.22 (0.43-3.50)	*0.710*
FSG	≤150mg/dl	1.00		1.00	
	>150mg/dl	4.65 (1.69-12.76)	*0.003*	3.66 (1.43-9.35)	*0.007*

FH-KD = Family history of kidney disease. FSG = Fasting Serum Glucose.

4. Discussion

Although several studies in developed countries show a high prevalence of CKD among patients with diabetes, this study was the first to assess the prevalence and risk factors of CKD among diabetic adults in Ethiopia with the use of estimated GFR derived from serum creatinine and estimating equations. The prevalence of CKD (eGFR <60 ml/min/1.73 m^2) was 18.2% using the MDRD study and 23.8% by C-G equations; CKD stage 3 was the most prevalent stage, 17.3 and 22.9% by both the MDRD and C-G, respectively.

Our prevalence estimate of CKD using the MDRD equations was higher than 15.1% reported in the US NHANES III study [17], but lower than that of 27.5% and 31% reported in two UK studies [18,19], and 33.1% in Japanese study [20]. These differences in CKD prevalence might be because of the differences in case-mix or differences in creatinine assays and calibration, or due to the incorporation of a 0.808 coefficient to the MDRD equation for Japanese population.

When using the C-G equation to assesses renal function, our prevalence estimate of CKD was comparable to the Sub-Sahara African, Tanzania study which reported 24.7% of patients with diabetes as having CKD as defined by eGFR <60 ml/min/1.73 m^2; with 20.9% stage 3 CKD [21]. 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.

As for risk factors, this study found a significant association between older age and CKD whatever the equations were used. This is consistent with findings from other studies [19,20,22,23]. It was reported that the eGFR diminishes with age, and at age ≥60 years; 25% of the diabetics will have eGFR <60 mL/min/1.73 m^2 (24). Thus, to screen diabetics in this age group is an important strategy for the detection of CKD and to improve the outcomes.

Gender differences have a significant association with CKD in this study when renal function was assessed by the MDRD equation, but not by C-G. This is in agreement with the findings of the UK and Sweden studies when using the MDRD [19,22], but not with the Japanese's study, in which the male gender was reported to be a non-modifiable risk factor for CKD [20]. Furthermore there was a strong association between female sex and CKD in the UK and Sweden studies using C-G equation [22,23]. The possible explanation for this might be due to the higher proportion of obese females than males and the equation being adjusted for BSA in this study, in which the C-G adjusted for BSA overestimated GFR in diabetics with obesity [25].

As expected, there was a significant association between CKD and the presence of longer duration of diabetes and a family history of kidney disease in this study subjects using either the MDRD or C-G equation. This corresponds with the findings of several studies, which reported that the like hood of developing reduced eGFR was greater among patients with longer duration of diabetes and among those with or whose parents has kidney disease [19,20,22].

This study also found a significant association between obesity and CKD when renal function was assessed by the MDRD equation, but not by C-G. This corresponds with the findings of two different UK studies using a similar definition of eGFR [20,22]. However, low BMI was independently associated with CKD by C-G in the UK study [22]. This might be explained by the C-G equation used in this study, which is adjusted for BSA [25]. A significant association between Type 2 diabetes and CKD was found in the study subjects when C-G equation was used to define renal function, but not by the MDRD. Similarly, the UK and Japanese studies reported that Type 2 diabetes was not associated with CKD when using the MDRD equation [19,20].

In this study, uncontrolled diabetes corresponding to high fasting serum glucose was associated with CKD when defined by either equation; in contrast with findings that identified patients with CKD (eGFR <60 ml/min/1.73m^2) had better glycaemic control [19,20]. However, our finding corresponds with the current guidelines reported that the prevalence of kidney disease was fivefold greater among patients with uncontrolled diabetes compared with controlled [3,12]. This is attributed to the early development of end-organ damage and late presentation for medical care in patients with poorly controlled diabetes.

Hypertension and elevated systolic blood pressure were not independently associated with CKD when renal function was defined by either equation in this study. It showed that the presence of elevated systolic BP was a significant risk factor for CKD by univariate analysis but not by multivariate analysis, and this was in contrast with other related studies, in which elevated systolic BP was independently associated with CKD when defined by the MDRD [19,22] or C-G equations [22,23]. The beneficial effects of controlling blood pressure and using antihypertensive agents on kidney function in diabetics has been described repeatedly in current guidelines [3,12].

Although this study is the first of its type in Ethiopia, it has a few limitations. First, it is limited by the fact that the K/DOQI proposed using eGFR and albuminuria to evaluate and classify the stages of CKD, were lack of information regarding albuminuria made it difficult to confirm whether patients with eGFR ≥60 ml/min/1.73m^2 were having CKD or not. Second, calculated GFR rather than measured GFR was used to diagnose renal insufficiency and the MDRD equation used in this study is not validated among adult populations of Ethiopian origin. The other limitation of this study is that the data are cross-sectional, not longitudinal, preventing assessment of whether risk factors caused or resulted from CKD. Moreover, due to the relatively small samples in this study, associations between different severity levels of CKD have not been studied. Follow-up data are required on how the identified associations with decreased eGFR predict clinical outcome. Our study also has major strengths, including the diagnosis of CKD based on eGFR on multiple measures to establish chronicity, and the provision of CKD within a high-risk group, a reliable scenario of the current diagnostic approach for targeted screening of CKD in primary care.

5. Conclusion

In conclusion, the study identified a high prevalence of CKD (ranging from 18.2-23.8% depending on the formula used to estimate GFR) among diabetic adults attending Butajira hospital of southern Ethiopia. Risk factors for CKD such as ageing, longer duration of diabetes and poorly controlled diabetes were similar to those reported in developed country studies. This study, therefore, proposes that a nationwide survey to be conducted encompassing the entire diabetes population to find out the prevalence of CKD and its associated risk factors, so that a preventive strategy or an entire defensive framework could be adopted or planned to reduce the disease and complications related to it in the community.

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