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Burden and Predictors of Diabetic Nephropathy in an Adult With Diabetes Mellitus Patients on Follow up at Ambo University Referral Hospital Central, Ethiopia

Delessa Hirpa¹, Bilisuma Girma²

¹ Ambo University

² Haramaya University

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Abstract

Background: Despite the growing evidence of Diabetic Nephropathy in adult patients with long-standing diabetes in sub-Saharan Africa, data on its burden and correlates in adult African patients with diabetes are limited. We, therefore, undertook this study to determine the burden and predictors of Diabetic Nephropathy among adult population with diabetes in Hospital.

Objective: We, therefore, undertook this study to determine the burden and predictors of Diabetic Nephropathy among adult population with diabetes in Ambo University Referral Hospital Central, Ethiopia.

Methods: A Hospital-based cross-sectional study was conducted from June to August, 2023 and a systematic random sampling method used to recruit participants. A total of 4,300 were interviewed using structured questionnaires to gather data from the study subjects. For data entry and analysis, Epi Data version 3.1.1 and SPSS version 25 were used. Multivariable logistic regression analysis was done after descriptive statistics. 95% confidence intervals (CI) and crude and adjusted odds ratios were presented.

Results: Diabetic Nephropathy (DN) was documented in population was 24.9% from the 369 participants (95%; CI 23.37– 26.43) participants among the study). Male sex [AOR = 2.215; 95% CI: 1.34, 3.45, $p = 0.002$], physically inactive [AOR = 1.983; 95% CI: 1.05, 3.70), $P = 0.034$], dyslipidaemia [AOR: 1.98, CI: 1.009, 3.5), $P = 0.024$] and poor controlled glycemia [AOR= 2.70; 1.40, 5.2), $P = 0.003$] were significant determinants for the development of Diabetic Nephropathy.

Conclusion: Among DM patients, sex, physical inactivity, dyslipidaemia, and poor glycaemic control were discovered to be the predictors of diabetic nephropathy. By enhancing programs for health information, education, and promotion, diabetes management should be better equipped to achieve glycaemic control and prevent diabetic nephropathy.

Delessa Hirpa¹, and Bilisuma Girma²

¹Department of Medical Laboratory, College of Health Science and Medicine, Ambo University, Oromia, Ethiopia

²Department of Medical Biochemistry, College of Medical and Health Sciences, Haramaya University, Harar, Ethiopia

*Corresponding author: Delessa Hirpa: delesakundi@gmail.com

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Introduction

Diabetes mellitus is one of the non-communicable diseases (NCDs) that account for 63% of mortality globally, which was originally considered a social illness. Globally, there is substantial evidence linking diabetes mellitus (DM) to the onset of a number of complications that raise the risk of premature death and place a significant financial burden on the health system^[1].

An American study found that the number of adults with diabetes would rise from 22.3 million (9.1%) in 2014 to 39.7 million (13.9%) in 2030 and 60.6 million (17.9%) in 2060^[2]. The prevalence of diabetes among people aged 20 to 79 has increased by more than threefold since 2021. According to the International Diabetic Federation (IDF), diabetes will affect 643 million people worldwide by 2030, or 11.3% of the entire population, and 783 million people, or 12.2% of the entire population, by 2045 if current trends continue^[3].

According to a meta-analysis, a study carried out in Iran between January 2000 and May 2020 showed that the prevalence of diabetic nephropathy in people with type 2 diabetes was 30.6%^[4]. A cross-sectional study was carried out in Thailand between October 2016 and September 2017 to look at the prevalence and risk factors of chronic kidney disease (CKD) in 1,096 primary care type 2 diabetes (T2DM) patients. The study depicted the overall prevalence of CKD to be 24.4% (21.9-27.0) of < 60 mL/min/1.73 m² based on glomerular rate filtration measurements^[5].

An increasing burden of DN has been reported in adult patients with diabetes in sub-Saharan Africa. Given that the illness is a major underlying cause of cardiovascular disorders, renal failure, and mortality, this is a crucial component of the consequences of the disease's outcome^[1]. According to a study conducted in Nigeria, out of 5078 patients, 1937 patients had DN (prevalence: 38.4%)^[6].

In Ethiopia, between 1990 and 2017, a study demonstrated an increase in the prevalence of DM and the microvascular and macrovascular issues it causes in diabetic people. Diabetic complications can be caused by a number of variables, including prolonged disease duration, lower socioeconomic status, the existence of additional issues, and advanced age^[7]. Besides, study done in Gondar, Ethiopia showed that the incidence rate of diabetic nephropathy was 14 (95% CI 10.8-17.7) cases per 10,000^[8]. The incidence rate of diabetic nephropathy was also found to be 14 (95% CI 10.8-17.7) instances per 10,000 patient-month observations, according to a study conducted in Gondar, Ethiopia. The development of diabetic nephropathy occurred in 63 (13.6%) DM patients as well^[9].

Diabetic nephropathy may appear at the time of diabetes diagnosis. The connection between diabetes mellitus and problems in the microvascular and macrovascular tissues is one of the most significant clinical characteristics. The primary contributing element to the onset of organ damage is the degree and duration of long-term hyperglycaemia. Nephromegaly and a modified Doppler are two early morphological indicators of renal impairment, although proteinuria and Glomerular Filtration Rate are the strongest indicators of how damaged the kidneys are (GFR)^[10].

The most important elements in the progression of DN are the level of blood pressure and glycemic control, dyslipidaemia, cardiovascular factors. However, recent studies have shown that, in addition to the classical albuminuric DKD phenotype, two new nonalbuminuric phenotypes of DKD exist, i.e., nonalbuminuric DKD and progressive renal decline, suggesting that progression of DKD can also occur through a non-albuminuric pathway and Patients with proteinuria >3 g/day reach the main end goal more quickly than those with baseline proteinuria <3 g/day^[11].

About 25-35% of people with type 1 or type 2 diabetes mellitus develop diabetic nephropathy. From hyper filtration to micro-albuminuria, macro-albuminuria, nephrotic proteinuria, and lastly to progressive chronic kidney disease, which eventually results in end-stage renal failure, the disease develops through numerous clinical phases. The glomerulus, the tubules, the vasculature, and the interstitial spaces of the kidney are all commonly affected by structural pathological alterations during these stages^[12].

Numerous epidemiological studies show that the main risk factors for the development of diabetic nephropathy are family history, high blood pressure, dyslipidaemia, obesity, and insulin resistance. Furthermore, glycated hemoglobin level (HbA1c), systolic blood pressure, proteinuria, and smoking are risk factors^[13].

In sub-Saharan Africa (SSA), the high costs of increased mortality and morbidity in this population as well as the cost of kidney replacement therapy provide a strong economic benefit for improving early detection of DN with diabetes a top priority in in sub-Saharan Africa (SSA)^[14]. In order to undertake a program that intends to lower the incidence and mortality of the disease as part of targeted interventions, it is necessary to have accurate information about DN.

According to research conducted in Tigray, Ethiopia, having hypertension, having poor glycemic control, having had diabetes for a long time before being diagnosed, and not adhering to diabetic medication, diet, and exercise were all significant predictors of diabetic nephropathy^[15]. Although numerous studies have been conducted in Ethiopia, many important associated factors such as smoking, family history, high blood pressure, dyslipidaemia, glycosylated hemoglobin, and obesity were overlooked. Additionally, there is no recent data on diabetic nephropathy in the research area. Therefore, the study objective was to determine this study aimed to investigate the prevalence, and predictors of diabetic nephropathy in an adult population with diabetes.

Method and Materials

Study area and period

A cross-sectional study conducted from June to August, 2023 among 369 diabetic patients attending their follow-up at chronic illness clinic of Ambo University Referral Hospital, Central Ethiopia. The West Shewa Zone is expected to have a total population of 2,058,676 people in 2018/2019, of which 1,028,501 are men and 1,030,175 are women, according to the Ethiopian census conducted in 2007. In this zone, there were 520 health posts, 92 health centers, and 9 hospitals.

Eligibility criteria

The study included all adult with type I diabetes who had it for longer than five years, had proven type II diabetes, were age of 18 and above, were being followed up in the study area, and could provide their informed consent. Patients who were seriously ill and had a severe cognitive or hearing impairment were excluded from the study.

Sample size determination

A single population proportion formula with a 95% confidence interval, 35.3% of a systematic review and meta-analysis of diabetic nephropathy from sub-Saharan countries, and a margin of error of 5% were used to compute the sample

size^[16] i.e. $N = \frac{(z^{\alpha/2})^2 p(1-p)}{d^2} = \frac{(1.96)^2 0.353(1-0.353)}{(0.05)^2} = 351$ and by adding 10% for nonresponse the final sample size was 369.

Sampling technique and procedure

The study subject in Ambo University Referral Hospital was selected by systematic random sampling. Six participants were excluded because of incomplete Laboratory investigations.

Variables used in the study

Dependent variable

Diabetic nephropathy was a dependent variable.

Predictor variables

Socio-demographic, clinical, anthropometric, and behavioural characterisation: Relevant data were collected, this included age at diagnosis, gender, smoking habits, education status, marital status, occupation, and religion, co-existing hypertension comorbidity, anti-glycemic agents, BMI, duration with DM since diagnosis, family history of hypertension, glycemic control, dyslipidaemia, Physical exercise, alcohol intake.

Data collection tool and procedure

Data were collected by using a structured interviewer administered questionnaire which was developed by researchers

from relevant literatures. Behavioural variables were assessed based on WHO Step wise approach for chronic disease risk factor surveillance ^[17]. Clinical variables were taken from patient record review and physical measurements were conducted.

Following standardised study procedures, biophysical measurements which included resting blood pressure and relevant anthropometric measurements (weight, height) and body mass index [BMI] were then performed.

Biophysical Measurements

A fasting blood sample was then collected for the measurement of blood glucose (FBG), glycated haemoglobin (HbA1c), lipid profile, and serum creatinine (for estimation of the e-GFR) using electro-chemiluminescence immunoassays manufactured by Roche diagnostics Limited, Germany on a Cobas 311 C-model SN 14H3-15 machine (Hitachi High Technologies Corporation, Tokyo Japan). Glomerular filtration rate (GFR) was measured using Cockcroft-Gault formula $(140 - \text{age [yr]}) \times \text{body wt [kg]} \times K / \text{serum creatinine [}\mu\text{mol/L]}$, $K = 1.23$ for men, 1.05 for women ^[18]. These values were then corrected for body surface area (1.73 m²).

Operational definition

Hypertension: if the SBP/DBP was >140/90mmHg and/or or patients on antihypertensive therapy.

Nephropathy: chronic micro vascular diabetic complication whose e-GFR <60 ml/min/1.73m²

Data entry, processing and Statistical Analysis

Data were categorized, cleared, compiled and coded, checked for completeness, accuracy then entered into Epi data version 3.1 and then exported to SPSS. Both bivariable and multivariable logistic regression analysis was done and variables that were significant in bivariable with a p-value of <0.25 were retained for further consideration with multivariable logistic regression to control confounders. Finally significance of statistical association was assured using 95% confidence interval and a p-value of (<0.05) was considered significant in multivariable regression. The necessary assumption of model fitness during logistic regression was checked using Hosmer-Lemeshow goodness-of-fit test statistics.

Data quality control

The principal investigator provided data collectors with a two-day intensive training on sampling techniques and the purpose of the study before they began collecting actual data. A questionnaire that was originally written in English was translated into the working regional language (Afaan Oromo), and then, in order to ensure accuracy, it was translated back into English by someone with strong two-language translation skills. On the basis of the pre-test, the study tool underwent all necessary revisions. The tool was pre-tested on 5% of the sample size at the nearby Holeta Hospital. For the data collection, experienced enumerators were hired, and selected participants were given an introduction to the

study. The two supervisors and the principal investigator conducted ongoing follow-up and supervision, and they also reviewed the collected data.

The analysis of all blood samples in the laboratory followed standard operating procedure. In accordance with the manufacturers' instructions, the tests were carried out. To guarantee a high-quality outcome, the pre-analytical, analytical, and post-analytical stages of quality assurance were all applied. To prevent cross contamination, visual checks of the lab's and working bench's cleanliness are made. The daily results were accurately recorded, and the principal investigator followed up every day.

Limitations of the Study

Cross-sectional research does not strongly suggest a cause-and-effect link. The most accurate nephropathy test is micro-albuminuria, although it is not currently available. Second, for several variables, we relied on patient data that could have been affected by recall bias. We also had difficulties figuring out the precise age at which diabetes first manifested itself. Another drawback was that kidney biopsy, the gold standard diagnostic test, was not carried out.

Result

Socio-demographic characteristics of participants

A total of 369 diabetic patients participated in the study over the research period, with a response rate of 100%. The participants' average age was 46 years old. Males made up 192 (52.0%) of the participants, or nearly half. Urban residents made up the majority of participants (228,61.8%). (In Table 1).

Table 1. Socio-demographic characteristics of participants at Ambo University Referral Hospital Central Ethiopia, 2023 (n=369).

Variable	Category	frequency	Percent
Sex	Male	192	52.0
	Female	177	48.0
Age (Year)	Median	46	
Income	Under 30	40	10.8
	30-50	261	70.7
	50 and above	68	18.4
	<1000	87	22.3
	1000-1999	80	21.7
	2000-3000	22	6.0
	>3000	180	48.8
Marital status	Married	293	79.4
	Single	76	20.6
Religion	Orthodox	186	50.4
	Protestant	146	39.6
	Muslim	37	10.0
Educational Level	No education	87	23.6
	primary education	80	21.7
	Secondary education	22	6.0
	Tertiary and above	180	48.8
Occupational status	House wife	52	14.1
	Gov't Employee	114	30.9
	Private	103	27.9
	Farmer	100	27.1
Ethic Group	Oromo	291	78.9
	Amhara	61	16.5
	Tigirie, Gurage	17	4.6
Residence	Rural	147	37.7
	Urban	243	62.3
Family History of Hypertension	Yes	79	21.4
	No	290	78.6
Family History of Diabetes Mellitus	Yes	201	54.5
	No	168	45.5

Clinical and behavioral characteristics of study participants

A total of 190 participants (51.5%) fell into the normal BMI range, compared to 117(31.7%) overweight participants and obese participants 40 (10.8%). The subjects' remaining clinical and behavioral information is displayed.

Table 2. Clinical and behavioral characteristics of participants at Ambo University Referral Hospital Central Ethiopia, 2023 (n=369).

Characteristics	Type	Frequency	Percentage
DM Type	T1DM	150	40.7
	T2DM	219	59.3
Duration of DM	<10yrs	227	61.5
	≥10yrs	142	38.5
Treatment regimen	Oral agents	212	57.5
	Injection (Insulin)	121	32.8
	Oral and injection	36	9.8
BMI (kg/m ²)	Low	22	6.0
	Normal	190	51.5
	Overweight	117	31.7
	Obese	40	10.8
Hypertension	Yes	163	44.2
	No	206	55.8
Alcohol intake	Yes	127	34.4
	No	242	65.6
Smoking habits	Yes	47	12.1
	No	343	87.9
physical activity	Yes	92	24.9
	No	277	75.1
HbA1C (%)	<7	85	23.0
	>7	284	77.0
Total cholesterol(mg/dl)	<200	259	70.2
	>200	110	29.8
Triglyceride(mg/dl)	<150	140	37.9
	>150	229	62.1
HDL-C(mg/dl)	>40	195	52.8
	<40	174	47.2
LDL-C(mg/dl)	<130	307	83.2
	>130	62	16.8

Burden of diabetic nephropathy

In this study, the eGFR scores were used for defining burden of DN for each study subject and Diabetes Nephropathy was then defined as score of ≤60ML/Minutes. Accordingly, the overall Burden of DN among the study population was 24.9% from the 369 participants (95%; CI 23.37– 26.43).

Independent predictors of Diabetic Nephropathy

In this study population, we report that DN was relatively common. In the multivariate logistic regression analysis, variables like sex, physical activity, dyslipidemia, and glycemic control were included since bivariate analysis revealed evidence of some association with the outcome variable at a p value of 0.25. The predictor variables that were found to be strongly linked to the development of DN at a p value of < 0.05 were; male sex, poorly controlled glycemia, dyslipidemia and being physically inactive.

One of the independent predictor of DN was individuals' male sex. Participants of the male sex were two times more likely than those of the female sex to develop DN (AOR = 2.215; 95% CI: 1.34, 3.45). After adjusting for other factors, Participants who were physically inactive had a twofold increased risk of developing DN compared to their counterparts [AOR = 1.983; 95% CI: 1.05, 3.70].

Diabetic patients with dyslipidemia had two times more likely to develop DN than those who had not [AOR: 1.98, CI: 1.009, 3.5]. Patients with poor controlled glycemia were 2.70 times more likely to develop DN than the good controlled glycemia [AOR= 2.70; 1.40, 5.2] (In Table 4).

Table 3. Bivariate and Multivariate analysis to identify predictors of DN, at Ambo University Referral Hospital Central Ethiopia, 2023 (n=369).

Variables	Category	DN (n)		Bivariate & Multivariate analysis				
		Yes	No	COR	(95% CI)	AOR	(95% CI)	P-value
Sex	Male	16	21			2.22	1.34, 3.64	0.002
	Female	135	154	1		1		
Physical Exercise	Yes	74	59	1		1		
	No	118	139			1.98	1.05, 3.73	0.034
Dyslipidemia	Yes	114	96	1.55	1.04,2.32	1.96	1.09, 3.51	0.024
	No	78	102	1		1		
A1c (%)	<7	34	57	1		1		
	>7	158	141	1.88	1.16,3.04	2.71	1.41, 5.21	0.003

AOR: adjusted odds ratio; COR-Crude odds ratio; 1: reference

Discussion

We found that Diabetes Nephropathy (DN) was highly widespread in this study population, that it is a public health burden, and that it is one of the main reasons of hospital admission and death in Ethiopia. We documented that Diabetes Nephropathy (DN), a serious public health concern that accounts for a considerable portion of hospital admissions and deaths in Ethiopia, was quite common in the study population. The objective of the current investigation was to identify the prevalence and risk factors for diabetic nephropathy in the studied population.

A wide variation in the prevalence of DN has been reported across African populations. This study revealed that 24.9% (95%; CI 23.37– 26.43) patients had DN which is in line with studies done, like in northern Thailand 24.4% (21.9-27.0), 24.7%; 95% CI 23.6% - 25.7%) in one systematic review studies performed in SSA respectively [19][20]. However, a different systematic review and meta-analysis that assessed the burden of DN and its association to hypertension in 27 research conducted in SSA found a combined prevalence of DN of 35.3%. [21], higher than to what we documented in our study. In one systematic review and meta-analysis of 21 medium- and high-quality studies performed in SSA to document the epidemiology of chronic kidney disease, the prevalence of DN in the included studies was reported to range between 7.3% and 24% [22], which is lower than the current study findings.

These variations may be due to the study design, the study period, sociodemographic characteristics, diagnostic criteria, as well as the techniques used to quantify creatinine. It may also be due to difference in the type and duration of diabetes, as well as the study period. In order to prevent the development of DN in high-risk DM patients, it is critical to recognize risk factors in clinical practice. According to this study, DM patients with current male sex, inactivity, dyslipidaemia, and uncontrolled glycemia were more likely to develop DN.

We also documented that Male sex increased the odds of DN in current study. This result was in align with prior studies [23]. Given that the hormone estrogen performs a significant protective role, this may be explained [23][24]. The alternative argument is that, despite gender difference, creatinine-based estimates of the glomerular filtration rate underestimate the renal function of women. Compared to our findings, previous studies [25] demonstrated that men were less likely than women to experience micro vascular problems from diabetes. Therefore, more research is required to ascertain whether this gender disparity influences the improved outcomes in diabetic females.

Diabetes-related nephropathy and physical inactivity were highly significant associations. This study's findings align with earlier research done at the Ayder Comprehensive Specialized Hospital in Tigray, Ethiopia. [15]. Possible explanation Physical exercise can improve DN and reduce its progression, according to one meta-analysis [26]. Similar to earlier research association between developing DN and poor glycemic control (high HbA1c) was observed [24][27]. It is possible to explain this association by the fact that hyperglycemia causes albuminuria and glomerular filtration rate decline [24][28].

A high glucose concentration in meningeal cells also causes hypertrophy, which raises gene expression and protein secretions while lowering the activity of the metalloprotease enzyme, which is in charge of eliminating waste from the body. Finally, our research showed that participants with dyslipidemia had a higher risk of developing DN than individuals without dyslipidemia did [27][29][30]. Activation of the Toll Like Receptor signaling pathway in the glomeruli appears to represent a unique mechanism of dyslipidemia-induced kidney injury in diabetic circumstances in a Toll Like Receptor4 (TLR4)-dependent manner [31].

Limitation of the study

Because the period from diagnosis and the actual onset of diabetes may occur before the diagnosis of diabetes, the

length of diabetes as determined in this study may not accurately reflect the length of the condition. The study's cross-sectional design, which does not support a strong causal association, is another drawback.

Conclusion

In this study, the burden of DN was relatively high. Additionally, among DM patients, sex, physical inactivity, dyslipidaemia, and poor glycemic control were revealed to be predictors of diabetic nephropathy. By enhancing programs for health information, education, and promotion, diabetes management should be better equipped to achieve glycaemic control and prevent diabetic nephropathy. Male sex, sedentary lifestyles, dyslipidemia, and patients with poor glycemic control need to receive more attention. The determinants of diabetic nephropathy should be investigated in a larger social context using qualitative research, and another study with a strong design should be conducted.

Abbreviations

A1C: Glycated hemoglobin, AOR: Adjusted Odds Ratio, BG: Blood Glucose, BMI: Body Mass Index, CI: Confidence Interval, DN: Diabetes Nephropathy, DM: Diabetes Mellitus, TLR4: Toll like Receptor4.

Statements and Declarations

Availability of data

The data sets used and/or analysed during this study are available from the corresponding author upon reasonable request.

Competing Interests

The corresponding author declares that there were no competing interests

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None

Ethics Consideration

The proposal was approved by the Department Research and Ethics Review Committee (Ref. No: CMHS-ERC: 048/12) and Institute Review Committee board of Ambo University. An official letter (SOM/BCHM/102/2023) was written from the Ambo University to Ambo University Referral hospital granted permission for sample collection. Written voluntary informed consent was signed and obtained from the study participants to start data collection. The result of the finding was

reported to the responsible bodies for any beneficiary or corrective measures. The study was performed in accordance with the Declaration of Helsinki.

Authors' contributions

All authors contributed regarding the conception, supervision, methods and all other works of this manuscript equally.

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