






Magnitude of, and Factors Associated with Cardiovascular Disease Among Type Two Diabetes Mellitus Patients

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Background: Diabetes mellitus is becoming one of the major health problems in developing countries. The number of adults living with type 2 diabetes mellitus (T2DM) worldwide is increasing over time. Cardiovascular disease (CVD) is the major cause of death in T2DM. The objective of this study was to determine the prevalence of cardiovascular disease and its associated factors among diabetic patients at the MRC clinic of Dilla University Referral Hospital (DURH).

Methods: A hospital-based cross-sectional study was conducted from April to May 2019. A total of 216 diabetic individuals were selected with a convenient sampling technique from patients on follow-up at DURH MRC. Data were collected using a structured format. The diagnosis of CVD was made with the necessary diagnostic tests and examination. The data analysis was done in SPSS software version 20. Bivariate and multivariable logistic regression analysis was carried out to identify factors associated with cardiovascular disease.

Results: A total of 216 patients participated in the study and the mean age of the study participants was 30 years; 83.3% of the study participants were male. The overall prevalence of cardiovascular disease was 25% of which 57% were ischemic heart disease, 32% were hypertensive and 10% were stroke. Duration of DM for more than 10 years and diabetic drug discontinuation were factors associated with cardiovascular disease. Odds of CVD was nearly four times more in those whose duration of DM is more than 10 years (AOR=4.00, 95% CI: 2.386–6.705) and odds of CVD among those who discontinued medication were almost three times more, (AOR=2.98, 95% CI: 1.287–6.080).

Conclusion: A quarter of the diabetic population studied developed CVD. Duration of DM for more than 10 years and drug discontinuation are independent associated factors of CVD. Hence appropriate intervention at early stages should be implemented at primary healthcare level.

Keywords: T2DM, cardiovascular disease, Ethiopia

Introduction

The International Diabetes Federation (IDF) estimates that worldwide, 415 million people have diabetes, 91% of whom have type 2 diabetes mellitus (T2DM). People with diabetes comprise 8.8% of the world's population, and the number of cases of diabetes is predicted to rise to 642 million by 2040.^{1,2} Individuals with T2DM and with chronically poor metabolic control can experience microvascular and macrovascular complications leading to a significant burden for the individual and for society. This burden includes direct costs of medical care and indirect costs, such as loss of

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productivity, which result from T2DM-related morbidity and premature mortality.^{3–5} Insulin resistance preceding long before the diagnosis of T2DM enhances atherogenic risk profile and has been delineated as a potential cause for subsequent increased risk of cardiovascular disease (CVD) among diabetic patients.⁶

Patients with T2DM disease are disproportionately affected by CVD compared with those without diabetes.^{7–10} CVD is a major cause of disability among people with T2DM^{2,11} and accounts for more than one-half of all the deaths due to T2DM.^{12,13} In persons with T2DM, the death rates were 15.4% for those with no prior myocardial infarction (MI) and 42.0% in patients having a history of MI which is in contrast with patients who did not have T2DM.¹⁰ Specifically, coronary artery disease (CAD) was most lethal, followed by stroke.¹⁴ A meta-analysis by Einarson et al. showed that atherosclerosis (29.1%) is the most prevalent CVD followed by CAD (21.2%) and heart failure (14.9%).¹⁵ Furthermore, diabetic patients with CVD have a worse prognosis for survival than CVD patients without T2DM and their quality of life also depreciates.

The elevated risk of cardiovascular events among diabetic versus non-diabetic patients emphasizes the need for screening of asymptomatic diabetic patients for CVD risk by the premise that earlier identification and stratification would lead to appropriate management of cardiovascular risk in both the long and short term.

There is a scarcity of comprehensive data on the prevalence and associated factors of CVD among patients with T2DM in Ethiopia, specifically in the study region. This study was therefore conducted to assess the prevalence of CVD and its associated factors among T2DM patients on follow-up at the diabetic clinic (MRC) of Dilla University Referral Hospital, Ethiopia.

Materials and Methods

Study Setting and Design

This was a hospital-based cross-sectional study conducted in Dilla University Referral Hospital, which is in Dilla Town, located 360 km away from the capital city, Addis Ababa, and 90 km from Hawassa in southern Ethiopia. Dilla University Referral Hospital serves a population of over 100,000 who are mainly (80%) rural. The hospital contains approximately 200 beds that provide surgical, gynecologic/obstetric, medical, and pediatric wards. It acts as a referral center for the surrounding primary health-care units. The study period was from April to May 2019.

Study Population

The sample size was computed using a single population proportion formula, with the following assumptions: 95% confidence level to be 1.96, degree of precision (d) to be 0.05, and adding 10% for non-response yielding a sample size of 216. All selected adult diabetic patients who visited chronic medical outpatients department at Dilla University Referral Hospital during the study period made up the study population. Patients who were critically ill and unable to communicate during the interview were excluded.

Socio-Demographic and Clinical Data Collection

Socio-demographic data such as age, sex, residency and educational status, clinical data such as blood pressure and anthropometric related data of the study participants were collected using a structured questionnaire including a review of patients' clinical records. Data were collected by face to face interview, followed by measurement of fasting blood glucose, blood pressure, height, and weight.

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured from each subject with a standard adult arm cuff (sphygmomanometer). Two trained medical doctors who were working in the chronic diseases follow-up clinic measured the blood pressure from the right arm after a patient had rested for at least 5 minutes. The precision of the measurement was checked by using two readings two minutes apart and the average of the two readings was taken as blood pressure.

Diagnosis of CVD was made by the necessary diagnostic tests and examination. Anthropometric data (weight and height) were collected according to WHO guidelines. Weight was measured using a digital bath balance, Seca, which is a German model for weight measurement. A portable height measuring device with standing scale which was calibrated regularly against known weight and recorded to the nearest 0.1 kg was used. Body mass index (BMI) was calculated with the weight divided by the square of height in kilogram per meters square formula ($BMI = \text{weight}/\text{height}^2$ in kg/m^2). The patients were classified on the basis of body mass index (BMI) using WHO classification.¹⁶

Dyslipidemia was defined by the presence of more than one abnormal serum lipid concentration and hyperglycemia was defined as having fasting blood glucose level >110 mg/dL.

Data Processing and Analysis

Socio-demographic and economic data were cleaned manually and then entered into the computer using EPI Info version 7 and statistical analysis was carried out using SPSS version 20, with descriptive summary used to summarize the variable. Continuous variables such as age and income were first transformed into categorical variables before they were analyzed. First, the frequency of all the variables in the questionnaire was determined. Secondly, cross-tabulation was done between important variables, their significance was checked by bivariate analysis and multivariable logistic regression was done to assess the association of factors. Variables with a p-value of less than 0.2 in the bivariate analysis were entered into the final model. Important variables were entered and analyzed using multivariable logistic regressions to find factors associated with CVD among T2DM. Finally, the results of the study were presented using graphs and tables. In all cases, a p-value of <0.05 was considered statistically significant.

Results

Socio-Economic, Demographic and Other Characteristics

Out of the 216 study participants, the mean age of the study participants was 30 years and 126 (58.3%) were older than 30 years. Most 180 (83.3%) were male and 162 (75%) were urban residents. 36 (16.7%) had no formal education while 54 (25%) were degree holders. 72 (33.3%) were farmers and 90 (41.7%) earned more than 2500 birr and 126 (58.3%) were married (Table 1).

About 90 (41.7%) were leading a sedentary life or were physically inactive and 38.5% were overweight (BMI >25). About 72 (33.3%) were cigarette smokers whereas 54 were khat chewers and another 54 (25%) were alcohol drinkers regularly.

Prevalence of CVD Among the Study Participants

The total prevalence of CVD among the study participants was 25% and 50% of the study participants were hypertensive. 41.7% had dyslipidemia and 16.7% had a family history of chronic illness. 33.3% had DM for more than 10 years and 33.3% of the study participants had diabetic drug discontinuation history (Table 2).

Table 1 Socio-Demographic Characteristics of Diabetic Patients on Follow-Up at DURH, April to May, 2019

Variables	Category	Frequency	Percent
Age	<30 years	90	41.7
	> 30 years	126	58.3
	Total	216	100
Sex	Male	180	83.3
	Female	36	16.7
	Total	216	100
Educational Status	Uneducated	36	16.7
	Grade 1–8	36	16.7
	Grade 9 & above	18	8.3
	Diploma	72	33.3
	Degree	54	25
	Total	216	100
Marital Status	Married	126	58.3
	Divorced	90	41.7
	Total	216	100
Residency	Urban	162	75
	Rural	54	25
	Total	216	100
Occupation	Farmer	72	33.3
	Employed	90	41.7
	Jobless	54	25
	Total	216	100
Income	Less than 1000 birr	72	33.3
	1000–2500 birr	54	25
	More than 2500 birr	90	41.7
	Total	216	100

Factors Associated with CVD Among T2DM Patients

Age, occupation, family medical history of DM, alcohol drinking, drug discontinuation, duration of treatment, physical inactivity and obesity/overweight were found to be associated with CVD at bivariate level analysis. Drug discontinuation and duration of treatment for more than 10 years remained statistically significant at multivariable analysis level with 95% CI (AOR= 4.0, CI=2.0–8.0, P=0.02) and (AOR=3.0, CI=1.3–6.1, P=0.03) respectively. The odds of CVD among those who discontinued medication are four times more than those who did not discontinue their medication. The odds of CVD among those who were on DM treatment for more than 10 years is almost three times higher than those who were on treatment for less than 5 years (Table 3).

Table 2 Clinical Characteristics of Diabetic Patients on Follow-Up at DURH, April to May, 2019

Independent Variables		Frequency	Percent
Ever Diagnosed with CVD?	Yes	54	25.0
	No	162	75.0
	Total	216	100.0
Ever Diagnosed Hypertension?	Yes	108	50.0
	No	108	50.0
	Total	216	100.0
Ever Diagnosed Dyslipidemia?	Yes	90	41.7
	No	126	58.3
	Total	216	100.0
Past History Medical Illness	Yes	36	16.7
	No	180	83.3
	Total	216	100.0
Family History of Chronic Illness	Yes	36	16.7
	No	180	83.3
	Total	216	100.0
Duration of DM	<5 years	90	41.7
	5–10 years	54	25.0
	More than 10 years	72	33.3
	Total	216	100
Diabetic Drug Discontinuation History	Yes	72	33.3
	No	144	66.7
	Total	216	100
IHD	Yes	16	57
	No	12	43
	Total	28	100
HHD	Yes	9	32
	No	19	68
	Total	28	100
Stroke	Yes	3	10
	No	25	90
	Total	28	100

Abbreviations: CVD, cardiovascular disease; DM, diabetes mellitus; HHD, hypertensive heart disease; IHD, ischemic heart disease.

Discussion

This study aimed to assess the prevalence of CVD and its associated factors among T2DM patients. 83.3% of the study participants were male and 75% of them resided in urban areas. 41.7% and 50% of the study participants had dyslipidemia and hypertension, respectively. The prevalence of CVD among the study participants is 25%. Duration of DM and unnecessary diabetic drug discontinuation are independent predictors of CVD among DM patients.

The prevalence of CVD among the study participants is 25% which is in agreement with reports from Cameroon (28.6%) and Southeast Asia (29.5%),¹⁷ but lower than reported in a systematic literature review on the prevalence of cardiovascular disease in T2DM, which revealed the highest prevalence of overall CVD in North America and the Caribbean (46.0%), Southeast Asia (42.5%) and the Western Pacific (including China) (33.6%).¹⁵ That review also reported a pooled prevalence of 32.2% of CVD.¹⁵ This difference could be due to the inclusion of diabetics under the age of 18 in the systematic review and differences in the study settings, study time, stage and types of overt complication of T2DM at which the data were collected. It also could be because of lifestyle differences of the study participants, which will be related with the each county's development index as most of the studies included in the meta-analysis were from developed countries.

The high prevalence of CVD in the current study may cause increased morbidity and mortality among diabetic patients due to the synergism of hyperglycemia with other cardiovascular risk factors.¹⁸ The prevalence of dyslipidemia among the study participants was 41.7% which is relatively comparable with a follow-up study done on a Korean population (49.5%) and DIAB-CORE project (49.4%).¹⁹ The current study results were much lower than the study done in Durame general hospital, Ethiopia (65.6%),²⁰ in Tanzania (94.1%)²¹ and Pakistan (95%).²² Another study also found dyslipidemia among hyperglycemic patients to be 92.4%.²³ The high prevalence could be explained by genetic differences, difference in study setup or because of the method used to classify dyslipidemia.^{24,25}

In the current study 50% of participants were hypertensive which is higher than the study done in southern Ethiopia (25.5%)²⁶ and lower than the study done from DIAB-CORE project data (83.9%).¹⁹ The difference could be explained by a difference in lifestyle, study setup, genetics and mean age of the participants. We also cannot exclude cases of elevated blood pressure caused by the stress of the unfamiliar situation.

Duration of DM and unnecessary diabetic drug discontinuation are independent predictors of CVD among DM patients. This is because the longer duration of DM and drug discontinuation brought about hyperglycemia which is an important etiologic factor leading to complications of DM. The mechanism by which hyperglycemia leads to diverse cellular and organ dysfunction may be explained by hyperglycemia-induced increased production of reactive oxygen

Table 3 Bivariate and Multivariable Analysis of the Associations Between Selected Characteristics and the CVD Risk Factors in Diabetic Patients, DURH, April to May 2019

Variables	Diagnosed CVD		Total	P-value		AOR (95% CI)
	Yes	No				
Age of Respondents						
> 30 years	18	108	126	<0.001		
<30 years	36	54	90	1		
Residence						
Rural	0	54	54	1		
Urban	54	108	162	<0.001		
Occupation						
Jobless	0	54	54			
Employed	36	54	90			
Farmer	18	54	72	<0.001		
Family medical history (DM)						
No	54	126	180			
Yes	0	36	36	<0.001	2.3(1.7–3.2)	
Duration of DM						
> 10 years	36	36	72	<0.001	4.0(2.4–6.7)*	3.0(2.0–8.0)**
5–10 years	0	54	54			
<5 years	18	72	90			
Diabetic drug discontinuation						
No	54	90	144			
Yes	0	72	72	0.003	2.0(1.4–2.8)*	2.8(1.3–6.1)**
Cigarette smoking						
Yes	54	90	144	0.001		
No	0	72	72			
Khat chewing						
No	18	144	162			
Yes	36	18	54	<0.001		
Alcohol drinking						
No	36	126	162			
Yes	18	36	54	<0.001	2.0(1.4–2.8)	
Physical inactivity						
No	36	90	126			
Yes	18	72	90	<0.001	2.0(1.4–2.8)	
Obesity						
No	36	108	144			
Yes	18	54	72	<0.001	2.0(1.4–2.8)	

Notes: *P-value<0.2; **p-value <0.05.

species or superoxide in the mitochondria causing different cytotoxicity in the cellular level and organ dysfunction.¹⁸

Limitation

The authors could not generalize the findings of the present study to the entire population as the current

study was small in sample size and cross-sectional in study design. These findings need to be validated further through various epidemiological study designs, large sample sizes, and inclusion of various other socio-demographic and biological parameters. Moreover measurements of blood pressure and lipids based on a single

testing opportunity provide evidence for the respective condition only.

Conclusion

A quarter of the diabetic population developed CVD. Duration of DM for more than 10 years and drug discontinuation are independent predictors of CVD.

Abbreviations

BMI, Body mass index; CVD, Cardiovascular disease; DM, Diabetes Mellitus; DURH, Dilla University Referral Hospital; HDL, High-density lipoprotein; HHD, hypertensive heart disease; IDF, International Diabetes Federation; IHD, ischemic heart disease; RBS, Random blood sugar; MRC, Medical referral clinic; MRFIT, Multiple risk factors intervention trials; WHO, World Health Organization.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki. The study was approved by Dilla University, Internal Review Board. An official letter of cooperation was written from Dilla University College of Health Science to all concerned bodies. The aim, purpose, benefits and method of the study were clearly explained to the participants. The entire study participants had been informed that, the data obtained from them were used only for this study purpose, the confidentiality of the data were maintained and their names were not recorded. Next, the study participants was informed that they can withdraw from the study at any time and being withdrawn would not have any negative impact on their diagnosis and treatment in the hospital. Finally, each study participant had provided a signed consent before any data were collected.

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Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it

critically for important intellectual content; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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