UNIVERSITY of RWANDA

COLLEGE OF MEDICINE & HEALTH SCIENCES

SCHOOL OF MEDICINE & PHARMACY

PREVALENCE OF MACROVASCULAR DISEASE AND ASSOCIATED RISK FACTORS IN DIABETIC PATIENTS –RWANDA .

A dissertation submitted to College of Medicine and Health Sciences, School of Medicine and Pharmacy in partial fulfillment for the requirement of award of a Masters degree in Internal Medicine, University of Rwanda.

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June, 2019

i. DECLARATION

I, Dr. NDIKUBWAYO Emmanuel, to the best of my knowledge hereby declare and certify that the work presented in this dissertation entitled "**PREVALENCE OF MACROVASCULAR DISEASES AND ASSOCIATED RISK FACTORS IN DIABETIC PATIENTS –RWANDA"** is entirely my own and original work and it has never been presented or submitted in whole or in part to any other university.

Dr. NDIKUBWAYO Emmanuel Signature: Date:Friday,14th June 2019

Supervisors:

We, hereby declare that this dissertation has been submitted with our approval as the supervisors.

Prof. RWABIHAMA Jean PaulSignature :

Fridray, June 14th, 2019

Dr Jeffrey A. Dixson, MD,Mmed

Signature ……

Dr SIBOMANA Jean Pierre,MD,Mmed

Signature…….

ii. DEDICATION

To God the Almighty

To my beloved parents

To my sisters and brothers

To my relatives and friends

To my wife :MANISHIMWE Sylvie

To my supervisors

I dedicate this work

iii. ACKNOWLEDGEMENT

I would like to express my deepest acknowledgement to my supervisors Prof RWABIHAMA Jean Paul, Dr Jeffrey Dixson and Dr SIBOMANA Jean Pierre for their full support, technical expertise and mentorship throughout my study and research. Thank you for your valuable guidance and inspiration that led me to be more interested in this diabetic research.

My deepest appreciation goes to the management of UR-CMHS,KUTH and BUTH for their permission to conduct this study.

It is my pleasure to acknowledge my classmates for their endless friendship and teamwork.

Finally, and most importantly, special thanks to my wife, MANISHIMWE Sylvie, and my family for their support and encouragement.

iv. ABBREVIATIONS

ABI	Ankle Brachial Index
AHA & ADA	American Heart Association and the American Diabetes Association
BUTH	Butare University Teaching Hospital
CVD	Cardiovascular Disease
CHD	Coronary Heart Disease
HbA1c	Glucated hemoglobin
IDF	International Diabetes Federation
IM	Internal Medicine
IRB	Institutional Review Board
IVD	Ischemic Vascular Disease
KUTH	Kigali University Teaching Hospital
LDL-C	Low-density-lipoprotein cholesterol
MD	Medical doctor
MMED	Masters of Medicine
MI	Myocardial Infarction
PAD	Peripheral Artery Disease
T1DM	Type 1 DiabetesMellitus
T2DM	Type 2 DiabetesMellitus
WHO	World Health Organisation

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I. INTRODUCTION

The International Diabetes Federation (IDF) estimates that worldwide, in 2017, 415 million people have diabetes, 91% of whom have type 2 diabetes mellitus (T2DM). Worldwide ,the prevalence of diabetes is 8.8% and IDF predicts that the number of diabetic patients will rise to 642 million by 2040 (1).

In Africa , in 2017, estimated 15.5 million adults aged 20-79 years were living with diabetes , representing a regional prevalence of 3.3% (1)

In Rwanda ,in 2015,we were counting a population of 11 610 000 ,with diabetic prevalence of 2,8%. (World Health Organization – Diabetes country profiles, 2016).

Macrovascular disease contributes to high mortality of diabetic patients with coronary Artery Disease responsible for 29.7% and cerebrovascular disease for 11.0%.(2)

In high- and middle-income countries, cardiovascular disease affected 32.2%; 29.1% have atherosclerosis, 21.2% have coronary heart disease and 7.6% have cerebrovascular disease. (2)

In Africa, cardiovascular disease complications are considered to be rare but are increasing and most of the time associated with classic cardiovascular risk factors. Prevalence of coronary heart disease varies between 5% to 8% of type 2 diabetic patients and up to 5% of diabetic patients present with stroke at diagnosis. Peripheral vascular disease prevalence varies across sites from 4% to 28%. (6)

There are known modifiable major risk factors for cardiovascular disease like diet, smoking, hypertension, dyslipidemia, physical inactivity, obesity, Diabetes mellitus control (considered a CHD risk equivalent).The presence of multiple risk factors confers at least additive risk. In Framingham, those with five risk factors had a 10 year risk of a first CHD event of 25 to 30 percent. (7) People with either type 1 or type 2 diabetes mellitus are at increased risk for cardiovascular disease and have worse outcomes after surviving a cardiovascular event.

The use of lifestyle modifications can decrease or delay the need for medical intervention. Appropriate lifestyle and medical interventions will reduce the occurrence of cardiovascular disease and allow people with diabetes to live healthier and longer lives.(7)

Unfortunately in Rwanda, with diabetes prevalence of 2.8% , little is known about macrovascular disease and Its associated risks factors. There is no research done before on macrovascular disease in Rwanda.

The aim of this study was to determine the prevalence of macrovascular disease and Its associated risk factors, among diabetic patients seen in referral hospitals in Rwanda.

II. PATIENTS AND METHODS

Type of study

This was a prospective descriptive cross-sectional study to determine the prevalence of macrovascular disease and associated risk factors, in diabetic patients.
The study recruited 147 patients from the outpatient departments of two referral hospitals: Kigali University Teaching Hospital and Butare University Teaching Hospital. The study was conducted from January 2018 to March 2019.

Inclusion criteria:

We included diabetic patients meeting the following criteria:
1. Adult patients, older than 18 years of age
2. Referred to outpatient clinics at Kigali University Teaching Hospital and Butare University Teaching Hospital
3. Have been diagnosed with diabetes
4. Are receiving treatment for diabetes

Exclusion criteria:

Participants will be excluded if they are unwilling to participate in the study

Data collection

-Data was collected by Internal Medicine resident and It was collected using conducting interviews and using questionnaire

-All of the process of data collection was done in private room and all information was kept confidential

For every patient:

1)Twelve lead electrocardiograms was done at initial enrollment time. And ECG was interpreted using Manual Minnesota code(8)

ECG is the main tool for diagnosing coronary heart disease, mostly in developing country where other tests are not available. In a study of different diagnostic criteria in 603 chest pain and 149 non-chest-pain admissions, the Minnesota code had a sensitivity of 56% and a specificity of 94% for AMI (defined by clinical history and biochemical evidence)(9)

2)Ankle Brachial Index measurements was performed and calculated

-Each patient had ankle and brachial blood pressure measurements performed at rest. The patient had a rest for at least 5 minutes before the measurement was taken. The cuff was placed just above the ankle for the lower limb measurements. The right and left arm was measured simultaneously, and the highest reading between right and left, of the systolic pressure over the brachial artery, on the arm, was recorded.

ABI was calculated as the highest ankle systolic pressure divided by the highest brachial systolic pressure. ABI values less than 0.90 were taken as denoting the presence of PAD

-Every participant was clinically assessed ,for the presence of cerebrovascular disease, basing on the WHO Monica criteria(10)

Dyslipidemia was considered if LDL is greater than 2.6 mmol/l or triglycerides greater than 1.7 mmol/l or total Cholesterol greater than 4.5 mmol/l (mmol/l) (7)

Statistical Analysis

Data were collected on questionnaires and medical records was entered using Excell.Data was analyzed using Statistical Package for the Social Sciences (SPSS) version 20. Prevalence of macrovascular diseases was expressed in percentage. Possible association between categorical variables was determined using Chi square test.

Ethical consideration

This study determined the prevalence of ischemic vascular disease in Rwandan diabetic population. This will help in strengthening preventive measures and better management of diabetes complications.

After explaining, to the participants ,the purpose, methods, risks and benefits of the study, participants who accepted to participate signed a consent form.

Both verbal and written consents were required from each participant and It was in the participant's language of preference (either English or Kinyarwanda).

Research was done respecting the privacy of participants and kept their private information confidential.

Participants had their right to change their mind and to withdraw without any penalty if the research does not match their interests.

Authorization to conduct the study was received from the College of Medicine ,Institutional Review Board and from KUTH, BUTH Research Committees.

III. RESULTS

In total 147 participants were enrolled into the study. Socio-demographic profiles and the burden of cardiovascular risk factors of the participants are displayed in Table 1.
Female participants were predominant, comparing to male participants 116/31(78.9/21.1). The mean age of study population was 58.9 years. Eight percent of participants were smokers. Furthermore, only 33 % of all participants had controlled BP,32% do regular exercise and only 44% adhere to diabetic diet.

Table1.Demographic details of the study population and the magnitude of potential risk factors of macrovascular disease

Number of participants	147
Area of enrollment	
BUTH	50 (34.0%)
KUTH	96(65.3)
Sex (Male/Female)	31/116 (21.1/78.9)
Age in years(mean)	58.93
10 - 19	**0 (0.0%)**
20 - 39	**10(6.8%)**
40 - 59	**56 (38.1%)**
60 - 69	**60 (40.8%)**
70+	**21 (14.3%)**
Duration of diabetes(years)	
Less than 5 years	40 (27.2%)
Between 5-10 years	36 (24.5%)
Between 10-20 years	50 (34.0%)
More than 20 years	21 (14.3%)
Adherence to Diabetic Diet	66 (44.9%)
Regular Physical exercise (≥150min per week)	47 (32.0%)
Tobacco smoking	12 (8.2%)
Systolic pressure(mmHg)	
< 130	**40 (27.2%)**
130 - 159	**64 (43.5%)**
160 - 189	**34 (23.1%)**
190+	**9 (6.1%)**
Diastolic pressure (mmHg)	
< 90	**112 (76.2%)**
90+	**35 (23.8%)**
HbA1c %	
< 7.0	**27(18.4%)**
7.0 +	**120(81.6%)**

Total Cholesterol (mmol/l)	
< 4.5	**64(43.5%)**
4.5+	**83(56.5%)**
LDL (mmol/l) (mmol/l)	
< 2.6	**55(37.4%)**
2.6+	**92(62.6%)**
HDL(mmol/l)	
< 1.0	**35(23.8%)**
1.0+	**112(76.2%)**
Trigyceride(mmol/l)	
< 1.7	**56(38.1%)**
1.7+	**91(61.9%)**
Use of Antiplatelets	**20 (13.6%)**
10 years Risk for cardiovascular events	
Low (<10 %)	**87 (59.2%)**
Intermediate:10% to <20%	**26 (17.7%)**
High: 20% to <30%	**9 (6.1%)**
Very high 30% to <40%	**12(8.2%)**
Extremely High:≥40%	**13(8.8%)**

Peripheral artery disease

PAD was present in 12 patients over 147 participants, which makes PAD prevalence of 8.2% . In women, PAD prevalence was significantly high 10.2% ,while there was no PAD in male participants 0%

All patients with PAD were females between the age 50 to 69 and the prevalence within this age group was 16,6 % for age group 50 to 59 and 10% for age group 60 to 69 years.

The variable more strongly associated with PAD was:
Duration of diabetes [p-value 0.017 (95%CI)], tobacco smoking [p-value 0.02 (95%CI)],elevated level of total cholesterol [p-value 0.009(95%CI)] and elevated level of LDL[p-value 0.024(95%CI)]

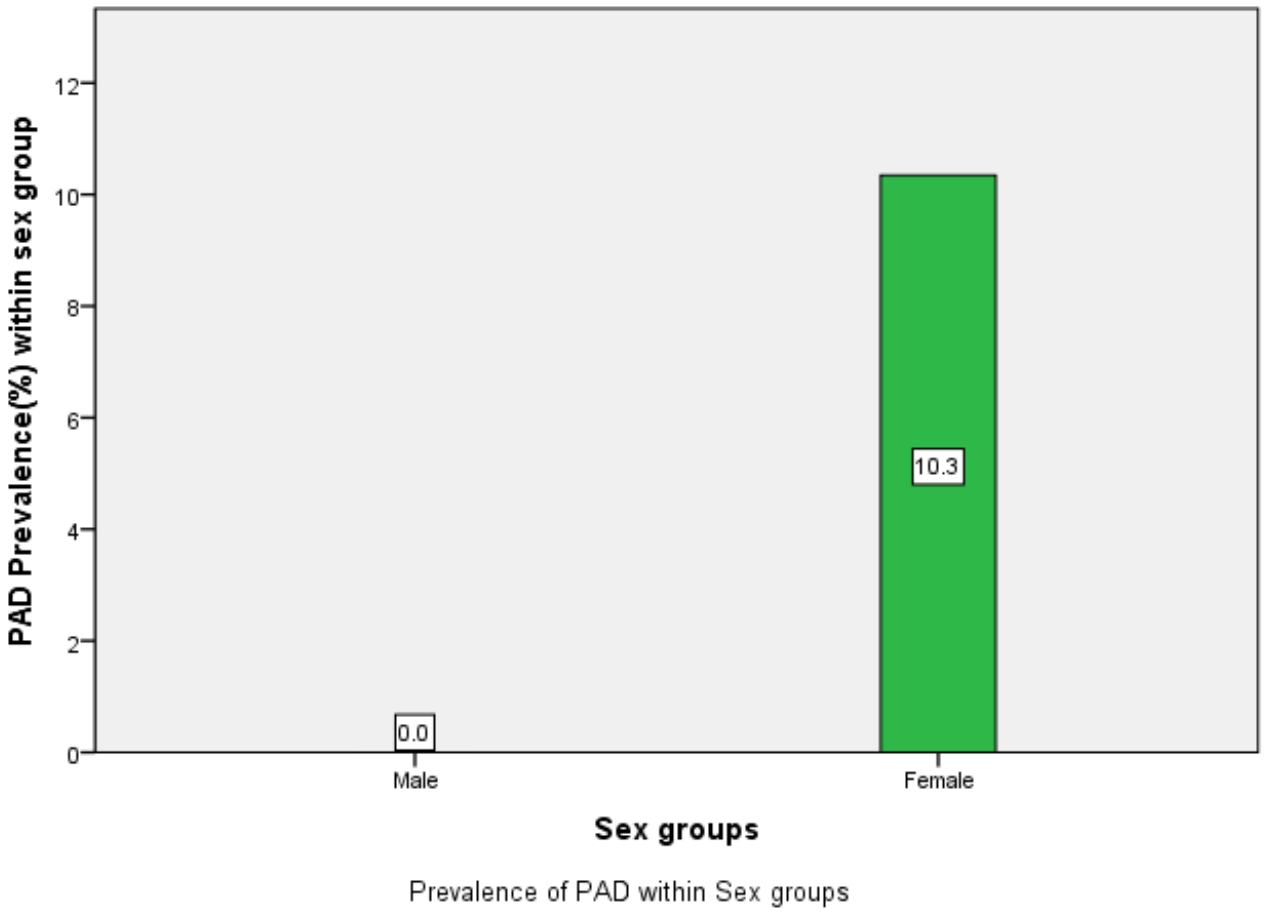

Figure 1. Peripheral artery disease distributions by sex

All 12 patients who had PAD were female, in a total of 116 female participants .This results in Peripheral Artery Disease prevalence of 10,3% in female patients versus 0% in male patients.

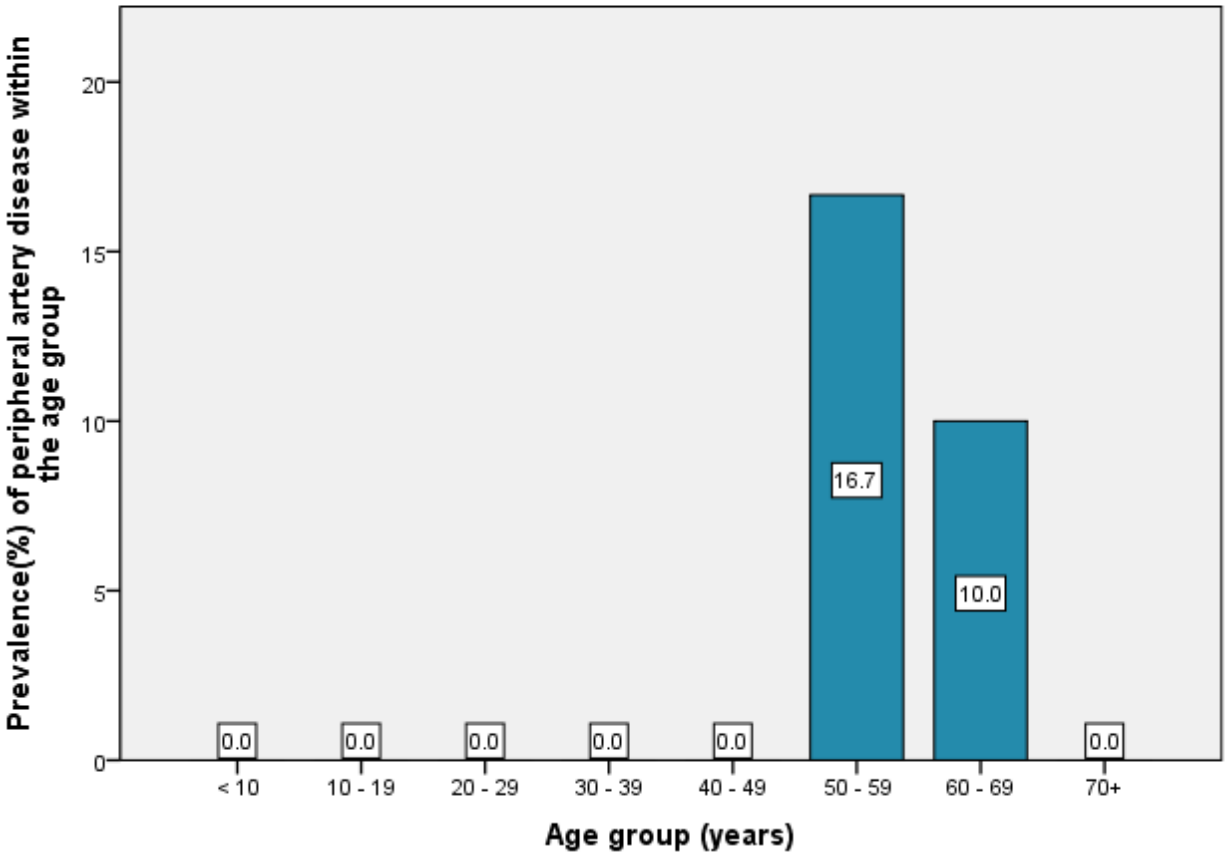

Figure 2.Peripheral artery disease distributions by age groups

Peripheral artery disease start above age 50 with highest prevalence of 16.7% in the age group 50-59,followed by prevalence of 10% in age group 60-69 years. No patient found with Peripheral Artery Disease above the age of 70.

Table 2 Risk factor distribution by PAD status

CHARACTERISTIC		*PAD(n=12)*	*No PAD(n=135)*	
		Frequency(%)	*Frequency(%)*	*p-value*
Age group(years)	<40	**0(0.0%)**	**10(7.4%)**	**0.142**
	40 – 49	**0(0.0%)**	**20(14.8%)**	
	50 – 59	**6(50.0%)**	**30(22.2%)**	
	60 – 69	**6(50.0%)**	**54(40.0%)**	
	70+	**0(0.0%)**	**21(15.6%)**	
Gender	Male	**0(0.0%)**	**31(23.0%)**	**0.062**
	Female	**12(100%)**	**104(77.0%)**	
Duration of diabetes (years)	Less than 5 years	**1(8.3%)**	**39(28.9%)**	**0.017**
	Between 5-10 years	**1(8.3%)**	**35(25.9%)**	
	Between 10-20 years	**5(41.7%)**	**45(33.3%)**	
	Above 20	**5(41.7%)**	**16(11.9%)**	
Systolic blood pressure (mmHg)	< 130	**2(16.7%)**	**38(28.1%)**	**0.853**
	130 – 159	**6(50.0%)**	**58(43.0%)**	
	160 – 189	**3(25.0%)**	**31(23.0%)**	
	190+	**1(8.3%)**	**8(5.9%)**	
Diastolic blood pressure (mmHg)	< 90	**11(91.7%)**	**101(74.8%)**	**0.189**
	90+	**1(8.3%)**	**34(25.2%)**	
Coronary Heart Disease	Present	**0(0.0%)**	**3(2.2%)**	**0.602**
	Absent	**12(100%)**	**132(97.8%)**	
10-year Risk for cardiovascular events	Low	**5(41.7%)**	**82(60.7%)**	**0.14**
	Intermediate	**2(16.7%)**	**24(17.8%)**	
	High	**0(0.0%)**	**9(6.7%)**	
	Very high	**3(25.0%)**	**9(6.7%)**	

	ExtremelyHigh	**2(16.7%)**	**11(8.1%)**	
Cerebrovascular disease	Present	**4(33.3%)**	**19(14.1%)**	**0.078**
	Absent	**8(66.7%)**	**116(85.9%)**	
Diet	Respect Diet	**3(25.0%)**	**63(46.7%)**	**0.148**
	Don't adhere to Diet	**9(75.0%)**	**72(53.3%)**	
Physical activity	Physical Exercises (>150 min/week)	**1(8.3%)**	**46(34.1%)**	**0.067**
	Physical Exercises (<150min/we)	**11(91.7%)**	**89(65.9%)**	
Blood Pressure control	BP >130mmHg	**2(16.7%)**	**31(23.0%)**	**0.616**
	BP <130mmHg	**10(83.3%)**	**104(77.0%)**	
Tobacco smoking	Smoker	**3(25.0%)**	**9(6.7%)**	**0.026**
	Non smokers	**9(75.0%)**	**126(93.3%)**	
Use of Anti-Platelets	On Anti-platelets	**1(8.3%)**	**19(14.1%)**	**0.578**
	Not Anti-Platelets	**11(91.7%)**	**116(85.9%)**	
HbA1c	< 7.0	**2(16.7%)**	**25(18.5%)**	0.874
	7.0 +	10(83.3%)	110(81.5%)	
LIPIDS PROFILE				
TotChol	< 4.5000	1(8.3%)	63(46.7%)	0.010
	4.5000+	11(91.7%)	72(53.3%)	
LDL	< 2.6000	1 (8.3%)	54(40.0%)	0.030
	2.6000+	11(91.7%)	81(60.0%)	
HDL	< 1.0000	5(41.7%)	30(22.2%)	0.130
	1.0000+	7 (58.3%)	105(77.8%)	
Triglycer	< 1.7000	2(16.7%)	54 (40.0%)	0.111
	1.7000+	10(83.3%)	81(60.0%)	

The variable more strongly associated with PAD was:

Duration of diabetes , tobacco smoking ,elevated level of total cholesterol and LDL**.**

For patients who had PAD: 83.4% had diabetes more than 10 years,25% were smokers, 91.7% had elevated LDL higher than 2.6 mmol/l and 91.7% total cholesterol higher than 4.5 mmol/l.

Coronary Heart Disease

Three participants , in a total of 147 participants ,had coronary artery disease. This results in Coronary Heart Disease prevalence of 2% for all participants. In men , Coronary Heart Disease prevalencewas higher than in women (3.2%) vs.(1,7)% .

All patients with CHD were above the age 40 ,with prevalence of 5% from 40 to 49 years of age and 3,3% ,from 50 to 59.

Coronary Heart Disease was significantly associated with the presence of cerebrovascular disease[p-value0.014 (95%CI)].

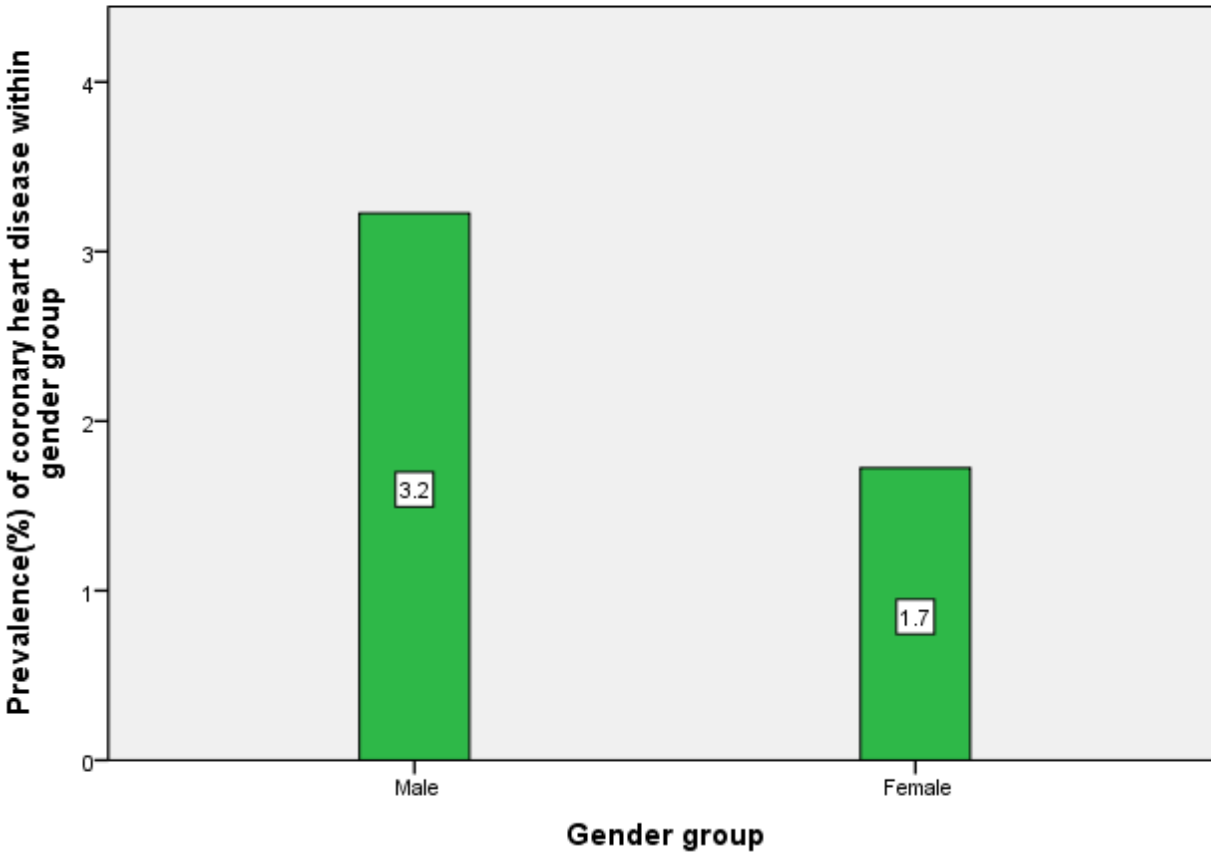

Figure3. Coronary heart disease distributions by sex

In a total of 31 male participants, only 1 had coronary artery disease, which make a prevalence of 3.2%.

For females, only 2 had coronary heart disease,out of 116 females. So prevalence of coronary heart disease was higher in male (3.2%) than in female (1.7%).

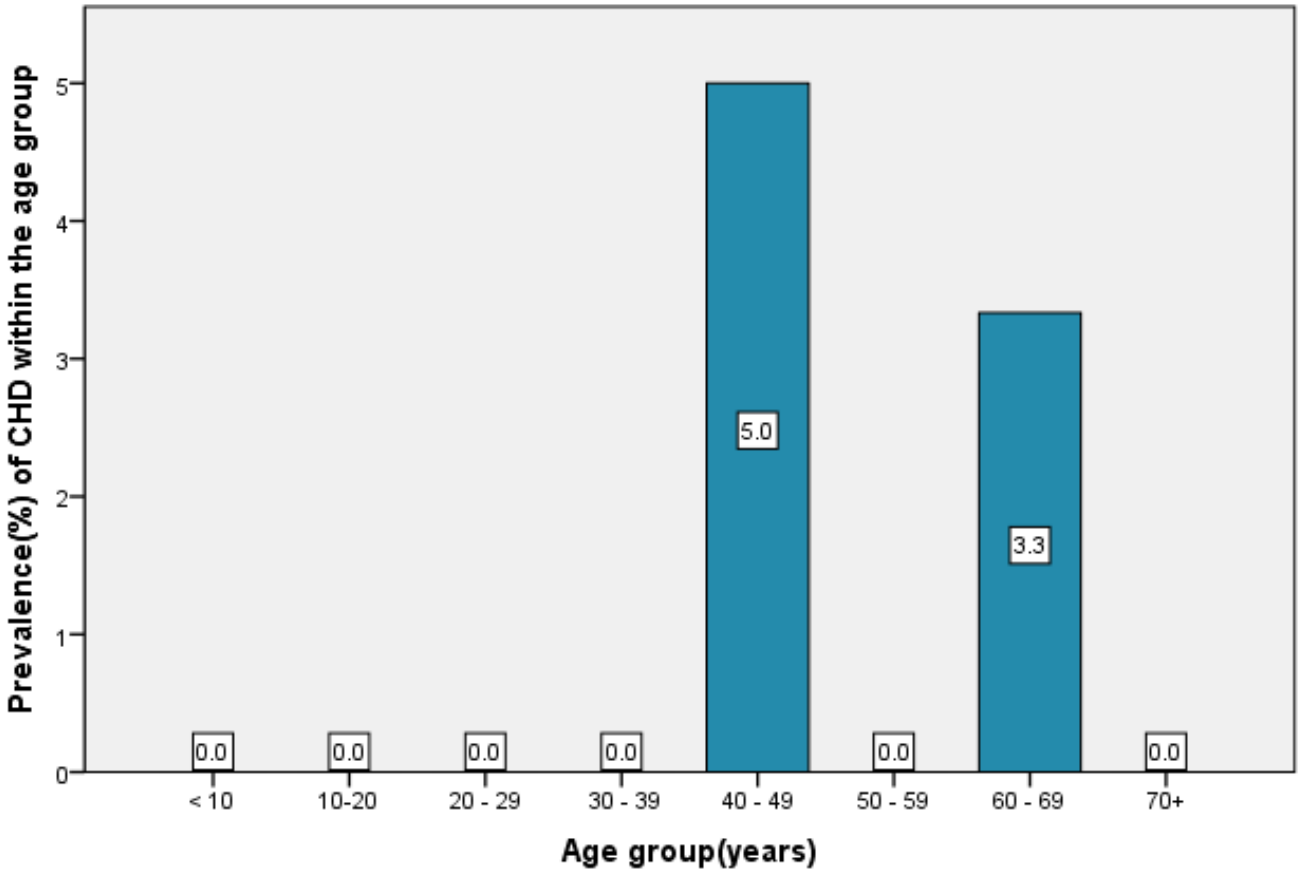

Figure 4.Coronary heart disease distributions by age group

There was no coronary heart disease below 40 while It was most prevalent in the age group 40-49,with a prevalence of 5%.The following prevalence was 3.3% in the age group 60-69 and there was no CHD above the age 70.

Table 3. Risk factors distribution by Coronary Heart Disease status

CHARACTERISTICS		CHD(n=3)	No CHD(n=144)	
		Frequency(%)	*Frequency(%)*	*p-value*
Age group(years)	< 40	**0(0.0%)**	**10(7.0%)**	0.735
	40 - 49	**1(33.3%)**	**19(13.2%)**	
	50 - 59	**0(0.0%)**	**36(25.0%)**	
	60 - 69	**2(66.7%)**	**58(40.3%)**	
	70+	**0(0.0%)**	**21(14.6%)**	
Gender	Male	**1(33.3%)**	**30(20.8%)**	0.599
	Female	**2(66.7%)**	**114(79.2%)**	
Duration of diabetes (years)	Less than 5 years	**1(33.3%)**	**39(27.1%)**	0.534
	Between 5-10 years	**0(0.0%)**	**36(25.0%)**	
	Between 10-20 years	**2(66.7%)**	**48(33.3%)**	
	Above 20	**0(0.0%)**	**21(14.6%)**	
Systolic Blood Pressure (mmHg)	< 130	**1(33.3%)**	**39(27.1%)**	0.157
	130 - 159	**0(0.0%)**	**64(44.4%)**	
	160 - 189	**1(33.3%)**	**33(22.9%)**	
	190+	**1(33.3%)**	**8(5.6%)**	
Diastolic blood pressure (mmHg)	< 90	**1(33.3%)**	**111(77.1%)**	0.078
	90+	**2(66.7%)**	**33(22.9%)**	
PAD	Present	**0(0.0%)**	**12(8.3%)**	0.602
	Absent	**3(100.0%)**	**132(91.7%)**	
10-year Risk for cardiovascular events	Low	**1(33.3%)**	**86(59.7%)**	0.124
	Intermediate	**0(0.0%)**	**26(18.1%)**	
	High	**1(33.3%)**	**8(5.6%)**	
	Very high	**1(33.3%)**	**11(7.6%)**	
	ExtremelyHigh	**0(0.0%)**	**13(9.0%)**	

Cerebrovascular disease	Present	**2(66.7%)**	**21(14.6%)**	0.014
	Absent	**1(33.3%)**	**123(85.4%)**	
Diet	Respect Diet	**0(0.0%)**	**66(45.8%)**	0.114
	Don't Resp Diet	**3(100.0%)**	**78(54.2%)**	
Physical activity	PhysicalExercises(>150 min/week)	**0(0.0%)**	**47(32.6%)**	0.230
	PhysicalExercises(<150 min/week)	**3(100.0%)**	**97(67.4%)**	
Blood Pressure control	BP <130mmHg	**1(33.3%)**	**32(22.2%)**	0.648
	BP >130mmHg	**2(66.7%)**	**112(77.8%)**	
Tobacco smoking	Smoker	**0(0.0%)**	**12(8.3%)**	0.602
	Non smokers	**3(100.0%)**	**132(91.7%)**	
Use of Anti-Platelets	On Anti-platelets	**0(0.0%)**	**20(13.9%)**	0.487
	Not Anti-Platelets	**3(100.0%)**	**124(86.1%)**	
HbA1c(%)	< 7.0	**0(0.0%)**	**27(19.0%)**	0.281
	7+	**5(100.0%)**	**115(81.0%)**	
LIPIDS PROFILE				
TotChol	< 4.5000	2(40.0%)	62(43.7%)	0.871
	4.5000+	3(60.0%)	80(56.3%)	
HDL	< 1.0000	2(40.0%)	33(23.2%)	0.387
	1.0000+	3(60.0%)	109(76.8)	
Triglycer	< 1.7000	3(60.0%)	53(37.3%)	0.305
	1.7000+	2(40.0%)	89(62.7%)	
LDL	< 2.6000	2(40.0%)	53(37.3%)	0.903
	2.6000+	3(60.0%)	89(62.7%)	

Coronary Heart Disease was significantly associated with the presence of cerebrovascular disease. In all patients who had Coronary heart disease 66.7% had cerebrovascular disease.

Cerebrovascular disease

Cerebrovascular disease was present in 23 over 147 participants which makes Cerebrovascular disease prevalence of 15.6% ,in diabetic patients.

In men, CVD prevalence was significantly higher than in women (29%) vs.(12,1%).Our study showed that Cerebrovascular disease starts at age of 40 with 5% ,reach 21% at age 60 and decline to 14% at age of 70.The variable more strongly associated with CVD was: Gender, being male[p-value 0.02 and presence of Coronary heart disease [p-value 0.014 (95%CI)]

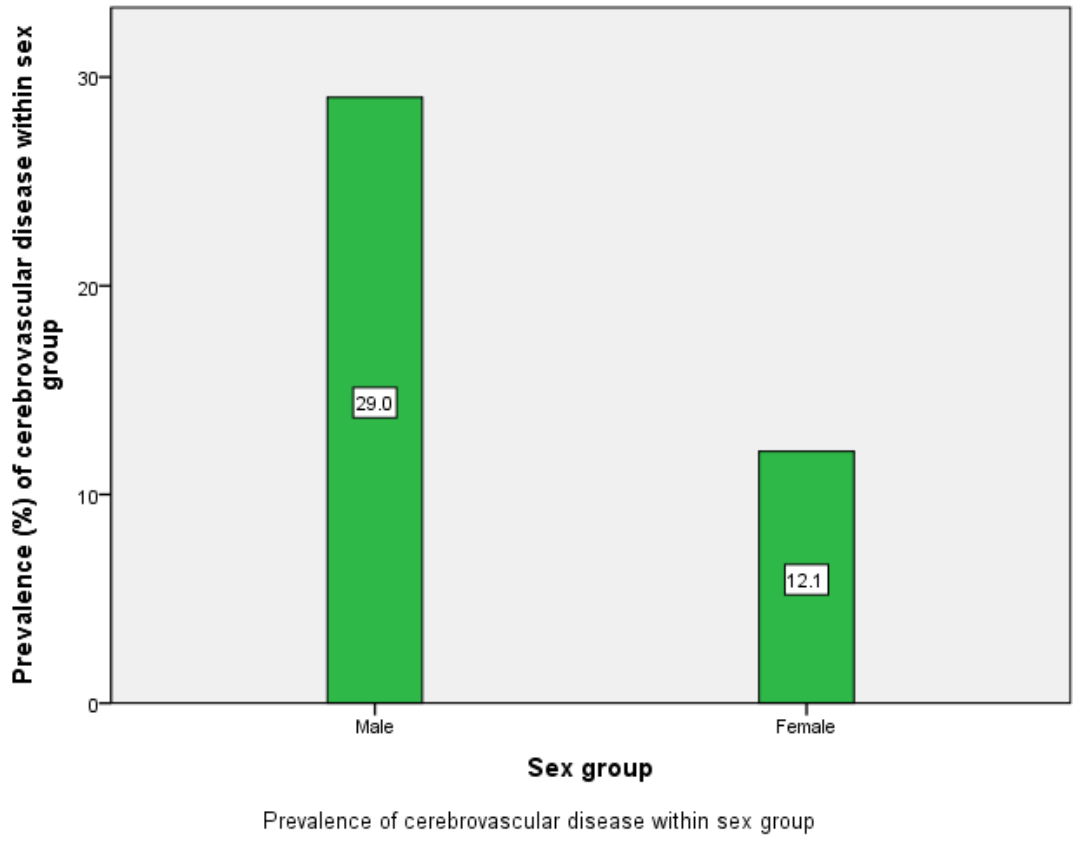

Figure 5. Cerebrovascular disease distributions by sex

In 31 male participants,9 had cerebrovascular disease and in female ,14 out of 116 got cerebrovascular disease.

So the prevalence of cerebrovascular disease is more common in male than in female, with a prevalence of 29% and 12.1% respectively.

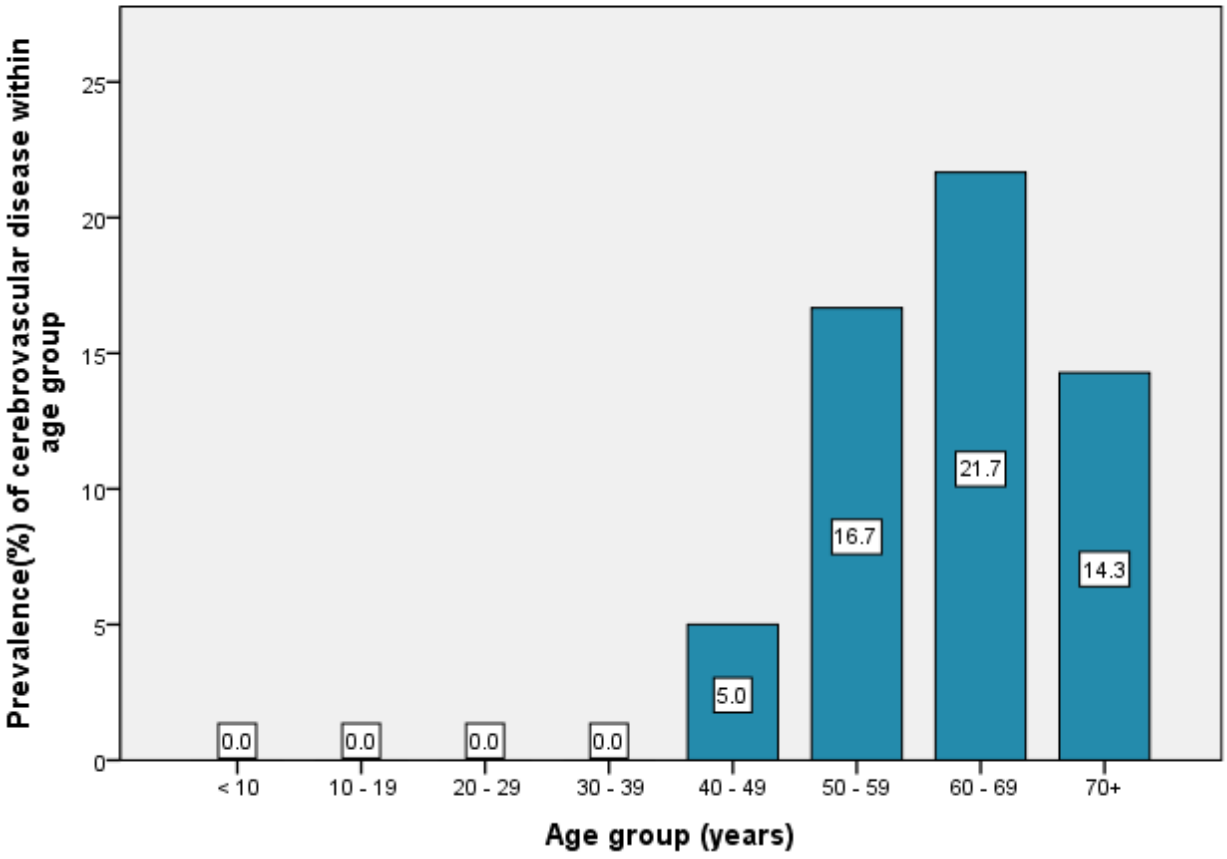

Figure 6.Cerebrovascular disease distributions by age group

Cerebrovascular disease, in diabetic patients start at the age 40 with a prevalence of 5% in the age group 40-49 . It shows a upward trend,with a prevalence of 16.7% in the age group 50-59 and reach the highest prevalence of 21.7% ,in the age group 60-69. It decline to a prevalence of 14.3% above 70 years.

Table 4 Risk factors distribution by Cerebrovascular disease status

		CerebroVD(n=23)	*NoCerVD(n=124)*	
		Frequency(%)	*Frequency(%)*	*p-value*
Age group(years)	<40	**0 (0.0%)**	**10(8.0%)**	0.383
	40 - 49	**1(4.3%)**	**19(15.3%)**	
	50 - 59	**6(26.1%)**	**30(24.2%)**	
	60 - 69	**13(56.5%)**	**47(37.9%)**	
	70+	**3(13.0%)**	**18(14.5%)**	
Gender	Male	**9(39.1%)**	**22(17.7%)**	0.021
	Female	**14(60.9%)**	**102(82.3%)**	
Duration of diabetes	Less than 5 years	**7(30.4%)**	**33(26.6%)**	0.625
	Between 5-10 years	**5(21.7%)**	**31(25.0%)**	
	Between 10-20 years	**6(26.1%)**	**44(35.5%)**	
	Above 20	**5(21.7%)**	**16(12.9%)**	
Systolic blood pressure (mmHg)	< 130	**5(21.7%)**	**35(28.2%)**	0.468
	130 - 159	**12(52.2%)**	**52(41.9%)**	
	160 - 189	**6(26.1%)**	**28(22.6%)**	
	190+	**0(0.0%)**	**9(7.3%)**	
Diastolic blood pressure (mmHg)	< 90	**17(73.9%)**	**95(76.6%)**	0.780
	90+	**6(26.1%)**	**29(23.4%)**	
PAD	Present	**4(17.4%)**	**8(6.5%)**	0.078
	Absent	**19(82.6%)**	**116(93.5%)**	
Coronary Heart Disease	Present	**2(8.7%)**	**1(0.8%)**	0.014
	Absent	**21(91.3%)**	**123(99.2%)**	
10-year Risk for	Low	**14(60.9%)**	**73(58.9%)**	0.939

cardiovascular events	Intermediate	**4(17.4%)**	**22(17.7%)**	
	High	**2(8.7%)**	**7(5.6%)**	
	Very high	**1(4.3%)**	**11(8.9%)**	
	Extremely High	**2(8.7%)**	**11(8.9%)**	
Diet	Respect Diet	**9(39.1%)**	**57(46.0%)**	0.545
	Don't Respect Diet	**14(60.9%)**	**67(54.0%)**	
Physical activity	Physical exercise >150 min/week	**5(21.7%)**	**42(33.9%)**	0.252
	Physical Exercise <150 min/week	**18(78.3%)**	**82(66.1%)**	
Blood Pressure control	BP <130mmHg	**4(17.4%)**	**29(23.4%)**	0.527
	BP >130mmHg	**19(82.6%)**	**95(76.6%)**	
Tobacco smoking	Smoker	**3(13.0%)**	**9(7.3%)**	0.352
	Non smokers	**20(87.0%)**	**115(92.7%)**	
Use of AntiPlatelets	On Antiplatelets	**5(21.7%)**	**15(12.1%)**	0.215
	Not AntiPlatelets	**18(78.3%)**	**109(87.9%)**	
HbA1c (%)	< 7.0	**5(**21.7%**)**	**22(**17.7%**)**	0.649
	7+	18(78.3%)	102(82.3)	
LIPIDS PROFILE				
TotChol	< 4.5000	7(30.4%)	57(46.0%)	0.168
	4.5000+	16(69.6%)	67(54.0%)	
LDL	< 2.6000	8(34.8%)	47(37.9%)	0.776
	2.6000+	15(65.2%)	77(62.1%)	
HDL	< 1.0000	9(39.1%)	26(21.0%)	0.060
	1.0000+	14(60.9%)	98(79.0%)	
Triglycer	< 1.7000	10(43.5%)	46(37.1%)	0.563
	1.7000+	13(56.5%)	78(62.9%)	

The variable more strongly associated with CVD was: Gender, the prevalence in male was 29% versus 12.1% in female and presence of Coronary heart disease as 8.7% of patients with cerebrovascular disease had coronary artery disease.

IV. DISCUSSION

The present study was done to determine the prevalence and associated risk factors of macrovascular disease in a sample of Rwandan diabetic patients. Our results showed that 21,7% of patients with diabetes had macrovascular disease. The most common condition was cerebrovascular disease 23 (15.6%), followed by peripheral artery diseases 12 (8.2%) and coronary artery diseases 3 (2%). In Zambia /Rofle study (3), the prevalence of peripheral artery disease 1.6% and cerebrovascular disease (1.1%) were lower than our findings. For coronary heart disease (2%),the prevalence was similar to our findings

The difference in prevalence of cerebrovascular disease and peripheral artery disease might be due to the Rofle study design.

For peripheral artery disease,Rofle used clinical questions while for our study ,we used Ankle brachial index measurements, which is more sensitive and specific than clinical questions.
To detect the presence of cerebrovascular disease, Rofle used only one question while for the present study we used the WHO Monica criteria, which has many questions.

The difference in lifestyles contributes to this difference
In Rofle study, the concentrations of total serum cholesterol and high density lipoprotein cholesterol were uniformly low even in patients with severe large vessel disease, reflecting consumption of a diet low unsaturated fats. And in 1988,people were more physically active than we are today.

The present study found similar rates to the Yemen study (11), for peripheral artery disease (8.2%) vs (9.1%). But the prevalence of cerebrovascular disease in our study was three time the prevalence of cerebrovascular disease in Yemen study 15.6% Vs5.8% and the prevalence of coronary artery disease in Yemen study was eight times the prevalence of coronary artery disease in our study 2% vs 17.8% .

The differences in gender ratio could explain this difference as females were (50.2%) in Yemen study vs 78.9% in our study. This could explain the low prevalence of coronary heart disease in our study as the prevalence of coronary heart disease , in our study, was double in male that of female (3.2% vs 1.7%). In addition the smoking ration was higher in Yemen study than in our study.

Overall in Yemen study 21.2% of patients reported being current cigarette smokers while in our study 8.2 % reported being current cigarette smokers .Significantly more men than women were smokers, (P = 0.005) in Yemen.
More poorly controlled hypertension in our study than in Yemen study 72.7% vs 48.2 %, could explain the high prevalence of cerebrovascular disease in our study.
And finally the ethnicity difference can contribute to the mentioned difference.

In a systematic literature review of scientific evidence from the developed world by Einarson et al(2) CVD affected 32.2% overall; 29.1% had atherosclerosis, 21.2% had coronary heart disease , and 7.6% stroke. Both peripheral artery disease and coronary artery disease prevalence was higher in developed countries than in our study but the prevalence of cerebrovascular disease in our study was double the prevalence of cerebrovascular disease in developed countries.
The probable explanations might be the difference in life styles, predisposing risk factors, diet and environment factors. Like obesity, hypertension ,tobacco smoking ,high fat diet which are higher in developed countries than in Rwandan population.

Some studies take in account ethnic differences to explain the variation in the risk of cardiovascular disease between populations. Among these ,an American study found that a substantial part of the risk associated with ethnicity can be attributed to socioeconomic status and geographic allocation rather than ethnicity(12)

The strong association of PAD with duration of diabetes, tobacco smoking ,elevated LDL and Total cholesterol was not surprising. These risks factors were previously reported in other studies like a *Review Article on Peripheral arterial disease in diabetes done by Jude et al.*(13). However HBA1c more than 7% and poorly controlled hypertension were not significantly associated with Peripheral Artery Diseases, which warrants further investigation in diabetic patients, in Rwanda.

Prevalence of different risk factors of macrovascular disease, as stated in "primary prevention of cardiovascular diseases in diabetic patients" by AHA&ADA(7):

In our study participants:

Female were 79%,Age more than 60 years 55.1 %,Diabetes duration more than 10 years 48.3%,Non adherence to diabetic diet 55.1%,Non-adherence to regular physical exercise 68%,tobacco smoking in 8.2 %,poorly controlled HTN in 72,8 %,Poorly controlled diabetes in 80%,Hypercholesterolemia in 54.4%,Elevated LDL in 59.2%,Hypertriglyceridemia in 60.5%,13.6 % use platelets as a primary prevention of CVDs, 10 years risk for cardiovascular events was low (<10 %) in 59.2%.

In a research done by Solomon Tamiru and **Fessahaye Alemseged**, on Risk Factors for Cardiovascular Diseases among Diabetic Patients In Southwest Ethiopia(14)**:** In two hundred and fifty six participants ,the prevalence of hypertension was 46.5%, dyslipidemia 63.5%, physical inactivity 55.1% and current smoking was5.5%.

Another study done by Mokta et al(15), on Prevalence of Cardiovascular Risk Factors among Diabetic Population and Awareness of Diabetes among Diabetic Patients at Himalayan ,in India: a total of 909 eligible adult diabetics were surveyed (59.73% male) with a mean duration of disease 38.14±4.56 months, 35.54% adults were smoker , 78.35% had A1C >7% and 61.50% had blood pressure measurements above target (>140/80mmhg), 56.74% had elevated LDL .

Prevalence of different risk factors of macrovascular disease ,in Rwandan diabetic patients, were similar to the prevalence in two previous studies except in smoking rate which is high in India and hypertension rate which is low in Ethiopia.

LIMITATIONS

Being cross sectional in nature, our study has the limitations to conclude on the associations between the risk factors and macrovascular disease

We did not use heart ultrasound and cardiac enzymes in detecting CHD: lack of availability and the cost. The use of cardiac ultrasound could have led to more detection of coronary heart disease

V. CONCLUSION

Overall macrovascular disease present in 1 out of 5 diabetic patients. The most frequent condition was cerebrovascular disease(15.6%), followed by peripheral artery diseases (8.2%) and coronary artery diseases (2%). Four participants had both Cerebrovascular disease and Peripheral Artery Disease and 2 participants had both Coronary Heart Disease and Cerebrovascular disease.

In the present study the prevalence of cerebrovascular disease was higher compared to the rest of the world and the rate of coronary heart disease was lower compared to the developed World

These differences maybe due to the high rate of uncontrolled hypertension**(72.8%)**,uncontrolled diabetes mellitus (**81.6%)** and high rate of dyslipidemia **(62.6%)** ,and further researches are needed to find out the real causes of this difference.

The most common associated factors were being male, duration of diabetes, tobacco smoking and dyslipidemia. And further cohort studies are needed on the association of macrovascular disease and different risk factors

VI. RECOMMENDATIONS

- Routines screening for Peripheral artery disease is encouraged in diabetic clinical visits and physician should focus on disease prevention, aiming at the modifiable risk factors.
- This study suggests that the prevalence of Macrovasculaer disease is high and physicians should develop preventive strategies to deal with the most common complications such as promotion of smoking cessation and control of dyslipidemia.
- Diabetic patients have to be regularly educated on diabetes management, diabetes complications and their management

VII. ABSTRACT:

Background:

Prevalence of macrovascular disease in diabetic patients in Rwanda is unknown. The aim of our study was to determine the prevalence of macrovascular disease and Its associated risk factors, in rwandan diabetic patients.

Method:

This study was cross-sectional that was undertaken to evaluate the prevalence of macrovascular disease and associated risk factors among diabetic patients, at Kigali University Teaching Hospital and Butare University Teaching Hospital . We enrolled adult diabetic patients who attended the outpatient departments, from 2018-2019.For every patient we did twelve lead electrocardiograms and It was done at initial enrollment time and interpreted using Manual Minnesota code. Ankle Brachial Index was calculated using measurements from automated calf sphygmomanometer and ABI values less than 0.90 were taken as denoting the presence of PAD.

Every participant was clinically assessed , for the presence of cerebrovascular disease, basing on the WHO Monica criteria.

Results:

Features of macrovascular disease were found in 32 (21.7%) of the 147 patients: the most common being cerebrovascular disease with 15.6% ,followed by Peripheral Artery Disease 8.2% ,then coronary heart disease with a prevalence of 2%. The variables associated with cerebrovascular disease were: being male[p-value 0.02] and presence of coronary heart disease [p-value 0.014 (95%CI)]

Peripheral vascular disease was associated with Duration of diabetes [p-value 0.017 (95%CI)], tobacco smoking [p-value 0.02 (95%CI)],elevated level of total cholesterol [p-value 0.009(95%CI)] and elevated level of LDL[p-value 0.024(95%CI)] while Coronary Heart Disease was significantly associated with elevated levels of triglyceride [p-value0.027 (95%CI)] and the presence of cerebrovascular disease[p-value0.014 (95%CI)].

Conclusion: Macrovascular disease affect one fifth of adult diabetic patients, in Rwanda. The most common associated factors were being male, duration of diabetes , tobacco smoking and dyslipidemia **.**

Key words: Prevalence ,macrovascular risk factors, diabetes.

VIII. ANNEXES

Informed consent form / Kwemerakwitabiraubushakashatsi

Number/code -------/-------

Dear participant,

My name is Dr NDIKUBWAYO Emmanuel. I am a student at the University of Rwanda (UR), pursuing Masters in Medicine (Mmed), in Internal Medicine. I am conducting a research study entitled: "PREVALENCE OF MACROVASCULAR DISEASE AND ASSOCIATED RISK FACTORS IN DIABETIC PATIENTS -RWANDA".

Ischemic vascular disease is common in diabetic patients. However, in our country, there has not been a study on ischemic vascular disease in diabetic patients. Therefore, this study hopes to determine the prevalence of ischemic vascular diseases , the cardiovascular risk profile and to assess whether diabetic patients are accessing appropriate preventive care for cardiovascular disease. It will help in elaboration of ischemic vascular diseases prevention policies. In addition ,every participant will be informed about what was learned from the research and he will receive a package of personal results and recommendations. -Data will be collected by a Medical Doctor and It will be collected using conducting interviews and questionnaire and for every participant Electrocardiogram ,Ankle and brachial Blood pressure will be measured and blood sample will be given.

-Electrocardiogram is a test that measures and records the electrical activity of the heartIn order to obtain an ECG, we will place small patches called "electrodes" over areas of the chest, arms, and legs and there will be 10 electrodes in total.The electrodes themselves are harmless. They do not emit electricity; they merely record and measure the natural electrical impulses that are emitted from the heart cells themselves.Other than some possible mild irritation from the electrodes placed upon your skin, there is no sensation associated with the test itself prior to undergoing the ECG, you will be asked to remove any jewelry or other accessories that could possibly interfere with the electrical readings. You will also be asked to remove clothing on the upper half of your body, so that your chest and arms are exposed, and you may be asked to wear shorts to better expose your legs.The ECG will only take a few minutes in total once the procedure is underway . For the duration of the test, it is important that you do not talk, move, or engage in any activity that could disrupt the test readings. Lie as still as possible in order to ensure the greatest accuracy of the results. Breathe normally (as you would at rest) as abnormal respiration could also interfere with test results.

-Each patient will have ankle and brachial blood pressure measurements performed at rest. The patient rests for at least 5 minutes before the measurement is taken. The cuff will be placed just above the ankle for the lower limb measurements. The right and left arm will be measured simultaneously, and the highest reading between right and left, of the systolic pressure over the brachial artery, on the arm, will be recorded.Finally you will give blood sample for lab testing. The blood will be drawn by putting a needle into a vein in your arm. One small tube of blood (about 10cc) will be taken and this will take about five minutes. It will be done by an experienced nurse .The needle stick may hurt but we will try to minimize the harm.

All of the process of data collection will be done in private room and all information will be kept confidential. You might be concerned providing your health information but we will respect your privacy and we will keep your private information confidential.

Participation in this study is voluntary and you can choose not to answer any individual questions or all of the questions .You will have your right to change your mind, to decide that the research does not match your interests, and to withdraw without any penalty. However, we hope that you will agree to participate in this study since your participation is very important. Whatever information you choose to provide will be kept strictly confidential, and no reference to your name or other family members will be made public.We do not anticipate that there would be any harmful event that would occur with this study, for any query, you can refer to the Chairperson of the CMHS IRB (0788 490 522) or the Deputy Chairperson (0783 340 040) or research committee (**researchcenter@ac.ur.rw** Tel +250 788563311). Thank you.I ……,understand the explanations given by ……..

about the risks and benefits of this research on "PREVALENCE OF MACROVASCULAR DISEASE AND ASSOCIATED RISK FACTORS IN DIABETIC PATIENTS –RWANDA" I accept willingly to participate in this research.……. ……..

Participant's signature Researcher's signature

Date:……../……/2018

Kwemerakwitabiraubushakashatsi

Nitwa NDIKUBWAYO Emmanuel,umunyeshuri muri kaminuzay'Urwandamw'ishamiry'indwara zo mu mubiri. Ndimogukoraubushakashatsikubijyanyenindwaraz'imitsikubantubafiteindwarayaDiyabete (indwaray'igisukari),buzakorerwa mu bitarobikurubyo mu Rwanda . Ahandiindwaraz'imitsikubantubafiteindwarayaDiyabeteninyinshi.Arikokugezubu mu Rwanda ntabushakashatsibwigeze gukorwakurizindwarazimitsiku bantu bafitediyabete.Ububushakashatsibuzerekanaukoindwarazimitsizingana mu barwayibacubafitediyabete,buzerekanakandinukoibyagobyokuzarwaraizondwarazingana mu gihekimyakaicumi,bwerekanekandinibaabarwayibirindaibiteraizondwara. Ibibizafasha mu guhamyauburyobwokurindaindwarazimitsi mu barwayibadiyabete.Burimuntuuzitabiraububushakashatsiazamenyeshwaibyavuye mu bushakashatsikandiazahabwaibaruwayibisubizo bye bwitenukoagombakwitwara.– Amakuruajyanyenubushakashatsiazajyaahabwamugangamukuru,hakurikijweibibazoazajyaabaza.

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QUESTIONNAIRE FOR "ISCHEMIC VASCULAR DISEASES IN DIABETIC PATIENTS, IN REFERRAL HOSPITALS –RWANDA"

Questionnaire number:…. Number of registration:…....

SOCIO-DEMOGRAPHIC CHARACTERISTICS
1.Age …….Years
2. Sex: F / M
3.Address:Province……
4. Residence: 1 Rural 2 Urban
DIABETES 5. When were you diagnosed with diabetes? O a.≤5years O b.5-10 O c.10-20 O d.>20
6.PAD O **Present** O Absentsystolic blood pressure in the ankle= systolic blood pressure at the arm=ABI:
CHD7.ECG FINDINGS:CHD O 1.Present O 2.Abscent.8.Estimated risk for Cardiovascular event over a period of 10 years: O1.Low: (<10 %)O 2.Intermediate:10% to <20% O 3.High: 20% to <30% O 4.Very high 30% to <40% O 5.ExtremelyHigh:≥40%
9.Cerebrovascular diseases O**1.Present**O **2. Abscent**
O1.Self-report of a diagnosis of stroke told to the patient by a physician 2. History of the abrupt onset of any of the following lasting more than 24 hours without another obvious cause: Oa.Unilateral or bilateral motor impairment (including dyscoordination) Ob.unilateral or bilateral sensory impairment Oc.aphasis/dysphasis (non-fluent speech) Od.hemianopia (half-sided impairment of visual fields) Oe.DiplopiaOf.Forced gaze (conjugate deviation) Og.Dysphagia of acute onset Oh.Apraxia of acute onset Oi.Ataxia of acute onset Oj.Perception deficit of acute onset
10.PREVENTIVE MEASURES
a. Diabetic Diet O Yes O No
b.How often do you do physical exercise? > 30 min/day? Yes No
c. BP ControlledO YES O NO
d. Smoking Cessation? O YES O NO

e. Do you take any antiplatelet agent ?O YES O NO If yes,which one?.....Statin? O YES O NO
f. Adherent to ALL strategies O Yes O No
LABORATORY INVESTIGATIONS: HbAlc: total cholesterol: LDL : HDL: Triglycerides: Albuminuria:

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