

Impaired Renal Function among Older People Living with Diabetes Mellitus and Hypertension in Southwestern Uganda

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ARTICLE INFO

Received Date: October 31, 2023

Accepted Date: December 01, 2023

Published Date: December 06, 2023

KEYWORDS

Hypertension; Diabetes; Chronic kidney disease

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Citation for this article: Rose Muhindo, Judith Owokuhaisa, Catherine Abaasa, Abel Mwine, Godfrey Rukundo, Elijah Bulega, Cyrus Biyinzika, Benjamin Mwine, Adrian Kayanja, Andrew Mutekanga and Grace Kansiime. Impaired Renal Function among Older People Living with Diabetes Mellitus and Hypertension in Southwestern Uganda. Journal of Nephrology & Kidney Diseases. 2023; 5(1):135

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ABSTRACT

Background: Hypertension and Diabetes Mellitus (DM) are linked to an increased risk of chronic kidney disease (CKD). As life expectancies rise, so will the proportion of the population over the age of 65 who have kidney disease, both in Uganda and throughout Africa and the world. We aimed to determine the prevalence of impaired renal function and related variables in patients aged ≥ 50 years with diabetes and/or hypertension.

Methods: From November 2022 to January 2023, a cross-sectional study on 222 people with diabetes mellitus, hypertension, or both who were 50 years of age or older was conducted at Mbarara Regional Referral Hospital (MRRH). Data on demographics, health, and laboratory tests were gathered. To identify the variables linked to impaired renal function, multivariate logistic regression was employed.

Results: Out of 222 patients, 68.9% were female. The mean age \pm standard deviation (SD) was 63.9 ± 10.2 years. 96(43.2%) had hypertension only, 34 (15.3%) had DM only while 92 (41.4%) had both diabetes and hypertension. The median serum creatinine level was 1.01 mg/dl (0.85–1.14), and the mean eGFR was 69.9ml/min/1.73m² (19.3). The overall prevalence of eGFR < 60 ml/min/1.73 m² was 32.8% (95% CI, 26.61–39.71). 40(18.2%) of the patients were classified as normal eGFR (≥ 90 ml/min/1.73 m²), 112(50.9%) as low eGFR (60–89 ml/min/1.73 m²), 62(28.2%) as moderately reduced eGFR (30–59 ml/min/1.73 m²), 6(2.7%) as severely reduced eGFR (15–29 ml/min/1.73m²). None of the patients had eGFR < 15 ml/min/1.73m². Factors associated with impaired renal function were age ≥ 65 years (aOR, 2.06; 95% CI, 1.04-4.09; P =0.037) and passage of frothy urine (aOR, 2.48; 95% CI 1.23-4.99; P =0.011).

Conclusion: 3 in 10 elderly patients with diabetes and/or hypertension have impaired renal function. The associated factors could help clinicians identify patients early and initiate renal protective treatment that could delay disease progression.

Keywords: Hypertension; Diabetes; Chronic kidney disease

ABBREVIATIONS AND ACRONYMS

AKI:	Acute Kidney Injury
AKIN:	Acute Kidney Injury Network
CBC:	Complete blood cell count
CKD:	Chronic kidney disease
DM:	Diabetes Mellitus
GFR:	Glomerular filtration rate
HIV:	Human Immunodeficiency Virus
MRRH:	Mbarara Regional Referral Hospital
MUST:	Mbarara University of science and Technology
NCDs:	Non- Communicable Diseases
RFT:	Renal function test
T2DM:	Type 2 Diabetes Mellitus
KDIGO:	Kidney Disease Improving Global Outcome

INTRODUCTION

The burden of kidney disease worldwide has increased, as has the number of persons with end-stage renal disease that require dialysis and transplantation. A significant global public health issue is the link between diabetes mellitus (DM), hypertension, and an increased risk of chronic kidney disease (CKD). Around the world, the incidence and prevalence of impaired renal function are increasing, affecting between 10% and 13% of the population [1,2]. According to some reports, 13.9 % of people in sub-Saharan Africa have CKD [3]. It has been determined that 15.3 % of the general in-patient population in Mbarara has CKD [4]. Studies among high-risk populations like the elderly with diabetes and/or hypertension are still lacking.

Renal impairment is greatly influenced by hypertension and diabetes. Globally, 639 million people with hypertension (672 million total) lived in low- and middle-income countries in 2000, adding a burden of 26% to society [5]. With an estimated global incidence of 4.4%, the number of people with DM is projected to increase from 171 million in 2000 to 366 million in 2030 [6]. Impaired renal function, diabetes, and hypertension are not properly identified or treated in settings with insufficient resources for a variety of reasons [7].

Patients with impaired renal function are susceptible to developing end-stage renal disease. The management of advanced CKD includes renal replacement therapy, which is costly and not widely available in resource constrained settings. A rise in renal disease is linked to a higher risk of unfavorable

outcomes and higher healthcare expenses for patients, caregivers, families, and communities [1].

Because impaired renal function is silent in early stages, it is recommended that patients at risk (for example patients with diabetes or hypertension) should be screened regularly. According to the UK guidelines, all adults at risk for obstructive kidney disease and those who have common cardiovascular diseases should be screened at least once a year, whereas US kidney disease outcomes quality initiative (US KDOQI) guidelines include patients aged >60 years as well. However, due to limited resources, patients at risk of CKD are not regularly screened.

In Uganda, Africa, and globally, the elderly population is most likely to rise with an increase in life expectancy, as is the prevalence of older persons with kidney disease [1]. With increasing age, there is a physiological decline in kidney function and patients will occasionally present with senile nephrosclerosis.

Most non-communicable diseases (NCDs) can be effectively controlled to reduce morbidity and mortality when identified early by instituting dietary changes, lifestyle adjustments, and the use of the appropriate medications when necessary.

Most sub-Saharan African nations, including Uganda, have not given impaired renal function the attention it deserves as a non-communicable disease [8]. It is well recognized that kidney disease has a major influence on one's quality of life and is associated with an increase in mortality [9].

An in-depth knowledge of the burden and factors associated with impaired renal function in patients aged 50 years and above with diabetes and/or hypertension paves the way for treatments that focus on modifiable risk factors to lower morbidity and mortality. Our main objective in this research was to identify the prevalence of impaired renal function, clinical characteristics and related variables in patients 50 years of age and older who also had diabetes or hypertension.

METHODOLOGY

A cross-sectional study was conducted from November 2022 to January 2023 and included patients aged 50 years and above attending the medical outpatient and diabetes clinics of Mbarara Regional Referral hospital (MRRH) and living with Diabetes Mellitus, hypertension or both and enrolled 222

patients. The distance between MRRH and Kampala, the country's capital, is roughly 260 kilometers. The hospital has a 350 bed capacity and acts as a teaching hospital for Mbarara University of Science and Technology (MUST). The medical outpatient and diabetes clinics run on a weekly basis and are managed by specialist physicians and resident doctors. These clinics manage an average of 80 patients weekly. The hospital has capacity for both imaging and laboratory tests.

Systematic random sampling was employed to recruit study participants. A questionnaire was administered to consented participants who were not known to have a prior diagnosis of kidney disease. The questionnaire was used to collect bio data, clinical presentation, other co morbidities, duration of disease and type of medication. Blood samples were obtained and taken to the Mbarara regional referral hospital laboratory and assayed for serum creatinine and urea. A single measurement of serum creatinine was taken.

The MUST Research and Ethics Committee (Ref; MUST-2022-586) and the management of MRRH gave their approval to this study. The Helsinki Declaration was strictly followed throughout the duration of this investigation, and all procedures employed in this study were completed in accordance with all applicable laws and regulations.

Definition of terms

Without utilizing the coefficient for African Americans, the estimated glomerular filtration rate (eGFR) was determined using the CKD-Epi equation [10]. Based on recommendations from the National Kidney Foundation, impaired renal function was divided into five stages similar to CKD, as follows (without including proteinuria): normal eGFR (90 ml/min/1.73 m²); low eGFR (60-89 ml/min/1.73m²); moderately reduced eGFR (30-59 ml/min/1.73m²); severely reduced eGFR (15-29 ml/min/1.73m²) [11]. Because we lacked measurements of urine protein excretion or a second creatinine after three or more months, we employed impaired renal function for the study.

Current alcohol use was defined as having consumed a drink containing alcohol within the last 12 months. A participant was considered to be a smoker if he/she reported a history of current use of cigarettes. Chronic Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) use was defined as the use of NSAIDs more than 3 times a week for more than 3 months. We also reported the use of herbal medicines as usage of any

herbal formulation for therapeutic purposes in the last 3 months. We considered engagement in physical activity if a participant reported engaging in physical exercises for a minimum of 30 minutes 3 times a week.

STATISTICAL ANALYSIS

In REDCap, a web-based data analysis program, data were entered and stored (Vanderbilt University, Nashville, NT, USA). STATA was used for statistical analysis (STATA Corp, College Station, Texas, USA version 16). For eligible individuals, descriptive statistics were presented as means with standard deviations or medians with interquartile ranges. Prevalence was defined as the percentage of patients with impaired renal function in relation to all patients. We employed simple and multiple logistic regression to determine the factors associated with impaired renal function. Factors which had biological plausibility and those with a p value <0.2 at univariate analysis were subjected to multiple logistic regression analysis. A p value < 0.05 was considered statistically significantly associated with impaired renal function.

RESULTS

Table 1: Socio-demographic characteristics of study participants.

Characteristic	N	
Female, n (%)	222	153(68.9)
Age, mean (± SD) -years-	222	63.9(10.2)
≤65 years, n (%)		121(54.5)
≥65 years, n (%)		101(45.5)
Level of education, n (%)	220	
Not educated		48(21.6)
Primary education		113(50.9)
Secondary education		38(17.1)
Tertiary education		23(10.4)
Type of residence, n (%)	222	
Rural		109(49.1)
Urban		113(50.9)
Marital status, n (%)	221	
Single		11(4.9)
Married		142(64.3)
Divorced/separated		67(30.3)
Widowed		1(0.5)
Peasant farmers, n (%)	220	117(53.2)
Smoking, n (%)	220	41(18.6)
Current alcohol use, n (%)	222	25(11.3)
Engage in physical activity, n (%)	220	113(51.3)
Use of herbal medications, n (%)	220	142(64.5)
Current use of NSAIDs, n (%)	196	4(2.04)

SD: Standard deviation; NSAIDs: non-steroidal anti-inflammatory drugs

From November 2022 to January 2023 a total of 226 participants aged 50 years and above and living with diabetes and/or hypertension were consecutively enrolled, a total of 4 patients were excluded because of missing results.

Of the 222 patients enrolled, 153 (68.9%) were female. The mean age \pm standard deviation (SD) was 63.9 ± 10.2 years. 41(18.5%) of the participants had a history of smoking while 25 (11.3%) reported current use of alcohol. 142/220 (64.5%) of the participants had a history of using herbal medications. Only 4/196 (2.04%) were taking non-steroidal anti-inflammatory agents. These results are presented in Table 1.

Clinical and laboratory characteristics of the study participants

96 (43.2%) of the participants had hypertension only, 34 (15.3%) had diabetes mellitus only, while 92 (41.4%) had both diabetes and hypertension. The median duration of disease was 5 (IQR, 2 - 10) years. 62(27.9%) of the participants reported a history of passing frothy urine. The median serum creatinine was 1.01 (IQR, 0.85 - 1.14) mg/dl, the mean eGFR was $69.9 (\pm 19.30)$ ml/min/1.73m². These clinical characteristics are shown in Table 2.

Table 2: Clinical characteristics of study participants.

Variable		N	
Comorbidities	Diabetes, n (%)	222	34 (15.3)
	Hypertension, n (%)	222	96 (43.2)
	Diabetes and Hypertension, n (%)	222	92 (41.4)
	HIV, n (%)	222	12(5.4)
Clinical presentation	Body swelling	222	87(39.2)
	Passage of frothy urine	222	62 (27.9)
	Reduced urine output (<400mls)	222	12 (5.4)
Duration of disease	Years, median, (IQR)	222	5 (2 - 10)
Blood pressure	SBP, median (IQR) – mmHg	222	150.5 (133-164)
	DBP, median (IQR) – mmHg	222	82 (75 – 92)
Laboratory parameters	RBS, median (IQR) – mmol/l	182	5.95 (4.13 – 8.9)
	HbA1C, median (IQR) - %	202	6.55 (5.9 – 7.8)
	Serum creatinine, median (IQR) –mg/dl	220	1.01 (0.85 – 1.14)
	eGFR, mean (SD) – ml/min/1.73m ²	215	69.9 (19.30)
	Total cholesterol, mean (SD), mg/dl	219	163 (57.20)
	LDL – C, mean (SD) – mg/dl	220	84.95 (40.11)
	HDL-C, mean (SD) – mg/dl	219	45.84 (17.26)
	Triglycerides, median (IQR) – mg/dl	219	148 (98 -218)

Abbreviations: HIV: Human immunodeficiency virus; IQR: Inter quartile range; SD: Standard deviation; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; RBS: Random blood sugar; HbA1C: Glycated Haemoglobin; eGFR: estimated Glomerular filtration rate; LDL-C: Low density lipoprotein cholesterol; HDL-C: High density lipoprotein cholesterol; mg/dl: milligrams per deciliter

Prevalence of impaired renal function among patients aged ≥ 50 years living with DM and/ or HTN

Impaired renal function with eGFR < 60 ml/min/1.73m² was prevalent overall at 32.8%. Majority of the patients, 112(50.9%) had low eGFR (60–89 ml/min/1.73m²) while 62(28.2%) had moderately reduced eGFR (30–59 ml/min/1.73 m²). 6(2.7%) had severely reduced eGFR (15-29 ml/min/1.73m²). This data is presented in Figure 1.

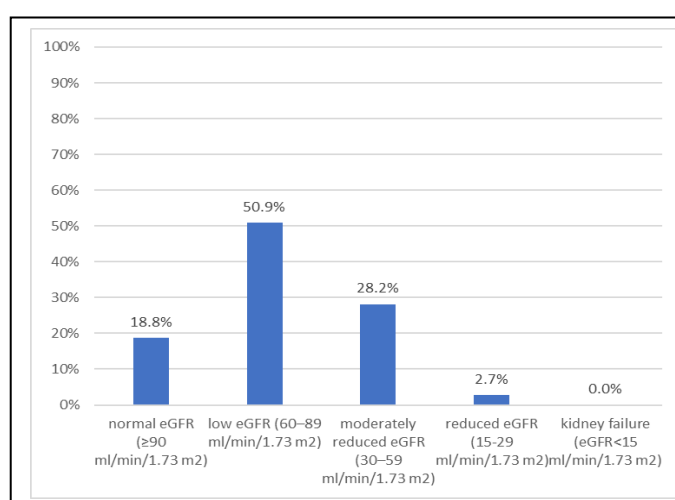


Figure 1: Prevalence of impaired renal function among patients aged 50 years and above, living with DM and /or HTN.

Factors associated with impaired renal function among patients aged 50 years and above, living with DM and /or HTN

The factors associated with impaired renal function were age ≥ 65 (aOR, 2.06; 95% CI, 1.04-4.09; P =0.037) and passage of frothy urine (aOR, 2.48; 95% CI 1.23-4.99; P =0.011). Table 3 displays specifics of the bivariate and multivariate analyses.

DISCUSSION

Our study reports a prevalence of impaired renal function (eGFR < 60 ml/min/1.73m²) of 32.8% among patients ≥ 50 years living with DM and/ or HTN. This finding highlights a high burden of undiagnosed impaired renal function among patients with hypertension and /or diabetes. Findings of a study done in the same region by Kalima et al., reported that hypertensive

patients were 4 times at risk of developing renal impairment [4]. The prevalence in our study is higher than what was found in hypertensive patients at the national referral hospital in Uganda (17.2%) [12]. Our prevalence may be higher than this because we enrolled much older patients. However, this prevalence is in the range of the one reported by a recent systematic review that reported a proportion of kidney disease in diabetes patients between 11% to 83% and 13% to 51% in those with hypertension respectively [13]. This study should typically raise concerns among medical professionals and even policymakers due to Uganda's lack of skilled specialists and dialysis facilities, which contribute to the country's higher than average burden of kidney disease [14].

Table 3: Multivariate analysis of factors associated with impaired renal function among patients aged 50 years and above and living with DM and/or HTN.

Variable	Category	cOR	p-value	aOR	p-value
Gender	Female	Ref			
	Male	0.62(0.32-1.21)	0.164	0.60(0.29-1.25)	0.178
Age (years)	≤ 65	Ref			
	>65	2.14(1.17-3.92)	0.013*	2.06(1.04-4.09)	0.037**
Duration of disease(years)	≤ 5	Ref			
	> 5	0.86 (0.47-1.57)	0.639	0.87(0.44-1.75)	0.714
Passage of frothy urine	No	Ref			
	Yes	2.43(1.28-4.62)	0.006	2.48(1.23-4.99)	0.011**
Use of herbal medication	No	Ref			
	Yes	1.38(0.73-2.60)	0.320		
Current alcohol use	No	Ref			
	Yes	1.08(0.45-2.61)	0.190		
Systolic BP (mmHg)	≤ 130	Ref			
	> 130	0.85 (0.41-1.86)	0.740	0.82(0.35-1.93)	0.663
Comorbidities	HTN	3.34 (1.23-9.10)	0.018	1.98(0.62-6.35)	0.246
	DM	0.61 (0.33-1.11)	0.107	0.83(0.39-1.72)	0.620
	DM/HTN	1.07 (0.59-1.95)	0.817		
	HIV	0.75(0.19-2.95)	0.687		
HbA1C (%)	≤ 7	Ref			
	> 7	0.83(0.44-1.57)	0.576		

cOR: Crude odds ratio; aOR: Adjusted odds ratio; mmHg: millimeters of mercury; %: Percent; DM: Diabetes mellitus; HTN: Hypertension; HIV: Human immunodeficiency virus; HbA1C: Glycated haemoglobin

In this study, majority of the individuals 112(50.9%) had eGFR 60 – 89ml/min/1.73m². This study's findings, which primarily demonstrate inadequate awareness of impaired renal function among both clinicians and affected patients, reinforces the notion that the disease is routinely overlooked.

We found out that old age above 65 years was significantly associated with impaired renal function. This demonstrates that aging has continued to be a potential risk factor for the development of kidney disease in people with diabetes or high blood pressure [15]. The association between age and impaired renal function has been widely recognized in previous studies. As people age, their kidney function naturally declines, which increases their risk of developing kidney disease. This patient population must be screened at every opportunity to detect impaired renal function early to reduce mortality and morbidity.

Additionally, this study found that passing frothy urine was associated with impaired renal function. Foamy urine is a symptom of excess protein in the urine, which could indicate renal impairment. This finding shows that clinical symptoms like the nature of urine could reveal those who are likely to have impaired renal function. This symptom is a known indicator of CKD [16] and hugely correlates with significant proteinuria [17].

Despite a high adjusted prevalence ratio from a study conducted in Uganda, HIV was not linked to impaired renal function in our analysis [18]. In this investigation, there was no evidence that drinking alcohol or other established risk factors, including smoking, were significantly associated with impaired renal function.

CONCLUSION

3 out of 10 patients aged 50 and above and living with DM and/or Hypertension have impaired renal function. Our findings suggest that age above 65 years and passage of frothy urine are significant potential risk factors for impaired renal function and should be considered in screening and diagnostic protocols for kidney disease. The study underscores the importance of regular health check-ups, especially for older adults, to prevent and manage kidney disease.

LIMITATIONS

We were not able to perform any radiological imaging tests for our participants and as such might not have fully

ascertained the kidney sizes in relation to the presence of impaired kidney function. The study was done at a single centre and therefore the generalizability of our findings is limited. Furthermore, we were unable to measure or demonstrate the sustained reduction of eGFR as we only measured a single creatinine reading. We were not able to perform urine studies to quantify proteinuria.

ACKNOWLEDGMENTS

We extend our gratitude to the study team, which includes the laboratory personnel, hospital administration, and the participants who agreed to participate in the study

AUTHOR CONTRIBUTIONS

All authors made significant contributions to the work, including the conception, design, and implementation of the research as well as the collection, analysis, and interpretation of the data. Additionally, they selected the journal to which the article would be submitted, contributed to its drafting, revision, or critical evaluation, gave their final approval for the version that would be published, and consented to take responsibility for every aspect of the project.

COMPETING INTERESTS

The authors state that they have no interests in conflict.

ETHICS APPROVAL AND INFORMED CONSENT

The institutional ethical review board at MUST gave its approval to this project. The study subjects were asked for their informed consent. The required approval bodies were contacted for their ethical approval. All the study's methodologies were carried out in accordance with the required laws and standards.

CONSENT TO PUBLISH: This work's publication was approved by all authors.

AVAILABILITY OF DATA AND MATERIALS: The datasets used for this study will be made available by the corresponding author upon reasonable request.

SOURCE OF FUNDING: The MUST First Mile Research Grant Project provided funding for this study.

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