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Atherosclerotic Cardiovascular Disease Risk Among Patients with Type 2 Diabetes in Uganda

William Lumu[1*], Ronald Mutebi[2], Emmanuel Ssendikwanawa[3], Davis Kibirige[4], Ronald Wesonga[5], Silver Bahendeka[6]

[1]*Department of Medicine, Mengo Hospital Kampala Uganda and Texila American University, George Town, Guyana*

[2]*Department of Medicine, College of Health Sciences, Makerere University, Uganda*

[3]*Clinical Epidemiological Unit, College of Health Sciences, Makerere University, Uganda*

[4]*Department of Medicine, Uganda Martyrs Hospital Lubaga, Kampala Uganda*

[5]*School of Statistics and Planning Makerere University, Uganda*

[6]*Department of Medicine, Mother Kevin Post Graduate Medical School, Uganda Martyrs University, Uganda*

Abstract

While atherosclerotic cardiovascular disease risk is increased in patients with type 2 diabetes, the magnitude and socio-demographic determinants of this risk are not known in Uganda. We aimed to establish the magnitude of the predicted 10-year atherosclerotic cardiovascular risk and describe its socio-demographic determinants among patients with type 2 diabetes in Uganda. This was a cross-sectional study conducted in eight (8) diabetes clinics from November 2020 to February 2021. We enrolled 500 patients with type 2 diabetes aged between 40 to 79 years. Patients were interviewed on their socio-demographic characteristics. Anthropometric and laboratory measurements were performed. The predicted 10-year atherosclerotic cardiovascular risk was categorized using the Pooled Cohorts Risks Equations. Bivariate and multivariate logistic regression was conducted to establish associated socio-demographic factors. The majority of participants were females (78%), with a mean age of 55.14years (SD±8.96). Of the patients studied, 20% were at low risk (score <5%), 14.2% borderline risk (score 5-≤7.5%), 45.2% intermediate risk (score7.5-<20) and 20.6% high risk (score ≥20%). Elevated risk of score ≥7.5% was found in 65.8%. The male gender (AOR= 5.456, 95% CI 2.998-9.932, p=0.001), at least 50 years of age (AOR=7.841 95% CI 4.863-12.642, p=0.001), part-time employment (AOR=1.726, 95% CI 1.221-2.441, p=0.002) and being widowed (AOR=2.4, 95% CI 1.192-4.833, p=0.002) were significantly associated with cardiovascular disease risk. The cardiovascular disease risk among patients with type 2 diabetes is high. The male gender, age of at least 50years, part-time employment, and being widowed are socio-demographic factors that should be prioritized at primary level management of cardiovascular disease.

Keywords: *Atherosclerotic cardiovascular risk, Diabetes mellitus, Uganda.*

Introduction

Atherosclerotic cardiovascular disease causes immense morbidity and mortality among patients with type 2 diabetes. Diabetic patients are at a two-to-four-fold increase in atherosclerotic cardiovascular disease risk compared with non-diabetic individuals [1]. Among diabetic patients, the atherosclerotic cardiovascular disease contributes to more than 75% of the overall cause of deaths [2].

For long, diabetes has been regarded as Cardiovascular disease (CVD) risk equivalent,

Corresponding Author: dhabaguma@gmail.com

and this was first suggested by Haffner and colleagues as patients with diabetes without prior myocardial infarction had a similar risk of coronary heart disease to those without diabetes with myocardial infarction (Haffner). This observational study in a Finnish population cohort underlies the suggestion that all people with diabetes should be treated as if they had existing coronary heart disease (CHD). This has since been challenged as this study lacked the power to detect differences between groups of patients. Additionally, patients in this Finish study were self-selected rather than obtained from a population-based cohort [3].

Moreover, a meta-analysis [4] did not show diabetes as a coronary heart disease equivalent and decisions to treat diabetic patients for primary CHD prevention should be based on patient's CHD risk estimate other than "one coat fits all" approach of treatment [4].

A population-based prospective cohort analysis where 1,586,061 adults aged 30-90 years were compared for the risk of subsequent CHD events among individuals with or without a history of diabetes or CHD in a large contemporary real-world cohort over a period of 10 years showed that the risk of future CHD for patients with a history of either diabetes or CHD was similar only among those with diabetes of long duration≥ 10 years [5].

Hence, the atherosclerotic cardiovascular disease (ASCVD) risk is no longer universal for all diabetic patients as there is now heterogeneity in this risk among the diabetic population most especially those younger than 40 years and those with recent onset of the condition [6].

In asymptomatic diabetic patients, there is need to screen for the ASCVD risk as early identification and stratification leads to appropriate management in both the long and short term [7].

Furthermore, quantification of ASCVD risk among diabetic patients is beneficial as it helps to rank patients according to absolute risk for the purpose of aiming therapy to those at greatest risk to fittingly apportion community and health resources.

Additionally, primary prevention modalities such as lipid-lowering therapy, blood pressure control, and antiplatelet therapy have been shown to be effective if used in appropriate patients [8]. Choosing these strategies is dependent on the determination of atherosclerotic cardiovascular risk.

The few diabetic patients in Uganda that are put on appropriate statin doses are those who have suffered from cardiovascular events. However, there is still lack of guidance on the appropriate statin dose for asymptomatic patients and with a short duration of diabetes.

With lack of local data on the predicted 10-year ASCVD risk, it is not clear when to intensify risk reduction strategies through use of newer drugs such as such as Sodium Glucose Co Transporter 2 inhibitors (SGLT2) or Glucagon like peptide 1 agonists (GLP-IA) that have demonstrated cardiovascular benefit in patients with high ASCVD risk or who have had Cardiovascular events [6].

Therefore, this study was conducted to provide data on the magnitude of the predicted 10- year atherosclerotic cardiovascular risk and its socio-demographic determinants among type 2 diabetic patients in Uganda to help guide appropriate early primary ASCVD prevention.

Materials and Methods

Study Design and Setting

This was a cross-sectional study that was conducted in eight (8) diabetes clinics in Central Uganda that referred most patients with cardiovascular disease to Mengo hospital in the preceding year.

Eligible diabetic patients were recruited from Entebbe grade B hospital, Mengo Hospital, Naguru Hospital, Kasangati Health Center IV, which are urban health facilities, and Wakiso Health Center IV, Mpigi Health Center IV, Mityana Hospital, and Kawolo Hospital, which are peri-urban health facilities. These facilities

run a weekly diabetes clinic where approximately 120 patients are treated.

Approximately 600 patients with type 2 diabetes attend these clinics per week. The facilities have well-organized manual patients registers. The diabetes clinics are run by medical officers, clinical officers, and nurses with varied knowledge and skills in diabetes and atherosclerotic cardiovascular disease care. The facilities were selected from both urban and peri-urban areas to enable comparison of predisposition to ASCVD hence generalizability of results. Additionally, the majority of patients with diabetes-related vascular complications that are referred to Mengo Hospital and Mulago hospitals come from Kampala, Wakiso, Mityana, Buikwe, Mpigi, and Mukono districts where these facilities are.

The study period was from November 2020 to February 2021.

Study Population

Patients with type 2 diabetics aged 40-79 years were eligible for the study if they consented and were asymptomatic for ASCVD. The revised Pooled Cohort Risks Equations used in this study are only validated among individuals aged 40 to 79 years. The Pooled Cohorts Risks Equations were used to quantify the ASCVD risk. Pregnant women and very sick patients were excluded from the study.

The sample size was calculated based on a cross-sectional survey using the formula [9]. Using the Uganda National Baseline survey data, the prevalence of the cardiovascular disease among type 2 diabetes was 40% compared to those without type 2 diabetes [10]. Basing on this data, the calculated sample size was 369. Due to the anticipated non-response rate for this study [11], the sample size was increased by 30%. Furthermore, 20 patients were added to adjust for the loss to follow up. Thus, the total sample size was 500 patients with sixty-three (63) patients from each of the eight [8] health facilities. The patients were selected consecutively from the diabetes registers. Trained Research Assistants educated them about the study. Written Informed Consent was obtained from the patients.

Socio-Demographic and Anthropometric Data Collection

Socio-demographic data such as age, sex, residency, employment status, level of education, marital status, family history of coronary heart disease, history of sudden cardiac death, alcohol, and smoking history were collected using a data collection form by the study nurses.

Anthropometric measurements such as blood pressure, weight, height, body mass index, waist circumference, hip circumference, and waist-hip ratio were taken.

Blood pressure was measured by study nurses using an automated OMRON® digital blood pressure machine with an appropriate cuff size. The cuff was placed on the upper arm so that the bladder of the cuff would be centered over the brachial artery. The readings were taken 5 minutes apart following 15 minutes of rest. Three measurements were taken, and an average of these was documented as the participant's blood pressure. Participants were refrained from talking, eating, or smoking for at least 30 minutes before the blood pressure measurements.

Hypertension was defined as systolic blood pressure (SBP)≥140mmHg and or diastolic blood pressure (DBP) ≥90mmHg as per the US 7th Joint National Committee on detection, evaluation, and treatment of hypertension [12].

Weight was measured to the nearest 0.1kg, with the subject standing motionless on the weighing scale. Each weighing scale was standardized every day with a weight of 50 kg. Participants were asked to remove slippers or shoes and any other articles of heavy clothing or jewelry. Participants were asked to step onto the scale in the middle of the platform with their heads erect and eyes looking straight in order to evenly distribute their weight.

Height was measured with the participant standing in an erect position using a portable stadiometer. Participants were checked to ensure the heels, buttocks, shoulder blades, and the back of the head are in contact with the vertical backboard.

The participants head was aligned in the Frankfort horizontal plane (the horizontal line from the ear canal to the lower border of the orbit of the eye is parallel to the floor and perpendicular to the vertical backboard. Arms were made to hang free at the sides with palms facing the thighs. The study nurses' eyes would be level with the headboard. As the headboard was lowered, the participant was instructed to take a deep breath and hold that position while the horizontal board was brought down firmly on top of the head. The headboard was held firmly on top of the head with sufficient pressure to compress the hair. The measurement was recorded to the nearest 0.1cm.

Body Mass Index

Body Mass Index was calculated as weight in kilogram divided by squared height in meters. Conventional BMI cut-offs were used to classify the study population into underweight (BMI <18.5 Kg/m^2) normal BMI (≥18.5 <25 Kg/m^2 overweight BMI >25 to <30 Kg/m^2) obese > 30 Kg/m^2.

Waist Circumference

Participants were instructed to unclothe their waist and hips and stand with their feet pointing forwards and approximately 25-30cm apart to distribute their weight evenly. The lower rib margin was felt, and a marker with a non-permanent marker was made at the exact level of the lowest rib margin. The iliac crest was palpated in the midaxillary line and make a mark on the skin surface. The distance between the two marks (rib cage and iliac crest) was measured. The Participant was instructed to breathe out gently while measurement was taken. A non-stretchable measuring tape was applied horizontally around the participant's body to take the measurements in centimeters. The waist circumference was measured twice to the nearest centimeter using a non-stretchable measuring tape, and the mean values were recorded in the data collection forms. Elevated waist circumference was defined as ≥102cm for men and ≥88cm for women.

Hip Circumference

Study nurses measured the hip circumference using a non-stretchable measuring tape applied at the widest portion of the buttocks at the level of the greater trochanters. The measurements were recorded in centimeters in the participant's data collection form.

Waist-Hip Ratio

The participant's average waist circumference was divided by the average hip circumference to obtain the waist-hip ratio. Elevated waist-hip ratio was defined as ≥0.95 for men and ≥0.88 for women.

Laboratory Data Collection

After 12-hour fasting, blood samples were aseptically collected on the day of appointment by venipuncture of the brachial vein in a 5ml EDTA tube and a 5ml plain tube. Samples were placed on ice(4^0c) and immediately transported to the biochemistry laboratory at Mengo Hospital, where plasma and serum specimen was separated by centrifugation at 3000r/min for immediate analyses. Standard calorimetric methods were used to assay fasting plasma glucose, total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C). Low-density lipoprotein cholesterol (LDLC) was calculated using the Friedwald formula when TG levels are equal to or less than 4mmol/l. Standard colorimetric procedures were used to directly measure LDL-c when TGs are >4mmol/l.

Low-density lipoprotein cholesterol and very low-density lipoprotein were determined as follows using the Friedwald formula:

VLDL=TG ÷ 5

LDL-C=(TC)-VLDL(TG/5) +HDL

Total cholesterol and high-density cholesterol values were fed into the revised Pooled Cohorts Risk Equation to calculate the predicted 10–year atherosclerotic cardiovascular risk.

Quantification of the Predicted 10-year Atherosclerotic Cardiovascular (ASCVD) Risk

Ten-year risk is defined as the risk of developing a first ASCVD event, defined as non-fatal myocardial infarction, fatal or non-fatal stroke over 10-year period among people free from ASCVD at the beginning of that period [13]. The revised Pooled Cohort Risk Equations [14] were used in this study to assess quantitively the atherosclerotic cardiovascular risk among participants with type 2 diabetes aged between 40 and 79 years.

The following independent variables, namely; sex, age, race, total cholesterol, high-density cholesterol, systolic blood pressure, treatment for high blood pressure, presence of diabetes condition, smoking status, were fed into the online Pooled Cohort Risk calculator to calculate the 10-year ASCVD risk. The scores were categorized as low risk with a score < 5%, borderline risk 5-≤7.5%, intermediate risk 7.5-<20% and high risk ≥20% [15]. The risk score was further categorized into a score of less than 7.5 and ≥7.5 % (elevated risk) which is regarded as the clinically relevant threshold [16].

Statistical Analysis

Continuous variables were described using the mean and standard deviation. The ASCVD risk scores were categorized, and their proportions and percentages were calculated with their confidence intervals of 95% (95% CI). The Proportion and percentages of the risk categories were used to obtain the magnitude of the ASCVD risk. The socio-demographic variables were described in terms of proportions, mean and standard deviation. Bivariate and multivariate analyses were done using logistic regression. While adjusting for clustering at health study site levels. The backward method was used to drop the most insignificant variables and to assess for interaction.

There were no significant interactions of the covariables. Confounding was assessed by at least 10% change in the crude and adjusted odds ratios. Statistical significance was set at a p-value of < 0.05.

Ethical Consideration

The study was approved by the Mengo Hospital Research and Ethics committee and registered by the Uganda National Council of Science and Technology. Written informed consent was taken from all study participant results.

Results

Socio-Demographic Characteristics

A total of 500 participants between the ages of 40 and 79 years were screened for the 10-year predicted atherosclerotic cardiovascular risk. Out of 500 participants, 387 (77.4%) were female and 113 (22.6%) were male. The mean age for female and male participants was 55.14 (sd±8.96) and 54.86 (sd±9.07) respectively. These are summarized in Table 1.

Moreover, more than a third of the participants, 141 (36.25%), were in the age range of 50-59 years.

Most of the participants, 323 (64.6%), lived in peri-urban/urban areas, and the majority were unemployed 195 (39%). More than half of the participants, 51.21% (n=256), were educated up to primary school level. No school attendance was noted among 7.6% (n=38) of the participants. The majority of the participants, 57% (n=285), were married. More than eighty percent (80%) of the study participants did not have a family history of coronary heart disease and premature coronary heart disease death. Only 6.8% (n=34) of the participants take alcohol. Smoking was reported among 0.2% (n=1) of the participants.

Table 1. Baseline Socio-Demographic Characteristics of Study Participants(N=500)

Variable		**n (%)**
Sex	Female	387(77.4)
	Male	113(22.6)
Age	40 - 49	144(28.8)
	50 - 59	187(37.4)
	60-69	133(26.6)
	> 70	36(7.2)
Residence	Urban	323(64.6)
	Rural	177(35.4)
Body Mass Index	Under weight	2(0.4)
	Normal	103(20.6)
	Over weight	179(35.8)
	Obese	216(43.2)
Level of education	None	38(7.6)
	Primary	256(51.2)
	Secondary	151(30.2)
	Tertiary	55(11.0)
Marital status	Single	114(22.8)
	Married	285(57.0)
	Widowed	80(16.0)
	Separated	21(4.2)
Employment status	Full time employment	131(26.2)
	Part time employment	24(4.8)
	Causal employment	70(14.0)
	Unemployment	195(39.0)
	House wife	80(16.0)
Family history of CHD	Yes	73(14.6)
	No	427(85.4)
Familial history of premature CHD death	Yes	36(7.2)
	No	442(88.4)
	Don't know	22(4.4)
History of hypertension	Yes	360(72.0)
	No	134(26.8)
	Don’t know	6(1.2)
Alcohol status	Yes	34(6.8)
	No	448(89.6)
	Quit	18(3.6)
Smoking status	Yes	1(0.2)
	No	491(98.2)
	Quit	8(1.6)
CHD Coronary Heart Disease, SD - standard deviation		

Anthropometric and Laboratory Measurements

The participants were majorly overweight 35.8% (n=179) and obese 43.2% (n=216) with a mean BMI of 27.83Kg/m (SD ±5.77). The female participants had a higher waist circumference, 37.8% (n=189), compared to male participants, 2.2% (n=11). Correspondingly, women had a higher waist-hip ratio 46.6% (n=233) than men 10.2% (n=51). The mean systolic blood pressure for participants was 137.5 (SD±1.658). The majority, 58% (n=290) of participants, had elevated total cholesterol. Most 68.4%(n=342) of the female participants had normal high-density lipoprotein cholesterol. More than half of the participants, 55.8 (n=279), had elevated triglyceride levels. Elevated low-density cholesterol (LDL) was found in more than three-quarters (78.6%) of the participants, and the mean LDL was 3.502mmo/l (SD±1.246). Details of anthropometric and laboratory measurements are shown in Table 2.

Table 2. Anthropometric and Laboratory Measurements of Study Participants(N=500)

Variable		**n (%)**	**Mean(±SD)**
BMI	Underweight<18Kg/m^2)	1(0.26)	
	Normal (18-24.99Kg/m^2)	104(20.8)	
	Overweight (25-29.99Kg/m^2)	179(35.8)	
	Obese (≥30Kg/m^2)	216(43.2)	
Mean BMI			27.83Kg/m^2±5.77
WC			
Females	<87.99cm	200(40)	
	≥88cm	189(37.8)	
Males	<101.99cm	100(20)	
	≥102cm	11(2.2)	
Mean WC			88.46cm±12.46
WHR			
Females	<0.879cm	156(31.2)	
	≥0.88cm	233(46.6)	
Males	<0.949cm	60(12)	
	≥0.95cm	51(10.2)	
Mean WHR			0.90±0.093
SBP	<140mmhg	289(57.8)	
	≥140mmhg	211(42.2)	
Mean SBP			137.5mmhg±1.65
DBP	<90mmhg	342(68.4)	
	≥90mmhg	158(31.6)	
Mean DBP			85.62mmhg±11.28
TC	<5.129mmol/l	210(42)	
	≥5.130mmol/l	290(58)	
Mean TC			5.405mmol/l±1.319
HDL-c			
Females	≥1.3mmol/l	342(68.4)	
	<1.299mmol/l	47(9.4)	
Males	≥1.0mmol/l	87(17.4)	

	<1.0mmol/l	24(4.8)	
Mean HDL-c			1.331mmol/l±0.372
TGs	<1.679mmol/l	221(44.2)	
	≥1.680mmol/l	279(55.8)	
Mean TG			2.0781mmol/l±.246
LDL-c	<2.559mmo/l	107(21.4)	
	≥2.56mmol/l	393(78.6)	
Mean LDL-c			3.502mmol/l±1.246

BMI=Body Mass Index, SD=Standard Deviation, Waist Circumference=Waist Hip Ratio, SBP=Systolic Blood Pressure, DBP=Diastolic Blood Pressure=Total Cholesterol-c=High Density Lipoprotein cholesterol, TG=Triglycerides, LDL-c=Low Density Lipoprotein cholesterol

Magnitude of the Predicted 10-year Atherosclerotic Cardiovascular Disease Risk

The mean predicted 10-year atherosclerotic cardiovascular score was 13.4%(sd±9.9). Figure 1 summarizes the categories of the ASCVD risk. Of all the study participants,100(20%) was at low risk,71(14.2%) was borderline,226(45.2%) were intermediate risk, and 103(20.6%) were high risk.

Both the intermediate and high-risk categories constituted the elevated risk (score ≥7.5%), and this was found among 329 (65.8%) participants as shown in Figure 2.

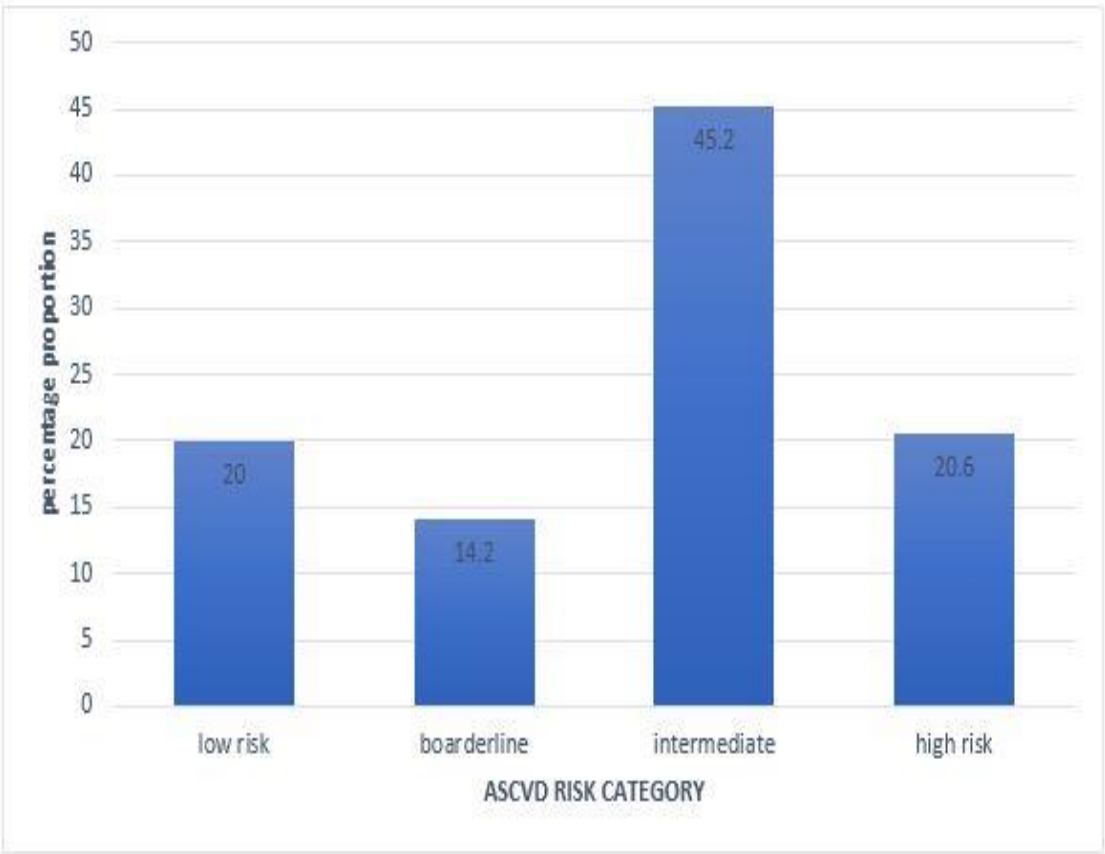

Figure 1. Atherosclerotic Cardiovascular Disease Risk Categories for Study Participants

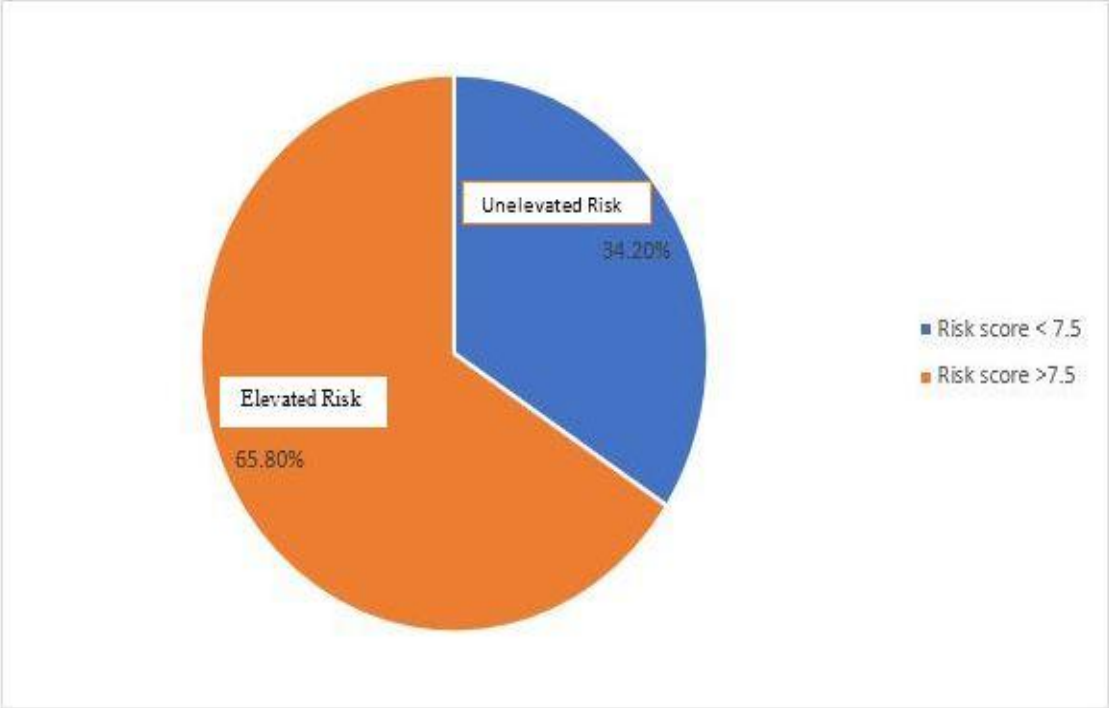

Figure 2. Study Participants with Elevated and Unelevated Atherosclerotic Cardiovascular Risk

Atherosclerotic Cardiovascular Disease Risk Across Socio-Demographic Characteristics

The male participants 81.08% (n=90) were at elevated ASCVD risk than female participants 61.44% (n=239). The proportions of participants with elevated risk progressively rose above 50 years. The participants who lived in rural areas had more elevated risk, 71.19% (n=126), than those in the urban areas, 62.85%(n=203). Elevated ASCVD risk was highest among participants with no Employment, 77.95% (n=152). The distribution of both the low and elevated risk categories were similar across all education levels. Participants who were widowed were at the highest ASCVD risk, 86.25% (n=69). Family history of coronary heart disease (CHD) conferred a higher risk, 72.6% (n=53) compared to those without 64.6% (n=276). The participants with a family of CHD had a similar elevated risk, 63.89 (n=23) compared to those without 65.61 (n=290). The proportions of the elevated risk were similar among smokers 65.99%(n=324) and those who quit 62.5%(n=5). Elevated risk was highest among those who quit alcohol at 77.78(n=14). Details are shown in Table 3.

Table 3. Magnitude of Atherosclerotic Cardiovascular Risk by Socio-Demographic Characteristics(N=500)

Variable	**ASCVD score**		***p* value**
	Low risk n (%)	**Elevated risk n (%)**	
Sex			
Female	150(38.56)	239(61.44)	<0.001
Male	21(18.92)	90(81.08)	
Age			
40 - 49	23(85.19)	4(14.81)	<0.001
50 - 59	144(47.37)	160(52.63)	
60 - 69	3(2.26)	130(97.74)	
> 70	1(2.78)	35(97.22)	

Residence			
Urban	120(37.15)	203(62.85)	0.06
Rural	51(28.81)	126(71.19)	
Employment level			
Full time	58(44.27)	73(55.73)	<0.001
Part time	10(41.67)	14(58.33)	
Casual	26(37.14)	44(62.86)	
None	43(22.05)	152(77.95)	
House wife	34(42.5)	46(57.5)	
Education level			
None	15(39.47)	23(60.53)	0.851
Primary	87(33.98)	169(66.02)	
Secondary	49(32.45)	102(67.55)	
Tertiary	20(36.36)	35(63.64)	
Marital status			
Single	45(39.47)	69(60.53)	<0.001
Married	109(38.25)	176(61.75)	
Widowed	11(13.75)	69(86.25)	
Separated	6(28.57)	15(71.43)	
Family history of CHD			
Yes	20(27.4)	53(72.6)	0.185
No	151(35.36)	276(64.64)	
Family history of CHD death			
Yes	13(36.11)	23(63.89)	0.765
No	152(34.39)	290(65.61)	
Don't know	6(27.27)	16(72.73)	
Smoking			
Yes	1(100)	0(0)	0.373
No	167(34.01)	324(65.99)	
Quit	3(37.5)	5(62.5)	
Alcohol			
Yes	14(41.18)	20(58.82)	0.39
No	153(34.15)	295(65.85)	
Quit	4(22.22)	14(77.78)	

Socio-Demographic Factors associated with the Predicted 10 year-ASCVD risk

The following factors were significantly associated with ASCVD risk; male gender AOR 5.456(CI 2.998-9.932, p<0.001), age 50years and above AOR 7.841(CI 4.863-12.642, p<0.001), part-time employment AOR1.726(CI 1.221-2.441, p<0.002) and being widowed AOR 2.4 (CI 1.192-4.833, p<0.002).

Table 4 shows socio-demographic factors that were significantly associated with ASCVD risk on multivariate analysis.

Table 4. Unadjusted and Adjusted Odds Ratios for the Socio-demographic Factors Associated with Atherosclerotic Cardiovascular Disease Risk

Variable	Unadjusted Odds Ratios (95% CI)	P-value	Adjusted Odds Ratios (95% CI)	P-value
Sex				
Female	1		1	
Male	2.661(2.135-3.317)	<0.001	5.456(2.998-9.932)	<0.001
Age- group				
40-49	1		1	
50-59	7.675(5.546-10.775)	<0.001	7.841(4.863-12.642)	<0.001
60-69	158.73(70.4-357.88)	<0.001	161.442(73.059-356.748)	<0.001
70&above	119.44((14.299-998	<0.001	103.2(11.2-946	<0.001
Employment Status				
Full time	1		1	
Part-time employment	1.130(0.441-2.892)	0.799	1.726(1.221-2.441)	0.002
Casual employment	1.356(0.896-2.051)	0.149	1.186(0.552-2.547)	0.662
Unemployed	2.807(1.249-5.436)	0.002	1.235(0.701-4.296)	0.233
House wife	1.065(0.46-2.462)	0,883	1.486(0.512-4.312)	0.466
Marital Status				
Single	1		1	
Married	1.149(0.795-1.661)	0.459	1.05(0.788-1.399)	0.741
Widowed	4.894(2.45-9.772)	<0.001	2.4(1.192-4.833)	0.014
Separated	2.033(0.929-4.493)	0.079	2.052(0.709-5.949)	0.185

Discussion

This study has revealed that most patients (45.2%) belonged to the intermediate-risk category. Further distribution of the risk was 20% in the low risk, 14.2% in the borderline, and 20.6% in the high-risk categories. Our findings underpin the heterogeneity of the ASCVD risk among patients with type 2 diabetes(4). Patients with diabetes in Uganda are universally treated for coronary artery disease since there is a paucity of data to guide primary prevention and management of this condition. This leads to indiscriminate use of the meagre resources available in a poor country facing a double burden of communicable and non-communicable diseases.

Since our study shows that not all patients are at the same ASCVD risk, there should be a varied approach in their management as regard to statin dose intensity, antiplatelet therapy, and choice of anti-diabetic agents. Without ASCVD stratification, diabetic patients are either under or over-treated [17]. Therefore, in Uganda where there is a high prevalence of dyslipidemia (88%) among patients with diabetes and low rates of its screening, and limited use of lipid-lowering drugs [18]. It is important to educate health workers on the utility of ASCVD risk stratification and management in a poor resource setting. A number of International guidelines such as the 2013 American College of Cardiologists (ACC)/ American Heart Association (AHA),2018 American Diabetes Association (ADA) standards of care, Brazilian Diabetes Society, and the 2016 European Society of Cardiology (ESC) no longer regard diabetes as coronary risk equivalent [19]. Therefore, the 2013ACC/AHA guidelines stipulate stratification for patients with diabetes aged 40 to 79 years into risk categories using a

global risk calculator, the Pooled Cohorts Risks Equations [19].

We have shown that the male gender, age of at least 50years, part-time employment, and being widowed are the socio-demographic determinants of a high ASCVD risk.

Basing on our findings, programs aimed at the control and management of ASCVD among patients with type 2 diabetes should prioritize; the male patients, those aged at least 50 years, the widowed, and those with part-time employment.

The heterogeneity of the ASCVD risk was also demonstrated in a study done in Qatar [20] to estimate the total 10-year cardiovascular disease risk using General Framingham Risk Prediction score and World Health Organization (WHO)/International Society for Hypertension (ISH), the WH0/ISH categorized 81.6% diabetic patients as low risk and 3.8% as high and very high risk while the Framingham score categorized 12.2% as low risk and 57.6% as high and very high risk. This study further confirms that not all diabetic patients are at the same ASCVD risk. Both our study and the Qatari study were of the same design and sample size, but there was a difference in the risk calculators used and, therefore, the difference in the risk categories and scores. We used a revised Pooled Cohort Risk Equations while [20] used WH0/ISH and the Framingham scores, but none of these calculators is specific for diabetic patients; they have a useful discriminative power although they tend to overestimate cardiovascular disease risk in diabetic patients, nonetheless, this does not preclude their usefulness in patients with diabetes [21].

Another study in the Middle East [22] also used general Framingham risk profile and the joint WH0/ISH risk calculator in Omani and showed that between 44% (WHO/ISH charts) and 74% (GFRP method) of patients with DM are at significant high risk for cardiovascular events (≥20% over 10 years).In contrast to the Omani study, our study had only 20.6% in the high-risk category, i.e. a score ≥ 20%, and this difference could be explained by the different study designs and risk calculators employed in both studies. The essence of atherosclerotic cardiovascular disease risk stratification is to implement primary prevention strategies in a cost-effective way, most especially in low resource settings.

In India, a study done to assess global CVD risk showed 68.8%,57%, and 0% in the high, moderate, and low-risk categories, respectively, with QRISK2 Risk Score and 67.7%,23.9%, and 3.2% in the high, moderate, and low-risk categories respectively with the Conventional risk score [23]. This study further shows that the CVD risk is heterogenous; again, the risk outcomes are different from our study as the risk calculators are different. The calculator we used was a revised version to reduce overestimation of the risk by the original version [13]. In a study done in Nigeria where the 10-years CVD risk was assessed with the Framingham score, among participants with type 2 diabetes, metabolic syndrome, and normal controls; low risk (score <10) was found in 27.5% diabetics,55% of metabolic syndrome patients and 72.5% normal controls [24]. The high risk (score>20%) was obtained in 52.5% diabetics,7.5% metabolic syndrome and 2.5% controls. This study had similar scores in the low-risk category and higher scores in the high-risk category compared to our study because the risk scores used were different, and our study had a larger sample size than the Nigerian study.

A Kenyan study done [25] examining the prevalence and correlates of metabolic syndrome and comparing 10-year cardiovascular disease (CVD) risk among Kenyan adults with and without HIV infection. The median ASCVD risk score was lower among people living with HIV compared to HIV negative participants (1.7% vs 3.0%, p=0.02). This study had lower scores compared to our study; participants in the Kenyan study were younger with a median age of 45 years (IQR39.5,53) and 40 years (IQR 31,55) for the People Living with HIV (PLWHIV) and HIV negative participants

respectively. Participants in our study were older, with a mean age of 55.14 (sd±8.96) females and 54.86 (sd±9.07) males. Additionally, there was a difference in the eligibility criteria, and the Kenyan study mainly enrolled people living with HIV with only 1.7% diabetics, while participants in our study were all diabetics. Human immunodeficiency virus (HIV) and diabetes may portend different ASCVD risks. The difference in the eligibility criteria could explain the difference. In a Ugandan Study looking at metabolic and renal complications, clinical and virologic outcomes among HIV positive Ugandan adults on long-term ant-retroviral therapy, 10-year ASCVD risk was assessed using Framingham risk score,16.6% of participants had a score above 10%. The difference in the score can be explained by the difference in the risk calculators and the study populations.

In the current study, male gender was significantly associated with ASCVD risk. This is consistent with a study done [20] where more males were in the high and very high-risk categories with both the General Framingham Risk Predictor (GFRP) and World Health Organization (WHO)/International Society of Hypertension (ISH)risk prediction charts [20, 22]. Similar findings were also found in India [23]. It is well documented that males are at more risk for CVD than females in the premenopausal period(6); in our study, there was no gender difference in mean age; females 55.14(sd±8.96) and males 54.86 (sd±9.07) thus, we would expect the risk difference to even out as women were post-menopausal. Menopause has been shown to increase cardiovascular risk [6]. The difference in our study findings could be explained by higher systolic blood pressure(p=0.008), higher diastolic blood pressure(p=0.109) and abnormal HDL(p=0.005) among males compared to females.

We report that age above 50 years progressively increased ASCVD risk. Our study underpins the relationship between age progression and increases in CVD risk that is directly related to age-dependent changes in the cardio-vasculature. Age is a major non-modifiable risk factor for CVD. The transition from low to moderate risk category occurs at 35 years and 45 years men and women respectively [6]. In our study, the mean age for men was 54.86 (sd±9.07), which transitioned them from low to higher risk categories. Our findings are similar to a study where cardiovascular risk was estimated with a pooled cohort Risk Equations among patients hospitalized in the internal medicine wards [26]. In this study, age greater or equal to 60 years was the main risk factor for high CVD risk.

Part-time employment was significantly associated with high ASCVD risk. Part-time employment is closely linked with job instability and periods of unemployment, all of which led to psychosocial stress [27]. Job instability and unemployment portend a low social, economic status which is associated with increased cardiovascular disease risk through psychobiological pathways that specifically slow recovery in blood pressure and heart rate variability following mental stress [28]. Our findings add to the evidence consistent with a study done among Whitehall II cohort of 228 British Civil servants aged between 47-58 years where the grade of employment (indicator of socio- economic status) was assessed against cardiovascular measures that were monitored during performance of two behavioral tasks and for 45 min following stress [28]. Post-stress return of blood pressure and heart rate variability to resting levels was less complete after 45 min in the medium and low than in the high-grade of employment groups. Furthermore, the odds of failure to return to baseline by 45 min in the low relative to the high grade of employment groups were 2·60 (95% CI 1·20–5·65) and 3·85 (1·48–10·0) for systolic and diastolic pressure, respectively, and 5·19 (1·88–18·6) for heart rate variability, adjusted for sex, age, baseline levels and reactions to tasks. We appreciate the significant difference between the British study

and ours but its findings are worth noting to explain this important association in our study.

Additionally, job instability and unemployment lead to unnecessary drug discontinuation, which is an independent determinant of cardiovascular disease among patients with diabetes [7]. In a population-based cohort study examining the association between employment status and risk of all-cause and cause-specific mortality [29] temporarily unemployed or never employed participants aged 18-65 years had a significantly increased risk of mortality from cancer, cardiovascular disease, chronic lower respiratory disease, diabetes and kidney disease [29] (temporary unemployed HR 1.76, 95% CI 1.67 to 1.86; never employed HR 1.63, 95% CI 1.47 to 1.81; retired HR 1.27, 95% CI 1.17 to 1.37).

Being widowed was significantly associated with high ASCVD risk in our study. Marital status has a protective effect on CVD, especially in men as they benefit from spousal support [29]. In a systematic review and meta-analysis on marital status and risk of cardiovascular diseases showed that partner loss or poor-quality relationships negatively impact on economic, behavioral and emotional well- being of an individual which reduces one's ability to prevent, detect and treat illness. [30] pooled 34 prospective cohort studies which differed from our study in terms of design, a number of participants, and a follow-up component nevertheless, we were able to show the association between ASCVD risk and being widowed.

Strengths of the Study

The strength of the study is that the study was done in a real-world setting with a fairly homogenous population.

Limitations of the Study

The risk calculator we used is not diabetes-specific so we could have overestimated the risk. Additionally, the risk calculator has not been validated in the Ugandan population. This being a cross-sectional study, no causal relationships can be inferred.

Conclusion

Participants in this study were at varied risk for atherosclerotic cardiovascular disease. The male gender, age, ≥50years, part-time employment, and being widowed are significant socio-demographic determinants of the ASCVD risk. Patients with diabetes should have their risk-stratified for appropriate resource allocation in primary prevention.

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Conflict of Interest

The authors declare no conflict of interest.

Authors' Contributions

WL, SB, RW, and DK, conceptualized and designed the manuscript and revised and approved its final version. WL was the Principal Investigator of this study. RW developed the statistical plan for the study. RM and ES analyzed data with the guidance of WL. SB was the supervisor of the study. All the authors revised and approved the final version.

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