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Prevalence and Correlation of Abnormal Atherogenic Cardiovascular and Ankle Brachial Indices with Predicted 10-Year Atherosclerotic Cardiovascular Disease Risk among Patients with Type 2 Diabetes in Central Uganda

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Aim: The aim of this study was to determine the prevalence of abnormal atherogenic cardiovascular indices, Ankle brachial index and their correlation with the predicted 10-year atherosclerotic cardiovascular disease risk (ASCVD) among type 2 diabetes patients in Central Uganda.
Methodology: Five hundred patients aged 40-79 were consecutively selected. Socio-demographic data was collected with a pre-tested questionnaire. Physical and laboratory measurements were performed. Atherogenic cardiovascular indices such as Atherogenic Index of

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Plasma (AIP), Atherogenic Coefficient and Casteri Risk Index I& II were determined. Ankle Brachial Index (ABI) was measured. We used the revised Pooled Cohorts Risk Equations to quantify the 10-year atherosclerotic cardiovascular disease (ASCVD) risk. The proportions and percentages of atherogenic cardiovascular indices, ABI and 10-year ASCVD risk were determined. Pearson chi-square correlation analyses were performed to determine correlation. Statistical significance was set at $P<0.05$.

Results: The prevalence of elevated AIP was 56.45%, Casteri Risk Index I 68.4%, Casteri Risk Index II 32.6 and Atherogenic Coefficient 64.8%. Low ABI of<0.9 was found among 25.4% while 0.6% had an ABI>1.3.Atherogenic cardiovascular indices significantly correlated with 10 year ASCVD risk with Casteri Risk Index I (r=0.185, $P<0.001$), Casteri Risk Index II (r=0.127, $P=0.004$), Atherogenic Coefficient r=0.186, $P<0.001$). AIP was positively but not significantly correlated with ASCVD risk (r=0.053, $P=0.241$). ABI negatively correlated with the ASCVD risk (r=-0.225, $P<0.001$).

Conclusion: Prevalence of abnormal atherogenic cardiovascular indices and ABI was high. They correlated with the ASCVD risk. Atherogenic cardiovascular indices and ABI can be used to screen and manage ASCVD in our setting.

Keywords: Atherogenic index of plasma; casteri risk index; atherogenic coefficient; ankle brachial index; type 2 diabetes.

ABBREVIATIONS

ABI : Ankle Brachial Index
ABPI : Ankle Brachial Pressure Index
AC : Atherogenic Coefficient
AIP : Atherogenic Index of Plasma
ASCVD : Atherosclerotic Cardiovascular Disease
BMI : Body Mass Index
CRI-I : Casteri Risk Index 1
CRI-II : Casteri Risk Index II
DBP : Diastolic Blood Pressure
HDLc : High Density Lipoprotein cholesterol
LDLc : Low Density Lipoprotein cholesterol
MH : Mengo Hospital
R : Correlation Coefficient
REC : Research Ethics Committee
SBP : Systolic Blood Pressure
SD : Standard Deviation
TC : Total Cholesterol
TG : Triglycerides
WC : Waist circumference
WHR : Waist Hip Ratio

1. INTRODUCTION

Atherosclerotic cardiovascular disease is the leading cause of morbidity and mortality among patients with type 2 diabetes mellitus (T2D) [1]. One of the major risk factors for atherosclerotic cardiovascular disease is diabetic dyslipidemia which is characterized by low levels of high-density lipoprotein (HDL), increased triglycerides and smaller dense LDL-Cholesterol particles (LDL-C) [2].

Diabetic dyslipidemia is characterized by both quantitative and qualitative abnormalities [3]. In clinical practice, it is the quantitative abnormality that is routinely assessed through estimation of lipid parameters. Atherogenic indices such as Castelli Risk Index I &II (CR-I&II), Atherogenic Index of Plasma (AIP) and Atherogenic Coefficient (AC) which are useful in assessing qualitative lipid abnormalities [4] are rarely ordered.

In usual care of patients with diabetes, a lipid profile is usually ordered and the individual parameters many times are border line or normal. A normal lipid profile doesn't exclude cardiovascular risk entirely [5] Therefore, cardiovascular indices (lipid fractions) can thus be used by the clinician to predict CAD risk and also determine treatment adequacy and efficacy at no added cost [6].

Cardiovascular disease is comprised of ischemic stroke, non-fatal myocardial infarction and peripheral arterial disease and accounts for 80% of deaths among patients with T2D [7]. Among CVD, CAD is the major contributor to CVD mortality among patients with T2D and is responsible for 29.7% of the mortality [8]. Whereas the predicted 10-year ASCVD risk assesses the global ASCVD risk (ischemic stroke, non-fatal myocardial infarction, peripheral arterial disease), the atherogenic indices are predictors of CAD which is a major component of ASCVD [8].

Notably, AIP is a major predictor of atherosclerosis and coronary heart disease (CHD) and reflects the relationship between protective and atherogenic lipoproteins [4,9] AIP

is an indicator of LDL particle size that is not determined by the usual lipid profile [9].

CRI-I and II are ratios of TC and HDL-C and LDL-C/HDL-C respectively are better predictors of CAD risk than absolute lipid or lipoprotein levels [6].

In circumstances where traditional lipid profile is limited, use of these ratios most especially when LDL-c level are under the target range is warranted. These ratios aid the clinician to identify at risk individuals who could be missed by the ordinary lipid profile [6].

In our setting, the prevalence of atherogenic cardiovascular indices of our patients is not known. It is worth noting that one of these indices that is AIP correlates with the LDL-C particle size [4,9]. In diabetic patients, it is not only the LDL quantity that is important to control but also small LDL-C particles that are easily oxidized and deposited on the vascular endothelium need to be assessed.

Patients with diabetes have both clinical and subclinical atherosclerosis that orchestrate diabetic macrovasculopathy [10]. For effective cardiovascular disease management, both entities of atherosclerosis must be taken care of. Several markers of subclinical atherosclerosis such as ankle brachial Index (ABI), carotid artery medial intimal thickness, coronary artery calcium and pulse wave velocity(PWV) have been described [10]. An ABI of < 0.9 does not only signify peripheral arterial disease but also generalized /multisystemic atherosclerosis [11].

In our setting, where 65.8% of people living with diabetes are at high CVD risk [12], the best way of tackling CVD mortality and CVD events is primary prevention through knowledge of all the vascular risk factors and how they relate or correlate with each other so that appropriate medications with proven cardiovascular benefits such as sodium glucose transporter inhibitors and glucagon like peptide agonists can be prescribed appropriately [13].

Knowledge of the ASCVD risk further helps the clinician decide on the statin dose intensity and when to use antiplatelet agents [13] most especially in a poor resource setting.

To our knowledge there is dearth of knowledge about the prevalence of atherogenic cardiovascular indices, ABI and their correlation with the predicted 10-year ASCVD risk among patients with diabetes in Uganda.

Therefore, the current study was conducted to understand the prevalence of atherogenic cardiovascular indices, ABI and their correlation with the predicted 10-year ASCVD risk among patients with T2D in Central Uganda so that clinicians are guided on when to use drugs with proven cardiovascular benefit, appropriate statin dose strength and antiplatelet prescription.

2. MATERIALS AND METHODS

2.1 Study Setting

This study was conducted in eight diabetes clinics in Central Uganda namely; Entebbe grade B hospital, Mengo Hospital, Naguru Hospital, Kasangati Health Center IV, Wakiso Health Center IV, Mpigi Health Center IV, Mityana Hospital and Kawolo Hospital.

These clinics are conducted by nurses, clinical and medical officers where about 80 patients are seen weekly per each clinic. This study was part of our clinical trial and details about the study setting are found in our published protocol [14].

2.2 Study Design and Population

This was a cross-sectional study conducted from November 2020 to February 2021.

Eligible participants were patients with T2D aged 40-79 years and who were asymptomatic for ASCVD. Pregnant women and very sick patients were excluded from the study.

2.3 Sample Size and Sampling Techniques

We calculated the sample size using Kish and Leslie formula [15] for cross-sectional studies. The calculation was based on the prevalence of cardiovascular disease among patients with T2D of 40% in a study by Guwattude et al [16] with the assumptions of 95% confidence interval and a 5% margin error.

In order to obtain adequate power, the sample size was increased by 30% due to the anticipated non-response rate for this study [17]. We added more 20 patients to cater for the loss to follow up. Therefore, a total of 500 patients were enrolled. Sixty-three patients from each of the eight health facilities were consecutively

selected from the diabetes registers. Eligible patients gave written informed consent.

2.4 Measurements

2.4.1 Socio-demographic characteristics

Socio-demographic data namely age, sex, level of education, employment status and smoking status was collected and entered into the data collection forms. Data was collected by face to face interview by trained study nurses.

2.4.2 Anthropometric and clinical measurements

Blood pressure was measured by study nurses using an automated OMRON® digital blood pressure machine with an appropriate cuff size. Participants were refrained from talking, eating or smoking for at least 30 minutes before the blood pressure measurements. The cuff was placed on the upper arm so that the bladder was centered over the brachial artery. Two measurements 5 minutes apart were performed. The average of the 2 measurements was documented [18].

Body weight was measured to the nearest 0.1kg using the Seca digital measuring scale with the subject standing motionless in light clothes without shoes. Each weighing scale was standardized every day with a weight of 50 kg [18].

We measured height to the nearest 0.1 cm with the subject standing in an erect position against a portable Seca digital stadiometer with the head positioned so that the top of the external auditory meatus was in level with the inferior margin of the bony orbit [18].

Body mass index(BMI) was obtained from the patient's measured weight and height calculated as weight (Kg)/height(M^2) and categorized according to WHO standard cut offs; underweight BMI <18.5 Kg/m^2) normal BMI (≥18.5 <25 Kg/m^2 over-weight BMI >25 to <30 Kg/m^2) obese > 30 Kg/m^2 [19].

Waist circumference was measured with a non-stretchable Seca 201 Ergonomic circumference measuring tape applied at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest. The waist circumference was measured twice to the nearest 0.1cm and recorded in the data collection forms. Elevated waist circumference was defined as ≥102cm for men and ≥88cm for women [19].

Hip circumference was measured using a non-stretchable Seca 201 Ergonomic measuring tape applied at the widest portion of the buttocks at the level of the greater trochanters. The measurements were recorded to the nearest 0.1cm in the participants data collection form.

Waist-hip ratio was obtained by dividing the participants average waist circumference by the average hip circumference. Elevated waist-hip ratio was defined as ≥0.95 for men and ≥0.88 for women [19].

2.4.3 Laboratory measurements

After a 12-hour fasting, 2ml of blood were aseptically collected on the day of appointment by venipuncture of the brachial vein into 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 were separated by centrifugation at 3000rpm/min for immediate analyses. Glycated Hemoglobin(HbAIc), total cholesterol (TC), HDL), triglycerides (TG) and LDL were measured using the Roche Hitachi Cobas C311 chemistry analyzer as described elsewhere [20].

2.4.4 Atherogenic cardiovascular indices

The atherogenic cardiovascular indices were Atherogenic Index of Plasma, Casteri risk Index I &II and Atherogenic Coefficient. These were calculated from the lipid parameters as shown below:

Atherogenic Index of Plasma (AIP) was calculated from Log10 (TG/HDL-C) ratio

Low CAD risk was when AIP was -0.3-0.1, medium risk 0.1 -0.24 and high CVD risk >0.24 [9]

Castelli Risk Index 1(CRI-I) or Cardiac Risk Ratio was estimated as: TC/HDL-C ratio, A low risk was defined as ≤4 (6)

Castelli Risk Index II (CRI-II) was determined as LDL-c/HDL-C ratio. A low risk was defined <3.0 [6].

Atherogenic Coefficient (AC) was calculated as follows:

AC= (TC-HDL-C)/HDL-C or (Non-HDL-C)/HDL-C ratio

A low risk was defined as < 3.0 [6].

2.4.5 Ankle brachial index

ABI was measured using the MESI ABPI MD device. The red cuff was positioned on the upper arm, green on the right ankle and yellow on the left ankle to determine ABPI [21]. A normal ABI was any value between 0.9 and 1.3. Values<0.9 indicative of arterial disease and >1.3 non-compressible blood vessels [22].

2.4.6 Quantification of the predicted 10-year atherosclerotic cardiovascular (ASCVD) risk

We defined the predicted 10-year risk as the risk of developing a first ASCVD event, such as non-fatal myocardial infarction, fatal or non-fatal stroke over a 10-year period among people with T2D free from ASCVD at the beginning of the study period [23].

In this study, we used the revised Pooled Cohorts Risk Equations [24] to quantity the predicted 10-year ASCVD risk among the participants.

Independent variables such as; sex, age, race, TC,HDL, SBP, 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 predicted ASCVD risk.

2.5 Data Quality Assurance

Study nurses were trained for two days at Mengo Hospital on data collection tools and methods. The data collection tools were pre-tested among 8 study nurses during the training and necessary modifications effected. We followed standard operating procedures during laboratory sample collection, storage, analysis and recording.

2.6 Data Processing and Analysis

The data collected was checked for completeness, coded and entered into Epi Data manager version 4.6 and exported to STATA version 14. Continuous variables were described using the mean and standard deviation. Categorical variables were expressed as frequencies and percentages and were compared using Chi-square tests. The correlation between atherogenic cardiovascular indices, ABI and ASCVD risk was determined by Pearson chi-square correlation analyses. A *P*-value of less than 0.05 was considered statistically significant.

3. RESULTS

3.1 Socio Demographic Characteristics

Out of the 500 study participants, majority (77.4%) were females and the mean age of the participants was 55.07±8.979. The majority 187(37.4%) were aged between 50 and 59 years. Most 323(64.6%) of the study participants were urban residents, 256(51.2%) attended Primary school. More than half 285(57.0%) were married, 195(39.0%) were unemployed, 427(85.4%) had no family history of coronary heart disease and 442(88.4%) did not have history of premature coronary heart disease death in the family. Details are shown in Table 1. The majority 448(89.6%) did not take alcohol and 491(98.2%) did not smoke.

3.2 Anthropometric, Clinical and Laboratory Measurements

The mean BMI of the study participants was 29.78±5.778. There was no significant difference in waist circumference between females and men though men had a higher mean waist-hip ratio 0.942±0. 106. Across all the study participants, the mean systolic blood pressure was 137.53mm Hg±19.65, HbA1c 8.919%±2.818, fasting blood sugar 9.514mmol/l±4.878,TC5.405mmol±1.319, HDL-C1.331mmol/l±0.372,LDL3.502mmol/l±1.181,CRI-I 4.284mmol/l±1.416,CRI-II 2.739±1.03, and A.C 3.282±1.43.There was no significant difference in triglycerides, AIP, AC and ABI between sexes. Details are in Table 2. The male participants had diabetes for a longer time (mean 7.072±6.992) and higher ASCVD score of 16.758%±10.182.

3.3 Prevalence of Abnormal Atherogenic Cardiovascular Indices and ABI

Out of 500 participants, 218(43.6%) had low, 101(20.2%) moderate and 181(36.2%) high AIP. Thus, 56.4% of the participants had intermediate and high AIP (atherogenic risk). More than 68% of the participants had elevated CRI-I and AC while the majority 337(67.4%) participants had normal CRI-II. About 127(25.4%) had a low ABI and 03(0.6%) had poorly compressible vessels. There was no significant difference in AIP, AC and ABI between sexes. Details are in Table 3.

Table 1. Socio demographic characteristics of study participants (N=500)

Variable	n (%)	Mean±SD
Age		
40-49	144(28.8)	
50-59	187(37.4)	
60-69	133(26.6)	
>70	36(7.2)	55.07±8.979
Gender		
Female	387(77.4)	
Male	113(22.6)	
Residence		
Urban	323(64.6)	
Rural	177(35.4)	
Education level		
None	38(7.6)	
Primary	256(51.2)	
Secondary	152(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	131(26.2)	
Part time	24(4.8)	
Casual Employment	70(14.0)	
Unemployment	195(39.0)	
House wife	80(16.0)	
Family History of Coronary Heart Disease		
Yes	73(14.6)	
No	427(85.4)	
Family history of premature coronary Heart Disease Death		
Yes	36(7.2)	
No	442(88.4)	
Don't Know	22(4.4)	
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)	

Table 2. Anthropometric, clinical and laboratory measurements of study participants

Variable	Mean ±SD					
	Female	**SD**	**Male**	**SD**	**All**	**SD**
BMI	30.249	5.755	28.15	5.583	29.783	5.778
W.C	88.388	12.658	88.876	11.832	88.496	12.44
W. H. R	0.89	0.086	0.942	0.106	0.901	0.093
SBP	136.191	19.509	141.652	19.713	137.539	19.658
DBP	85.191	11.423	87.124	10.72	85.62	11.289
HBA1C	8.9	2.845	8.986	2.734	8.919	2.818
FBS	9.586	5.144	9.262	3.809	9.514	4.878
T.C	5.544	1.288	4.917	1.317	5.405	1.319
HDL-C	1.36	0.373	1.227	0.35	1.331	0.372
LDL-C	3.627	1.155	3.065	1.174	3.502	1.181
TGs	2.062	1.06	2.138	1.755	2.078	1.246
Diabetes Duration	6.918	6.207	7.072	6.993	6.952	6.383
ASCVD score	12.478	9.637	16.758	10.182	13.428	9.911

Table 3. Atherogenic Cardiovascular Indices and AB1

Variable	Frequency	Percentage
AIP		
Low risk (-0.3-0.1)	218	43.6
Moderate risk (0.1-0.239)	101	20.2
High risk (≥0.24)	181	36.2
CRI- I		
Normal (<4)	158	31.6
Abnormal (≥4)	342	68.4
CRI-II		
Normal (<3.0)	337	67.4
Abnormal (≥3.0)	163	32.6
AC		
Normal (<3.0)	158	31.6
Abnormal(l≥3.0)	342	68.4
ABI		
Normal (≥0.9-1.3)	370	74.0
Low (<0.9)	127	25.4
Poorly compressible Vessels (≥1.3)	03	0.6

Table 4. The mean and standard deviations of atherogenic cardiovascular indices and ankle brachial index

Variable	Mean ±SD					
	Female	SD	Male	SD	All	SD
CRI-I	4.294	1.381	4.25	1.539	4.284	1.416
CRI-II	2.789	1.031	2.567	1.015	2.739	1.03
AIP	0.177	0.436	0.177	0.321	0.177	0.413
A.C	3.184	1.28	3.246	1.16	3.282	1.43
ABI	0.979	0.158	0.954	0.0.148	0.973	0.156

Table 5. Correlation between ASCVD risk with atherogenic cardiovascular disease indices and ankle brachial index

Parameter	r	P value
AIP	0.053	0.241
CRI-I	0.185	<0.001
CRI-II	0.127	0.004
AC	0.186	<0.001
ABI	-0.225	<0.001

r= Pearson's correlation coefficient

The mean±SD of CRI-I was 4.284mmol/l±1.416,CRI-II 2.739±1.03, and AC 3.282±1.43.The mean ABI was 0.97± 0.156. Details are shown in Table 4.

3.5 Correlation between Atherogenic Cardiovascular Indices, ABI and Predicted 10-Year Atherosclerotic Cardiovascular Disease Risk

Atherogenic cardiovascular indices were positively and significantly correlated with ASCVD with CRI-I (r=0.185, *P*<0.001), CRI-II (r=0.127, *P*=0.004) and AC r=0.186, *P*<0.001). Details are shown in Table 5.

AIP was positively but not significantly correlated with ASCVD risk (r=0.053, p=0.241).

ABI was negatively but significantly associated with ASCVD risk (r=-0.225, p<0.001). The correlation is further depicted in Fig. 1.

4. DISCUSSION

In this cross-sectional study, we assessed the prevalence of abnormal atherogenic cardiovascular indices and ABI and their correlation with the predicted 10-year ASCVD risk among patients with T2D in in 8 rural and urban clinics in Central Uganda. Our study showed 56.4% of the participants had high and intermediate AIP (atherogenic risk). CRI-I and AC were elevated in 68.4% of the study participants. The majority (67.4%) of participants had normal CRI- II. About 25.4 % and 0.6% of the study participants had a low ABI and poorly compressible vessels respectively. The current study showed positive and significant correlation between CRI-I(r=0.185, p<0.001), CRI-II (r=0.127, p<0.004), AC (r=0.186, p<0.001) and the predicted 10-year ASCVD risk.AIP (r=0.053, p=0.241) was positively but not significantly correlated with the ASCVD risk.

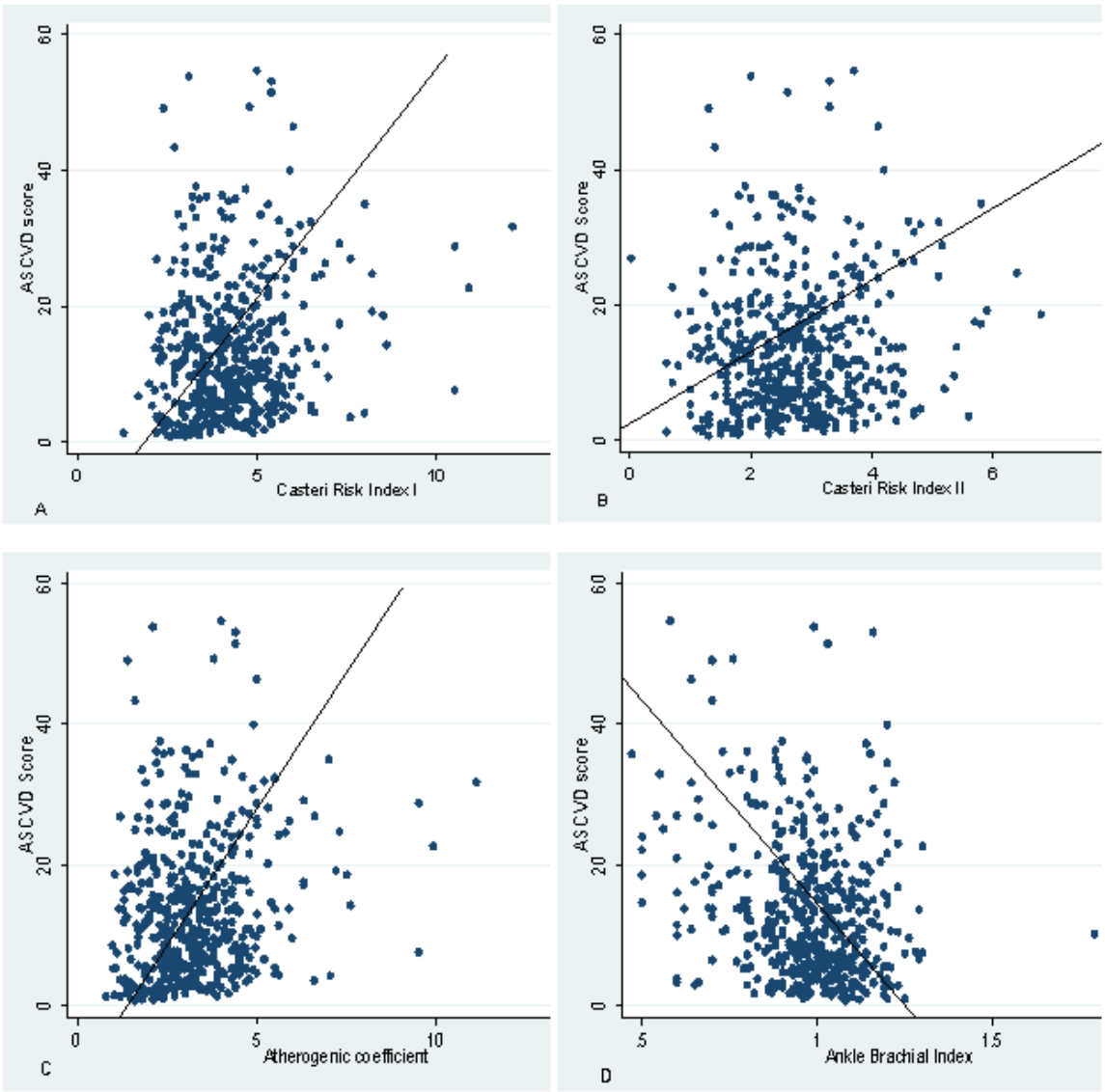

Fig. 1. Correlation of ASCVD risk with A) Casteri Risk Index I, B) Casteri Risk Index II, C) Atherogenic Coefficient D) Ankle Brachial Index

In this study, ABI was negatively but significantly correlated with the ASCVD risk (r=-0.225, p<0.001).

To the best of our knowledge, this is the first study to assess the prevalence of abnormal atherogenic cardiovascular indices, ABI and their correlation with the predicted 10 year ASCVD risk among patients with T2D in Central Uganda. Atherogenic cardiovascular indices most especially the AIP are predictors of coronary artery disease which is the major cause of death among the ASCVD spectrum (4) whereas the predicted 10-year ASCVD risk estimates an individual's global CVD risk (23) of which CAD is a component. Correlation between these two important measures of ASCVD risk is not known among our patients.

In a study done in India, CRI-I, CRI-II, AC and AIP were significantly elevated in diabetic patients compared to controls and identified CV risk better than the individual lipids alone. In the same study, AIP was a better marker in identifying cardiovascular risk with a high sensitivity of 92% and specificity of 96% specificity [4]. Comparatively, our study did not show a significant correlation between AIP and ASCVD risk and reasons for this were not clear.

Similar to our study, a significant increase in CRI-I and CRI-II was observed in diabetic

atherosclerotic subjects compared to age and sex matched non-diabetic atherosclerotic and normal controls [4] and this increase was noted with increasing age in both genders. We did not show age and sex matched distribution of these indices since our study design was cross-sectional.

Atherogenic cardiovascular indices namely CRI-I/II, AIP and AC are useful indices for CAD risk prediction [4,6].

In our study, atherogenic cardiovascular indices were significantly elevated underpinning a high CAD risk in our study population. S. Bhardwaj et al showed that atherogenic cardiovascular indices were elevated significantly in angiographically confirmed patients of CAD [6]. Similarly, atherogenic cardiovascular indices were elevated in our study signifying a high CAD risk in our patients. AIP contributed 31% to the total CAD risk, CRI-I 20%, CRI-II 13% and AC 17% in the Indian study. There was significant positive correlation between these indices and CAD in the same study [6].

Consistent with our study, a high AIP was shown in 31.4% of diabetic and hypertensive patients in a Nigerian hospital [5] similarly, the Nigerian study was also cross-sectional with similar patients studied.

Wekesa et al showed that 42 % of individuals in a large population based survey in Uganda had high and intermediate atherogenic risk [25]. The differences in the findings between the two studies could be explained by the differences in the study design, population sample, nature of patients studied and specimen collected.

We used the revised Pooled Cohort Risk Equations [24] to estimate the global 10-year ASCD risk which includes ischaemic stroke, non-fatal myocardial infarction and peripheral disease while the atherogenic indices are predictors of CAD a major component of global ASCVD. Understanding the correlation between the predicted ASCVD risk and the atherogenic cardiovascular indices is useful in daily practice because in poor resource settings indices can be easily calculated from routine lipogram so that patients at high CVD risk can be easily identified so that they can be started on medications with CVD benefit such as SGLT2 inhibitors and GLP 1 Agonists [13] and appropriate statin dose strength. In routine diabetes care, quantitative assessment of lipids may be normal or at target yet patients may have qualitative lipid abnormalities such as small density LDL (sdLDL) particles that easily invade, deposit and oxidize on arterial wall compared with LDL [4,9]. Incidence of CAD has been associated with low HDL, high TG and high LDL-C levels. However, CAD cannot be ruled out by a normal lipid profile [6]. Therefore, different combinations of the lipid parameters are useful in identification of such high-risk individuals.

In such circumstances, atherogenic cardiovascular indices that assess qualitative lipid abnormalities are very useful in our setting since they are non-invasive, cheap and widely available in our clinics.

Additionally, atherogenic cardiovascular indices can aid the clinician identify at risk individuals that could be missed by ordinary lipid profile [4].

Corroborating from our study, atherogenic cardiovascular indices can be used by clinicians in daily practice to predict CAD, determine statin therapy adequacy in all clinical settings including rural areas. These indices most especially the atherogenic index of plasma correlate with the LDL-C particle size and thus can be used to determine the plasma atherogenicity [6].

In the Ugandan setting where few patients have their lipograms performed, the LDL-C levels are near normal or normal and therefore patients are deemed “ASCVD safe” and no statin is prescribed. In a study by Kibirige et al, lipogram was performed in 14 % of patients whereas an LDL target of <100mg/dl was achieved in only 20% [26]. This study shows that there is little done in our setting to screen and effectively treat diabetic dyslipidemia.

Additionally, among those who are started on statins, follow up lipograms are not performed [26]. For those whose follow up lipograms are performed, adequacy of therapy is determined by quantity of LDL-c which may be normal or slightly reduced. Therefore, use of atherogenic cardiovascular indices that are easy to calculate help to determine qualitative and kinetic abnormalities that orchestrate ASCVD risk in diabetic dyslipidemia.

In our study, CRI-I, CRI-II and AC positively and significantly correlated with the 10-yearASCD risk and this underpins urgent change in practice of routinely calculating these ratios to predict the 10-year ASCVD risk for effective primary prevention of CVD among our patients with T2D.

Abnormal ABI of <0.9 and ≥ 1.3 were obtained in 26% of the study participants. In Uganda and other parts of the world, the prevalence of ABI< 0.9 among patients with T2D has varied from 24%-68% [11,27–31]. The difference in terms of study design, population studied and method used in determining ABI could explain the difference in magnitude in our study. The magnitude of PAD could have been higher had we included patients with symptomatic PAD. We did not include symptomatic patients since the 10-year predicted ASCVD risk is determined among asymptomatic individuals. Ankle brachial Index is a marker of subclinical atheroma and high cardiovascular risk (31). An ABI of < 0.9 is not only diagnostic of peripheral arterial disease but it is a marker of CAD, cerebral vascular disease and atherosclerosis in other vascular beds [11,31].

In the current study, ABI was negatively but significantly correlated with the predicted 10-year ASCVD risk that assesses ischaemic stroke, non-fatal myocardial infarction and peripheral disease risk in an individual. In a study conducted in Iran, patients with ABI < 0.9 had significant coronary artery stenosis with higher means of stenosis for all vessels [32]. Compared to our study, patients enrolled were fewer, symptomatic for CAD with only 40% being diabetic [32].

Similar findings were observed in a population-based cross-sectional study by FGR Fowkes et al that evaluated subclinical atherosclerosis using ABI in a rural African Population; ABI was related to certain cardiovascular disease risk factors such as cigarette smoking, high systolic blood pressure [31]. However, this study differed in terms of population studied and used individual traditional CVD risk factors rather than a CVD risk score.

In another study that assessed the relationship between ABI, toe-brachial index and cardiovascular mortality in persons with and without diabetes, a U-shaped relationship was demonstrated between ABI categories and CVD death [30]. Patients with low (<0.90) and high(>1.30) were at higher CVD mortality after a 7-year follow up. This study further corroborates our finding that patients with a low ABI are at higher risk of CVD death [30] despite the marked difference in study designs in both studies.

However, in a study by So Young Park et al, ABI was not correlated with 10-year ASCVD risk score or metabolic syndrome risk factors whereas Cardio-Ankle Vascular Index, Intimal Medial Thickness were correlated [10]. It is worth noting that this study had only 3 patients (1.4%) with an ABI<0.9 compared to 25.4% in our study. This could explain the failure to demonstrate a correlation.

One of the limitations for the use of ABI as a surrogate marker for subclinical atherosclerosis in DM is the presence of medial arterial calcifications (MAC) at the level of ankle vessels that decreases its sensitivity and specificity [30]. Ankle Brachial measurements of >1.3 signify poorly compressible vessels and MAC. In our study, only 3(0.6%) of the participants had ABI> 1.3 thus ABI measurements were assumed to be fairly sensitive and specific.

ABI is a simple objective, reliable and non-invasive test and is one of the tests for subclinical atherosclerosis which underpins macro vasculopathy in T2D. In our recent study, majority of T2D patients have a high ASCVD risk [12] and hence interventions in our setting are urgently needed. Much as determination of the predicted 10- year ASCVD risk using the Pooled Cohorts Risks Equation requires measurement of the lipid profile which is inexpensive; it is not readily available in remote poor settings in the country, therefore the 10year ASCVD risk can be easily assessed with the ABI measurement that can be performed by any health worker with minimal training .ABI measurement is simple, non-invasive and cheap [27]. Despite recommendations by several studies [11,27]. ABI is not routinely performed among patients with T2D in our clinical setting.

The strengths of our study are that the sample size was fairly large and the population studied was quite homogenous as it comprised of mainly Baganda in the same area.

However, the study was limited by its cross-sectional and correlational design as no causal relationships can be inferred from it. Secondly, it was a hospital-based study whose findings may not be generalizable to the general population as we could have had a selection bias. Thirdly, the revised Pooled Cohorts Risk Equations have not been validated in the Ugandan Population. Fourthly, single measurements of the laboratory parameters could have affected accuracy of the results.

5. CONCLUSIONS

This study has shown that majority of patients with T2D in Uganda have abnormal atherogenic cardiovascular indices. We have also shown that there is a high prevalence of abnormal ABI among our patients. The current study has shown that abnormal atherogenic cardiovascular indices and ABI correlate significantly with the predicted 10- year ASCVD risk. These parameters can be used to estimate the 10-year ASCVD risk in our setting most especially when quantitative lipid parameters are normal or subnormal. Estimation of the ASCVD risk helps to start patients on drugs with cardiovascular benefit such as SGLT2 inhibitors, GLPA agonists and also use appropriate statin dose strength and antiplatelet agents so that meagre resources are used cost effectively in our setting.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

Written informed consent was obtained from each study participant.

ETHICAL APPROVAL

The study was approved by Mengo Hospital Research and Ethics Committee (Approval number MH/REC/100/9-2019) and Uganda National Council of Science and Technology (Registration number HS2738).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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