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From the Editor's Desk

This issue covers a diversity of topics from South Africa and other countries in sub-Saharan Africa.

With the projected increase in prevalence of diabetes mellitus, a corresponding increase is expected in associated complications. Ojobi and co-workers reviewed the bacteriology of diabetic foot ulcers in Nigeria (page 4). Most of the patients were farmers. *Staphylococcus, E coli, Pseudomonas* and *Streptococcus* were the major isolates. Their resistance pattern favoured quinolones and not penicillin. A number of antibiotic choices are available for use in diabetic foot ulcers,[1] but local resistance patterns determine the final choice.

Ntuli *et al.* investigated risk factors for diabetic foot ulcers in a primary healthcare setting in Johannesburg, South Africa. They show a high prevalence of neuropathy, structural abnormalities and peripheral vascular disease in the primary care setting and make a strong case for the provision of adequate podiatry services at this level. While infectious diseases make up a large part of the disease burden in South Africa, non-communicable diseases also contribute to this burden and healthcare services need to cater for this.[2]

Since morbidity from cardiovascular disease is a major burden in Nigerians with type 2 diabetes, predicting and quantifying cardiovascular risk could help in the management of diabetes and its complications. Udenze and Amadi (page 8) assessed the risk of cardiovascular disease in adult Nigerians with type 2 diabetes or the metabolic syndrome, using the Framingham risk score, and concluded that patients on treatment had high cardiovascular risk scores and risk factor control was not optimal.

A large proportion of cardiovascular disease is the result of modifiable risk factors, such as tobacco and alcohol consumption, unhealthy diet and physical inactivity. These risk factors can result in obesity, hypertension, diabetes or hypercholesterolaemia. Pedro and co-workers (page 13) determined the prevalence, awareness, treatment and control of cardiovascular risk factors in Angolan patients. They also compared rural and urban populations and describe important factors, such as a high rate of obesity in this group of patients, representing the nutritional transition in Africa. These findings are important in guiding public health programmes

Gulmez and colleagues studied left atrial function in patients with early type 2 diabetes. Patients had significant alterations in cardiac parameters and this study suggests early cardiac functional impairment in diabetes. Left atrial volume may be an important indicator of left ventricular dysfunction and even risk of atrial fibrillation.[3]

Bashir and Cumber reviewed cerebrovascular disease in Sudan (page 29). They point out that stroke is a major cause of disability in the country and that a sound health-systems approach is needed for adequate stroke care in Sudan.

The 2017 SEMDSA diabetes management guidelines are summarised by Webb in an easy-to-read, well-written article (page 37).

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Tribute to Professor Bongani Mawethu Mayosi

'A friend, a brother, a mentor, a leader, a champion, a warrior and a true son of Africa'

Prof Bongani Mayosi, 51-year-old dean of Health Sciences at the University of Cape Town tragically passed away on Friday, 27 July in Cape Town.

PASCAR joins many, with great sadness, in mourning a man who truly impacted on and inspired all who crossed his path. No one was left untouched by Bongani's presence.

Bongani Mayosi made his name as one of the world's top cardiology researchers and his legacy will continue in the African research and networks he fostered in especially rheumatic heart disease in Africa. As a leader, he truly believed in inclusive leadership, and *ubuntu* was ingrained in who he was. Bongani at his time of passing was ex-officio president of the Pan-African Society of Cardiology (president 2013–2017). We can only hope to emulate him and carry his legacy forward.

PASCAR expresses its condolences to his spouse Nonhlanhla Khumalo, their two daughters, the extended family and his cardiology colleagues in Africa and all over the world. Africa has lost a truly exceptional leader.

Profile, bacteriology and antibiotic susceptibility pattern of diabetic foot ulcers at the Federal Medical Centre, Makurdi, Nigeria

JE OJOBI, P MBAAVE, A UBUMNEME, M ABONYI

Abstract

Objectives: **The projected increase in the prevalence of diabetes mellitus (DM) is expected to be accompanied by a corresponding increase in associated complications. Foot problems are an increasingly important public health complication of DM. A major obstacle in the management of foot ulcers in diabetes is the colonisation of wounds by virulent pathogens, causing increasing rates of morbidity and mortality. In this article, we present a review of the profile, bacteriology and antibiotic susceptibility pattern of foot ulcers in individuals living with type 2 diabetes mellitus (T2DM), hospitalised at the Federal Medical Centre (FMC), to aid planning of services and provide a sensible approach to empirical antibiotic therapy while awaiting culture and sensitivity reports.**

Methods: **This was a hospital-based, retrospective, descriptive study that reviewed the profile, bacteriology and antibiotic susceptibility pattern of foot ulcers in individuals living with T2DM who were admitted for foot ulcer(s) over a three-year period (2012–2014) at the FMC. Approval for the study was obtained from the ethics committee of the institution. Relevant data (gender, age, residence, occupation, DM duration, ulcer duration, glycosylated haemoglobin status) were extracted from the files.**

Results: **One hundred and nine T2DM case files, made up of 44 females and 65 males (1:1.5) with a mean age of 53.5 ± 11.4 years, were extracted. They were mostly farmers in their fifties with poor glycaemic control who had had T2DM for more than a decade and foot ulcers for more than six months. *Staphylococcus aureus* was the commonest organism isolated from swabs of foot ulcers. There was a high level of sensitivity to quinolones and resistance to penicillins.**

Conclusion: **Late presentation, poor glycaemic control, high rate of wound infection with *S aureus*, resistance to penicillins and sensitivity to quinolones were noted.**

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Keywords: profile, diabetes mellitus, ulcer, bacteriology, antibiotic susceptibility pattern

Background

Reliable estimates have projected an astronomical increase in the prevalence of diabetes mellitus worldwide in the near future.[1] The rise in prevalence will be associated with a corresponding increment in associated complications. Foot problems are an increasingly important complication of diabetes mellitus (DM), ranging from mild discomfort to debilitating paraesthesiae and fungating ulcers. They are known to be a leading cause of admission to hospitals and prolonged stay on admission, straining manpower, draining resources and often associated with unnecessary and untimely death.[2,3] Diabetes-associated foot conditions constitute different percentages of diabetes admissions from different reports, even in the same country.[2-5] A major obstacle in the management of diabetes-related foot ulcer is the colonisation of wounds by virulent bacterial pathogens,[5] leading to increasing costs and morbidity and mortality rates.

In this article, we present a review of the profile, bacteriology and antibiotic susceptibility pattern of foot ulcers in type 2 DM patients (T2DM) hospitalised at the Federal Medical Centre (FMC), Makurdi. This will engender better understanding of the patients that presented, and the bacteriological and antimicrobial susceptibility patterns of foot ulcer(s), with a view to providing a sensible approach to empirical antibiotic therapy while awaiting results of wound swab microscopy, culture and sensitivity.

Methods

This was a retrospective, descriptive, hospital-based study to determine the profile, bacteriology and antibiotic susceptibility of foot ulcer(s) in individuals with T2DM over a three-year period (2012–2014) at FMC, a 400-bed tertiary referral centre in Makurdi, Benue State, Nigeria. Benue state is located in the north-central region of Nigeria on geographical co-ordinates of latitude 7° 42′ and 10° 0′ east, longitude 6° 25′ and 6° 8′ north. Approval for the study was obtained from the ethics committee of the institution.

Relevant data (gender, age, residence, occupation, duration of DM, ulcer duration, glycaemic control at presentation using HbA_{1c} level, co-morbid conditions) were extracted from the case files. As a hospital policy, all wounds were swabbed using sterile swab sticks and taken to the laboratory within the hour. All swabs were subjected to Gram staining, microscopic examination and culture. Blood, MacConkey and chocolate agar were used as primary

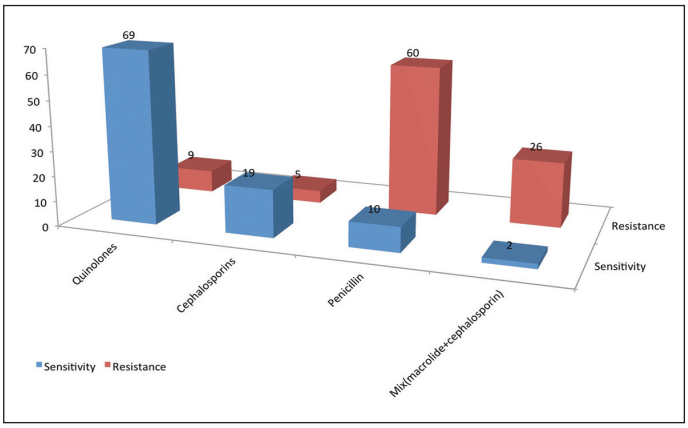

Fig. 1. Antibiotic sensitivity and resistance pattern.

isolation media for gram-positive and -negative bacteria. The wound specimens were inoculated on these media and incubated appropriately at 35–37°C. All isolates were subjected to antibiotic sensitivity testing using the disc diffusion technique.

The data generated were subjected to simple descriptive statistical analysis using frequencies and percentages. Chi-squared statistics was also employed where necessary. Statistical significance was set at $p < 0.05$.

Results

Six-hundred and four individuals living with diabetes were admitted within the three years this study lasted. There were 127 (21%) diabetic patients living with foot ulcer(s). Eighteen (14.2%) had incomplete records and were subsequently not included in the analysis; 109 (85.8%) had complete results. All subjects had T2DM. There were 44 females and 65 males (1:1.5) with a mean age of 53.5 ± 11.4 years. Other aspects of socio-demographic data are depicted in Table 1.

Table 1. Socio-demographic characteristics of participants

Parameter		Frequency	Percentage
Age (years)			
mean		53.5 ± 11.4	
range		38–92	
distribution:	30–39	3	2.8
	40–49	17	15.6
	50–59	38	34.8
	60–69	28	25.7
	70–79	15	13.8
	80–89	7	6.4
	≥ 90	1	0.9
Residence			
Rural		49	44.9
Urban		60	55.1
Educational level			
Primary		65	59.7
Secondary		30	27.5
Tertiary		14	12.8
Occupation			
Farmers		58	53.2
Civil/public servant		34	31.2
Self employed		5	4.6
Unemployed (including retired)		12	11.0

Table 2. clinical characteristics of participants

Parameter	Frequency	Percentage
DM duration (years)		
< 5	24	22.0
5–10	33	30.3
≥ 11	52	47.7
Ulcer duration (months)		
< 3	30	27.5
3–6	31	28.4
> 6	48	44.1
HbA_{1c} at presentation		
good (< 6.5)	24	22.0
poor (6.5– 8)	35	32.1
very poor (> 8)	50	45.9

Relevant clinical data in Table 2 show that the majority had had DM for more than a decade, had had the foot ulcer for more than six months and had poor glycaemic control on presentation. Most patients admitted were in the age group 50–59 years, as depicted in Table 3, while Table 4 shows the observed microbes and their relative frequencies. Repeated swabs from three ulcers did not grow any organism on bacterial culture. While one of these swabs eventually became positive for fungi, two remained negative on standard preparation for organisms, with very strict handling, and for non-bacterial pathogens.

Fig. 1 is a graphical presentation of antibiotic sensitivity and resistance pattern showing a high sensitivity to quinolones and high resistance to penicillins.

Discussion

This was a retrospective study of adults living with T2DM who presented with ulcers on the feet. They were mostly in the prime of their lives, as evidenced by a mean age of 53.5 years. The zenith of the impact of DM and its complications is thought to be highest in individuals less than 60 years of age.[6,7] The majority of the patients

Table 3. Admission pattern in each age range

	Age range (years)							
Year	30–39	40–49	50–59	60–69	70–79	80–89	≥ 90	Total
2012	1	4	12	11	3	2	0	33
2013	0	7	16	10	9	3	1	46
2014	2	6	10	7	3	2	0	30
Total	3	17	38	28	15	7	1	109

Table 4. Implicated microbial organisms and their relative frequencies

Organism	Frequency	Percentage
Staphylococcus aureus	34	31.2
Escherichi coli	28	25.7
Pseudomonas	20	18.4
Streptococcus	12	11.0
Kliebsiella	8	7.3
Candida albican	1	0.9
Staphyloccoci + coliforms	4	3.7
No growth	2	1.8
Total	109	100.0

(58%) in this study were under this age. The relatively young age of people developing limb ulcer(s) may have economic implications in any economy. Also, complications generally ascribed to older age groups are frequently being encountered in younger patients with diabetes, contributing to early mortality.[6]

There were more patients from the urban areas than from rural areas but the relationship was not statistically significantly different ($p > 0.05$). Type 2 diabetes is closely associated with (rapid) urbanisation, westernisation, sedentary lifestyle and obesity.[1,6,7] These are common descriptive terms applicable to most urban locale with many a rural area threatening to catch up.[1,8]

Both civil and public servants are known to farm extensively in Benue State, where this health institution was located. In the peasant agrarian setting that most of these patients were drawn from, poverty, inadequate footwear, increased risk of physical trauma, infection during farming activities and spontaneous blisters in bare-foot peasants and farmers were quite common.[7,8]

Farmers constituted more than half of those presenting with foot ulcers in this study. In addition, a situation where almost 60% of participants had primary or no Western education, widespread ignorance about appropriate health promotive and preventative activities would be expected. The higher the educational level, the lower the incidence of foot ulcers.[8] Other researchers have observed an even higher level of poor Western literacy rate among their respondents. Akanji *et al*. observed that up to 68% of their sample in a prospective study was without Western education.[9]

A number of research bodies on foot ulcers in people living with diabetes from the developing world feature late presentation to hospital as a common threat.[8,10,11] Up to 72.5% of patients in this study sought medical attention after three months of home/alternative/unorthodox treatment, for several reasons, including ignorance, fear of orthodox medical practices and inadequate transport.[10,11] This problem is still begging for a solution.[10] Sadly, many of the reasons were eminently solvable through education of individuals living with DM and their (primary) health providers.[12,13]

Generally, the patients in this study had poor glycaemic control, as evidenced by HbA_{1c} levels > 6.5%, which occurred in 78% of patients in this study. The Diabetes Control and Complications Trial (DCCT) research group were able to demonstrate a direct relationship between poor glycaemic control and microvascular complication.[14] Also, the United Kingdom Prospective Diabetes Study (UKPDS) clearly showed that each percentage point reduction in A_{1c} was associated with a 35% reduction in microvascular complications, such as neuropathy, a cardinal cause of foot disease in people living with diabetes.[15]

Other researchers have also noted varying degrees of poor glycaemic control in their subjects, especially using casual and fasting plasma glucose estimations.[14-17] However, comparisons are rather difficult due to lack of uniformity in testing. Some researchers have determined HbA_{1c} level, while others have used random or fasting plasma glucose assessments due to cost, convenience or unavailability of HbA_{1c} tests.[14,16,17]

Because of prolonged exposure of tissue proteins to glycation processes, the duration of diabetes mellitus is thought to be a predisposing factor to diabetic complications in general, especially in poorly controlled patients.[14,15] This is understandable in view of the variably long latency in the natural history of diabetes mellitus from the time of the initiating injury to clinical detection (as evidenced by the development of hyperglycaemia), up to the development of complications.[16]

Wound infection is a common occurrence in diabetic ulcers.[5,18,19] This often leads to prolonged hospital admission[18,19] and increased costs.[19] On the whole, Gram-negative bacilli were the predominant organisms observed on Gram stain in this study, making up 50.9% of all the bacteria. However, the Gram-positive coccus, *Staphyllococcus aureus*, constituted the majority of individual isolates, at 31.2%. This is in agreement with the findings from other publications that demonstrated a preponderance of *S Aureus*.[20-23]

S aureus is a common skin commensal, harboured in the anterior nares of nearly half of the global population and colonising the armpits, perineum and the respiratory tract of countless others. Coupled with the relatively reduced immune activity of people living with diabetes mellitus, *S aureus* would become more ubiquitous, invasive and virulent. However, this is not a universal finding, as studies equally exist demonstrating the pre-eminence of a variety of other bacteria.[6,19]

Apart from a mono-microbial pattern, other researchers have been able to culture more than one organism from an ulcer. Indeed, poly-microbial culture is quite common.[5,9,18,19,21] In this study, a combination of staphylocci and coliforms were cultured from only four ulcers out of the 109 studied.

Many factors could explain the 'no growth' observed in three cultures. While it could be true that the ulcers were indeed sterile, poor swab technique, wrong storage conditions, long 'wait' interval between collection and inoculation in the laboratory, wrong growth media/conditions, strict aerobes and anaerobes, and inappropriate antibiotic use should be borne in mind as possible factors in interpreting and making decisions on this observation. It would be better to err on the side of caution, judging from the history, local findings around and on the ulcer, and systemic examinations in evaluating this type of occurrence.

One of the 'no growth' swab samples, which was finally identified as a fungus, was further characterised to be yeast. Undiagnosed and with inappropriate anti-infective drugs, this ulcer may not heal. The time-tested teaching emphasising the need for further efforts in carrying out cultures of samples from refractory ulcers to ensure fungal colonisation (especially yeast) should be borne in mind, especially in resource-constrained areas.[18]

Two important observations stand out on antibiotic susceptibility testing: the high degree of resistance to penicillins (especially Ampicillin) and the relatively high rate of sensitivity to quinolones. The cephalosporins were seldom effective and unless suggested from antimicrobial susceptibility testing, these drugs should not be used as initial therapy for diabetic foot infections in our environment.[19]

The resistance to antibiotics of many of these microbes is not surprising because of drug misuse, which is widespread in sub-Saharan Africa. It is not uncommon to observe antibiotics being marketed in commercial vehicle parks, open markets and supermarkets by unlicensed vendors. Some of the strains of bacterial isolates that colonised the refractory diabetic ulcers in this study may have acquired genes for drug resistance through antibiotic misuse.[5] Quinolones were therefore recommended as the initial therapy for people living in this environment with diabetes with infected ulcers while awaiting culture results, which should be used to guide further antibiotic therapy.

Limitations

Bacterial culture results were a very important component of this study. The observed results may have been different if certain factors affecting the patient and/or their investigations were different. For

instance, where pathogen yield is a major determinant, wound biopsy is superior to wound swab. However, the centre where this study was undertaken lacked punch biopsy capability at the time these patients were documented.

The patients in tertiary hospitals in poor countries often have attempted home management[8,24] or unorthodox involvement[8,11,24] before they finally seek attention or are referred to primary/secondary centres.[8,11,24,25] Along this delivery chain of presentation to the tertiary centre, it has been observed that antibiotic use (and misuse) is very common in individuals living with DM nursing an ulcer.[5]

Since this was a retrospective study, it was difficult to interrogate prior antibiotic use among the study population. The type(s), duration and timing in relation to the onset of ulcer are important. Documented references to prior antibiotic use were scanty in this study, with patients not knowing the types of drugs used before presentation. This may also have affected the types of bacteria cultured while they were being managed in this facility.

Fastidious organisms, strict aerobes and anaerobes and the procedure through which swabs were taken, stored and handled were important determinants of the types of bacterial yield observed. Because of the retrospective nature of this study, it was not possible to assess anaerobic culture documentation.

Conclusion

In these patients, there was a high degree of late presentation as well as poor glycaemic control and a high rate of wound infection due to colonisation by opportunistic pathogens, especially bacteria. *Staphylococcus aureus* was the commonest organism isolated from swabs of foot ulcers in this study. Most of the organisms identified from swab cultures were sensitive to quinolones and resistant to penicillins. This is a major challenge in the management of foot ulcers in individuals living with diabetes where culture and sensitivity tests are not available or reliable, as the correct choice of antibiotics should be made only after antibiotic sensitivity testing. We therefore advocate the use of a quinolone while awaiting sensitivity results.

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Cardiovascular disease risk assessment in Nigerian adults with type 2 diabetes or the metabolic syndrome, using the Framingham risk score

IFEOMA CHRISTIANA UDENZE, CASMIR EZENWA AMADI

Abstract

Background: **Cardiovascular morbidity is a major burden in Nigerian patients with type 2 diabetes mellitus (DM). Predicting and quantifying cardiovascular risk could help in more focused and aggressive management of type 2 DM and its cardiovascular complications.**

Aim: **The aim of this study was to compare the cardiovascular risk scores of type 2 diabetes subjects on treatment with those of individuals with the metabolic syndrome, and healthy controls, and to examine the impact of glycaemic control and lifestyle on cardiovascular risk in adult Nigerians**

Methods: **This was a cross-sectional study of 40 adult men and women with type 2 diabetes attending the Diabetic Clinic, 40 adult men and women with the metabolic syndrome, and 40 age- and gender-matched males and females, who were recruited as healthy controls. The metabolic syndrome was defined based on the NCEP-ATP III criteria. Socio-demographic and clinical data were collected using a structured questionnaire. Venous blood was collected after an overnight fast.**

Results: **There was a statistically significant difference in the cardiovascular risk scores between the group with diabetes (20.41 ± 12.98), the group with the metabolic syndrome (10.00 ± 6.35), and the control group (6.79 ± 7.81) ($p < 0.001$). There was also a statistically significant difference in the glycated haemoglobin (HbA_{1c}), high-density lipoprotein cholesterol, total cholesterol and triglyceride concentrations between the three study groups ($p < 0.05$). Cardiovascular risk correlated positively and significantly with HbA_{1c} level, body mass index and waist circumference, and negatively with education level ($p < 0.05$). Only 52.2% of the diabetics on treatment achieved an HbA_{1c} target of < 7%.**

Conclusion: **Type 2 diabetes patients on treatment had high cardiovascular risk scores, and control of cardiovascular risk factors was not optimal in adult Nigerians, especially in individuals with type 2 diabetes or the metabolic syndrome. Strategies to achieve better glycaemic control, weight reduction and increased literacy levels would help achieve cardiovascular risk reduction in adult Nigerians.**

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Keywords: cardiovascular disease risk score, type 2 diabetes, metabolic syndrome, Framingham study

Introduction

The prevalence of type 2 diabetes is increasing globally and factors such as aging of the population, increasing prevalence of obesity and sedentary lifestyles have contributed to this trend.[1,2] In 2009, global estimates put the world prevalence of diabetes among adults at 6.4%, affecting 285 million adults in 2010, and projected to increase to 7.7%, affecting 439 million adults by 2030.[3] There was also an estimated 69% increase in numbers of adults with type 2 diabetes in developing countries, compared to a 20% increase in developed countries between 2010 and 2015.[3] In Nigeria, the estimated prevalence rate for type 2 diabetes was 4.3% and over five million people are projected to be affected by 2030.[3]

Diabetes is an independent risk factor for cardiovascular disease (CVD).[4,5] Type 2 diabetes is associated with a two- to four-fold increase in the risk of both coronary heart disease and stroke.[6,7] CVDs are listed as the cause of death in approximately 65% of persons with diabetes,[8] and strategies to reduce CVD risk is an important part of the management protocol for type 2 diabetes.[9]

Quantifying the risk of developing CVD in patients with diabetes has important strategic benefits in patient management.[10-12] CVD risk quantification is useful in ranking individuals and groups according to absolute risk for the purpose of targeting therapy to those at greatest risk in order to appropriately allocate community and health resources.[11] It also provides prognostic information or accurate estimations of the likely absolute benefit from a therapeutic intervention.[11,12] In addition to being part of a preventative strategy to motivate patients to change their behaviour and adhere to medical treatments,[10] CVD risk quantification can also be an assessment tool for clinicians to examine the effectiveness of their therapeutic interventions.

Todays' lifestyle choices are characterised by increased physical inactivity and the consumption of calorie-dense foods, which fuel the obesity pandemic. Obesity and physical inactivity have been implicated in the development of insulin resistance in individuals who are genetically susceptible.[1,13] Insulin resistance is the first defect in a cascade of metabolic abnormalities leading up to the onset of type 2 diabetes. These dysmetabolic features include cardiovascular risk factors such as dyslipidaemia, hypertension, inflammatory and prothrombotic factors.[14]

The clustering of these risk factors in a single individual is termed the metabolic syndrome. The metabolic syndrome commonly precedes the development of type 2 diabetes by many years,[15] and is also an independent risk factor for CVD. Therefore, early detection of the risk factors associated with the metabolic syndrome is

needed for institution of appropriate primary prevention measures in patients at risk for diabetes.

The Framingham risk-assessment tool, which was developed in the general population and validated in people with diabetes, is used to estimate a person's 10-year risk of developing CVD in order to identify high-risk individuals for primary prevention.[10] An individual's risk score can aid clinical decision making on how intensively to intervene in lifestyle-modification strategies, when to include drug therapy,[10] and also to assess the efficacy of these interventions.

This study compared the cardiovascular risk scores of type 2 diabetes subjects on treatment, with those of individuals with the metabolic syndrome, and healthy controls. It examined the impact of glycaemic control and lifestyle on cardiovascular risk reduction in adult Nigerians.

Methods

This was a cross-sectional study of 40 adult men and women with type 2 diabetes mellitus (DM), 40 adult men and women with the metabolic syndrome, and 40 age- and gender-matched males and females who were recruited as healthy controls. The Ethical Research and Review Committee of the Lagos University Teaching Hospital (LUTH) approved the study protocol, and informed consent was obtained from the participants.

The study participants were patients attending the Diabetic Clinic and the Obesity and Metabolic Clinic of the Lagos University Teaching Hospital. Adult men and women between the age of 30 and 70 years who agreed to participate in the study were consecutively recruited. Socio-demographic and clinical data were obtained from the participants using a structured questionnaire. Anthropometric measurements such as weight, height, waist and hip circumference and blood pressure readings were taken. Lipid profile results were also determined.

The diagnosis of type 2 diabetes was based on the WHO criteria,[16] and the diagnosis of the metabolic syndrome was based on the NCEP-ATPIII criteria.[17] Subjects who did not meet the criteria for the metabolic syndrome were matched for age and gender with the cases and recruited as controls.

The inclusion criteria included adult males and females between 30 and 70 years of age who had been diagnosed as having DM by the WHO criteria,[16] with a blood glucose level controlled with diet and hypoglycaemic drugs, and non-diabetics who had the metabolic syndrome, described by the presence of any three of the following: abdominal circumference ≥ 102 cm in males or ≥ 88 cm in females, high-density lipoprotein cholesterol (HDL-C) < 1.03 mmol/l (< 40 mg/dl) in males or < 1.3 mmol/l (< 50 mg/dl) in females, triglycerides (TG) ≥ 1.7 mmol/l (≥ 150 mg/dl), blood pressure ≥ 130/85 mmHg or the patient receiving hypotensive treatment, and fasting glycaemia > 6.1 mmol/l (> 110 mg/dl).[17] Pregnant women were excluded from the study.

The study participants reported on the morning of the study after an overnight (10–12 hours) fast; 5 ml of venous blood was collected from the ante cubital vein and transferred into plain tubes for lipid profile assay, into fluoride oxalate tubes for glucose analysis, and into EDTA tubes for glycated haemoglobin (HbA_{1c}) assay.

Abdominal obesity was determined by measurement of the waist circumference. The measurement was taken using an inelastic tape, at the end of several consecutive natural breaths, at a level parallel to the floor, midpoint between the top of the iliac crest and the lower margin of the last palpable rib in the mid-axillary line.[18] The hip circumference was measured at a level parallel to the floor, at the largest circumference of the buttocks.[18]

Blood pressure was determined using the Accoson's mercury sphygmomanometer (cuff size 15 × 43 cm). The subjects were seated and rested for five minutes before measurement. Systolic blood pressure was taken at the first Korotkoff sound and diastolic at the fifth Korotkoff sound.[19]

Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), HDL-C and triglyceride levels were determined on fasting serum samples, and glucose concentrations were determined from fasting fluoride oxalate plasma using reagents from Randox Laboratories Ltd (Antrim, UK, BT 29 4QY) on a semi-automatic biochemistry analyser (BS3000P-Sinnowa Medical Science and Technology Co, Ltd, Nanjing, China, 211135). An ion-exchange chromatographic-spectrophotometric method was used for HbA_{1c} determination,[20] with reagents from Fortress Diagnostics, UK. The Framingham risk score was estimated from a cardiovascular disease risk calculator based on the equation from the Framingham heart study.[21]

Table 1. Gender and age distribution of the study participants

Characteristics	Subjects with type 2 diabetes *n* = 40 (%)	Subjects with the metabolic syndrome *n* = 40 (%)	Healthy controls *n* = 40 (%)	*p*-value
Gender				
Males	13 (32.55)	13 (32.55)	13 (32.55)	1.00
Females	27 (67.5)	27 (67.5)	27 (67.5)	
Age (mean ± SD)	55.65 ± 10.54	54.87 ± 9.80	56.17 ± 10.2	0.78
Age group (years)				
30–40	5 (12.5)	5 (12.5)	7 (17.5)	0.83
41–50	14 (35)	15 (37.5)	12 (30)	
51–60	18 (45)	18 (45)	19 (47.5)	
61–70	3 (7.5)	2 (5)	2 (5)	

Table 2. Socio-demographic characteristics of the study participants

Characteristics	Subjects with type 2 diabetes *n* = 40 (%)	Subjects with the metabolic syndrome *n* = 40 (%)	Healthy controls *n* = 40 (%)	*p*-value
Level of Education				
None	2 (5)	0 (0)	1 (2.5)	0.075
Primary	9 (22.5)	3 (7.5)	5 (12.5)	
Secondary	13 (32.5)	11 (27.5)	6 (15)	
Tertiary	6 (15)	26 (65)	28 (70)	
Exercise				
Yes	5 (12.5)	6 (15)	4 (10)	0.81
No	35 (87.5)	34 (85)	36 (90)	
Alcohol				
Yes	11 (27.5)	6 (15)	6 (15)	0.64
No	29 (72.5)	34 (85)	34 (85)	
Smoking				
Yes	0 (0)	2 (5)	3 (7.5)	0.86
No	40 (100)	38 (95)	37 (92.5)	

Statistical analysis

The data were analysed using the IBM SPSS version 20.0 package. The chi-squared test was employed to test the differences in the categorical variables and ANOVA was used to test the differences in the mean values for the continuous variables. Spearman's correlation analysis was employed to determine the association between variables. Statistical significance was set at $p < 0.05$.

Results

Forty individuals with type 2 diabetes, 40 with the metabolic syndrome, and 40 healthy controls participated in the study. Each group consisted of 13 men and 27 women. Table 1 shows the gender and age distribution of the study participants. The participants did not differ statistically in their age and gender distribution. Table 2 shows the socio-demographic characteristics of study participants. The participants did not differ statistically in their socio-demographic characteristics.

Table 3 shows the clinical and laboratory parameters of the study participants. The differences between the groups are seen in the lipid profile parameters, HbA_{1c} levels and in the absolute values of cardiovascular risk. The group with the metabolic syndrome had higher TG, TC and LDL-C levels than both the control group and the DM group on treatment.

Table 4 shows a comparison of cardiovascular disease risk categories among subjects with type 2 diabetes, those with the metabolic syndrome and the healthy controls. Over 50% of the diabetic group were in the high-risk category, compared to 7.5 and 2.5% in the metabolic syndrome and control groups, respectively.

Table 3. Clinical and laboratory parameters of the study participants

Parameters	Subjects with type 2 diabetes *n* = 40 (%)	Subjects with the metabolic syndrome *n* = 40 (%)	Healthy controls *n* = 40 (%)	*p*-value
Age (years)	50.52 ± 8.70	49.65 ± 7.74	49.82 ± 8.9	0.832
SBP (mmHg)	130.22 ± 19.36	131.92 ± 17.31	126.00 ± 17.30	0.922
DBP (mmHg)	78.27 ± 12.03	82.77 ± 11.30	77.67 ± 17.33	0.130
BMI (kg/m^2)	29.43 ± 4.39	30.73 ± 4.43	29.03 ± 5.12	0.073
WC (cm)	98.26 ± 13.43	99.75 ± 9.04	95.22 ± 12.80	0.220
Waist/hip ratio	0.93 ± 0.13	0.88 ± 0.05	0.88 ± 0.06	0.051
HbA_{1c} (%)	8.56 ± 4.07a	4.79 ± 1.04	4.55 ± 1.76	< 0.0001*
HDL-C (mmol/l)	0.90 ± 0.45a	1.25 ± 0.12a	1.83 ± 0.62a	< 0.0001*
TG (mmol/l)	1.09 ± 0.33	1.90 ± 0.13a	1.03 ± 0.52	< 0.0001*
TC (mmol/l)	4.16 ± 1.07	5.03 ± 0.44a	4.53 ± 0.92	< 0.0001*
LDL-C (mmol/l)	2.78 ± 1.16	2.91 ± 0.42a	2.23 ± 1.22	0.045*
CVD risk (%)	20.41 ± 12.98a	10.00 ± 6.35	6.79 ± 7.82	< 0.0001*

SBP: systolic blood pressure, DBP: diastolic blood pressure, BMI: body mass index, WC: waist circumference, HbA_{1c}: glycated haemoglobin, HDL-C: high-density lipoprotein cholesterol, TG: triglycerides, TC: total cholesterol, LDL-C: low-density lipoprotein cholesterol, CVD: cardiovascular disease.
*Statistically significant, [a]*Post hoc* analysis showing the group(s) contributing to the observed differences.

Table 5 shows the correlation of glycaemic control and lifestyle variables with cardiovascular risk. Obesity, level of education and glycaemic control showed statistically significant relationships with cardiovascular risk.

Table 6 shows the percentage of DM patients who achieved optimal treatment goals for modifiable cardiovascular risk factors. Most of the study population with DM did not attain optimal treatment goals for the modifiable cardiovascular risk factors.

Table 4. Comparison of cardiovascular disease risk categories among subjects with type 2 diabetes, the metabolic syndrome and healthy controls

CVD risk category	Subjects with type 2 diabetes *n* = 40 (%)	Subjects with the metabolic syndrome *n* = 40 (%)	Healthy controls *n* = 40 (%)	*p*-value
Low risk (< 10%)	11 (27.5)	22 (55)	29 (72.5)	< 0.0001*
Medium risk (10–20%)	8 (20)	15 (37.5)	10 (25)	
High risk (> 20%)	21 (52.5)	3 (7.5)	1 (2.5)	

*Statistically significant

Table 5. Correlation of glycaemic control and lifestyle variables with CVD risk

Variable	Correlation coefficient	*p*-value
Smoking status	0.055	0.548
Alcohol consumption	0.079	0.389
Exercise	0.072	0.432
Level of education	–0.271	0.003*
Body mass index	0.203	0.026*
Waist circumference	0.252	0.006*
HbA_{1c}	0.402	< 0.001*

HbA_{1c}: glycated haemoglobin. *Statistically significant.

Table 6. Percentage of type 2 diabetes subjectswho achieved optimal treatment goals for modifiable cardiovascular risk factors

Treatment goals for type 2 DM[22]	Percent
Blood pressure < 130/80 mmHg	50
HbA_{1c} < 7%	52.5
HDL-C > 1.56 mmol/l	16
LDL-C < 2.6 mmol/l	40
TC < 5.2 mmol/l	80
TG < 1.7 mmol/l	95
Low WC (cm)	37.5

Low WC = waist circumference < 102 cm in men or < 88 cm in women.
HbA_{1c}: glycated haemoglobin, HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, TC: total cholesterol, TG: triglycerides.

Discussion

This study showed that a statistically significant proportion of the diabetic group belonged to the high cardiovascular risk category, compared to the group with the metabolic syndrome and the healthy control group, despite being on treatment. Diabetes is a major risk factor for CVD,[4,5] and findings by Haffner *et al*.[22] suggested that patients with type 2 diabetes without previous myocardial infarction have as high a risk of myocardial infarction as non-diabetic patients with previous myocardial infarction, indicating that type 2 diabetes is a coronary heart disease equivalent.[23,24]

A recent meta-analysis by Bulugahapitiya and colleagues,[25] however, did not support this hypothesis, asserting that it was not the diabetic status *per se* but the additional coronary artery disease risk factors that confer the coronary artery disease equivalent state in diabetic subjects. However, more than 70% of patients with type 2 diabetes die of cardiovascular causes.[26]

Chronic hyperglycaemia has been implicated in the microvascular complications of diabetes, and more recently it has also been associated with the macrovascular complications of CVD, including coronary heart disease, stroke and peripheral vascular disease.[27]

A higher proportion of subjects with the metabolic syndrome in our study were in the medium CVD risk category. The metabolic syndrome is an insulin-resistant state and several studies have shown that insulin resistance, characterised by impaired glucose tolerance (two-hour plasma glucose levels between 7.8 and 11.0 mmol/l) or impaired fasting glucose (plasma glucose between 5.6 and 6.9 mmol/l) have about a two-fold higher risk for CVD events than normoglycaemic subjects.[28]

Glycated haemoglobin level, a surrogate marker of chronic hyperglycaemia, has correlated strongly with the micro- and macrovascular complications of diabetes.[27] A glycated haemoglobin level less than 6% was the target of the intensive-treatment arm of the Diabetes Control and Complications Trial (DCCT) and the Epidemiology of Diabetes Interventions and Complications (EDIC) studies, which recorded a significant 42% reduction in CVD outcomes and a significant 57% reduction in the risk of non-fatal myocardial infarction, stroke or CVD death, compared with those previously in the standard-treatment arm with a glycated haemoglobin target of 7–8%.[27]

From our study, only about 50% of the diabetics achieved an HbA_{1c} target of < 7%[29] and this may explain the high proportion of diabetes patients in the high CVD risk category.

Chronic hyperglycaemia alone cannot explain the relationship between diabetes and CVD.[30] Findings from the United Kingdom Prospective Diabetes Study (UKPDS) group[31] showed that the most important risk factors for coronary heart disease were classic risk factors, particularly dyslipidaemia. In this study, the diabetic group also had higher glycated haemoglobin values and lower HDL-C values than the non-diabetic groups with and without the metabolic syndrome, which further explains their increased CVD risk.

This study showed that the diabetics on treatment had comparable TC, LDL-C and TG values with the healthy controls, although only 40% of the diabetics met the LDL-C treatment target of < 2.6 mmol/l.[29] The group with the metabolic syndrome had significantly higher levels of TC, LDL-C and TG. Lifestyle modification rather than drug therapy has been the management option for CVD risk factor levels above the cut-off point for the metabolic syndrome.[17] This study shows that a very low percentage of the study population participated in physical exercises, side-lining one of the avenues to target weight loss, reduce insulin resistance and effectively control the metabolic syndrome and its components.[32]

Correlation analysis in this study identified chronic hyperglycaemia, obesity and level of education as factors associated with CVD risk in this population. Alcohol consumption and smoking were not associated with CVD risk in this population, compared to other climes,[33] probably because a very low percentage of the study population smoked or used alcohol.

A study by Khaw *et al*.[34] reported that increasing values of glycated haemoglobin > 5% was associated with cardiovascular mortality and all-cause mortality in diabetic men, and glycated haemoglobin also appeared to be a continuous risk factor for cardiovascular mortality in the non-diabetic population. Strategies to reduce glycaemia in both diabetic and non-diabetic populations, including creating awareness of the effectiveness of increased physical activity and weight reduction in reducing insulin resistance, and increasing literacy levels would help reduce CVD risk scores in adult Nigerians.

Conclusion

Cardiovascular risk factors were high in these adult Nigerians with type 2 diabetes. Strategies to control the cardiovascular risk factors of the metabolic syndrome, achieve better glycaemic control and increase literacy levels would help to achieve cardiovascular risk reduction in adult Nigerians.

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Single blood test accurately diagnoses diabetes

A combination of elevated fasting glucose and HbA_{1c} levels from a single blood sample was found to be accurate for diagnosing diabetes. This is significant because current guidelines state that a second blood test, conducted a separate point in time, is requited to confirm a diagnosis of diabetes.

Glucose has been the standard measure of diagnosis of diabetes and current guidelines recommend repeated testing to confirm an elevated fasting glucose or haemoglobin A_{1c} level. Whether glucose and HbA_{1c} from a single point in time can be used in combination to diagnosis diabetes has been uncertain.

Researchers from Johns Hopkins Bloomberg School of Public Health evaluated a single fasting blood sample for 12 268 participants without diagnosed diabetes enrolled in the Atherosclerosis Risk in Communities (ARIC) study to determine the prognostic value of a single-sample confirmatory definition of undiagnosed diabetes. Patients in the ARIC study were enrolled between 1987 and 1989 with 25 years of follow up for incident diabetes, cardiovascular outcomes, kidney disease and mortality.

The researchers found that a single fasting blood sample showing both elevated glucose and HbA_{1c} levels was strongly predictive of a subsequent diagnosis of diabetes (almost everyone meeting the definition eventually developed diabetes) and was also strongly associated with complications of diabetes (cardiovascular disease, kidney disease, peripheral artery disease and mortality).

According to the researchers, this new approach to diagnosis could prove useful in clinical practice because it would eliminate the need for a second patient visit for a second blood draw and because the HbA_{1c} test result could be used to guide treatment.

Source: Medical Brief 2018

Prevalence, awareness, treatment and control of hypertension, diabetes and hypercholesterolaemia among adults in Dande municipality, Angola

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Abstract

Objectives: **To estimate the prevalence, awareness, treatment and control of hypertension, diabetes and hypercholesterolaemia in an Angolan population aged 15 to 64 years and to determine relationships with sociodemographic, behavioural and anthropometric characteristics.**

Methods: **A total of 2 354 individuals were assessed for behavioural, sociodemographic and physical characteristics in a cross-sectional, community-based survey. Post-stratification survey weights were applied to obtain prevalence levels. Adjusted odds ratios for each variable related to the conditions were calculated using logistic regression models.**

Results: Overall, the prevalence of hypertension was 18.0%, diabetes 9.2% and hypercholesterolaemia 4.0%. Among hypertensive individuals, the awareness rate was 48.5%; 15.8% were on treatment and 9.1% had their blood pressure controlled. Only 10.8% were aware they had diabetes, 4.5% were on treatment and 2.7% were controlled. The awareness level for hypercholesterolaemia was 4.2%, with 1.4% individuals on treatment and 1.4% controlled.

Conclusions: **The prevalence levels of hypertension and diabetes, which were higher than previous findings for the region, together with the observed low rates of awareness, treatment and control of all conditions studied, constitute an additional challenge to the regional health structures, which must rapidly adapt to the epidemiological shift occurring in this population.**

Keywords: epidemiology, hypertension, diabetes, hypercholesterolaemia, sub-Saharan Africa

Cardiovascular disease (CVD), a major cause of non communicable diseases (NCDs), was responsible for 17.5 million deaths worldwide in 2012, most occurring in low- and middle-income countries (LMIC). In Africa, the frequency of NCDs is rising rapidly, reflecting the combined effect of population growth and ageing, as well as nutritional and epidemiological transitions.[1]

A large proportion of CVD is the result of exposure to modifiable risk factors (tobacco and alcohol consumption, unhealthy diet and physical inactivity), which influence metabolic pathways and ultimately result in obesity, hypertension, diabetes or hypercholesterolaemia.[1,2] Together, these known adverse conditions explain approximately half of CVD cases, as demonstrated in the MONICA project and the INTERHEART study.[3,4]

Among the African population participating in the INTERHEART study, five risk factors (smoking, diabetes, hypertension, abdominal obesity and an elevated apolipoprotein B to apolipoprotein A-1 ratio) accounted for 89.2% of the population-attributable risk for the first myocardial infarction.[5]

The same study suggested that uncontrolled major risk factors have a larger impact on the burden of CVD in Africa than elsewhere in the world.[5]

If the current trends persist, the risk of dying from NCDs will increase in the African region. However, this rising risk could be reversed by reaching the proposed targets for six behavioural and physiological risk factors (tobacco and alcohol use, salt intake, obesity and increased blood pressure and glucose levels) out of the nine global targets proposed by the World Health Organisation (WHO) in the Global Action Plan for the Prevention and Control of NCD 2013–2020.[6,7]

To follow the achievement of those goals, there is a need for sound and updated epidemiological data from all regions of the world. The majority of published studies for the African region are conducted at hospital services, which does not allow one to detect risk factors, awareness rates and prevalence of such conditions in the general population.[8-10] To provide core data on established risk factors for the major NCDs within the context of low-resource settings, WHO designed the STEPwise approach to Surveillance (STEPS).[11] STEPS uses a modular structure with standardised questions and protocols, allowing adjustment of its application and appropriate comparisons across surveys.[11]

In Angola, infectious disease and maternal and child health-related problems remain the major causes of morbidity and mortality.[12] However, an increased burden of NCDs has been observed, particularly CVD, which was responsible for 9% of adult deaths in 2013.[13] Beyond general vital statistics, specific epidemiological information on CVD risk factors in Angola is based on only four local studies published after 2000: a survey of 667 adult students of Health Sciences in Lubango (prevalence of hypertension of 23.5%),[14] a study conducted among 615 active employees of the University Agostinho Neto, Luanda (prevalence of hypertension 45.2% and hypercholesterolaemia 11.1%),[15] 1 464 participants surveyed in the Dande Health and Demographic Surveillance System (Dande-HDSS) catchment area (23% prevalence of hypertension),[16]

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and a study of 421 subjects from a rural community of Angola (2.8% prevalence of diabetes).[17]

Building on the work carried out by Pires and colleagues,[16] and based on the STEPS methodology,[11] this study aimed to expand the sample population to the 15- to 24-year-old group, and to estimate the prevalence, awareness, treatment and control of hypertension, diabetes and hypercholesterolaemia, and its association with sociodemographic (gender, age, education and area of residence), behavioural (alcohol and tobacco consumption) and anthropometric [body mass index (BMI) and abdominal obesity] variables among 15- to 64-year-olds in the Dande-HDSS population.

Methods

A cross-sectional, community-based survey was conducted from September 2013 to March 2014 in the catchment area of the Dande-HDSS, located in Dande municipality of Bengo Province, Angola.[18] A representative gender- and age-stratified random sample list of 3 515 individuals, aged between 15 and 64 years, was drawn, as described previously.[19] Of these, we were able to examine 2 484 (70.7%) individuals, 750 (21.3%) were unreachable and 281 (8.0%) refused to participate, thus approaching the predicted non-participation rate of 30%.[19]

For analysis, we excluded participants with missing anthropometric values (n = 14) and pregnant women (n =116) due to the fact that anthropometric parameters vary during pregnancy. Therefore 2 354 individuals (67.0%) were included in the final analysis.

Information on age, completed years of school education, alcohol and tobacco consumption, and the previous measurement of any of the conditions under investigation, were collected through a structured interview conducted by trained interviewers, following a previously published protocol for data collection based on the WHO STEPS manual version 3.0.[11,19]

For this analysis, age was categorised into five 10-year age groups: 15 to 24, 25 to 34, 35 to 44, 45 to 54 and 55 to 64 years old. Education was categorised according to the number of completed years of schooling: none, one to four years, five to nine years, and 10 years or more. Area of residence was classified as rural or urban, as previously described.[18] Alcohol consumption was defined as none if participants reported no alcohol consumption; occasional if participants reported drinking alcohol two or less days per week; and frequent if drinking any alcohol three or more days per week. Current tobacco smokers were defined as participants who reported smoking at least one cigarette per day.

Previous measurements of blood pressure, and glucose or cholesterol levels in the last year were requested from all participants. In the case of a positive answer, participants were questioned about their awareness of a previous diagnosis of hypertension, diabetes or hypercholesterolaemia made by a healthcare worker. Any individual was considered under treatment if he/she indicated the use of a specific medication; a participant was considered controlled if they had a current normal value.

Certified health professionals conducted all anthropometric and clinical measurements, as described previously.[19]

Anthropometric measurements were performed with individuals wearing light clothing and no footwear, and an overnight fast was requested of all participants.

Body mass and height were measured using a digital scale SECA 803 (SECA United Kingdom, Birmingham, UK) and a portable stadiometer SECA 213 (SECA United Kingdom, Birmingham, UK). BMI was defined as the body mass (kg) divided by the square of the body height (m^2), and further categorised according to WHO as underweight (< 18.5 kg/m^2), normal (18.5 to 24.99 kg/m^2), overweight (25.0 to 29.99 kg/m^2) and obese (≥ 30 kg/m^2).[20]

Waist and hip circumferences were measured using circumference tape SECA 203 (SECA United Kingdom, Birmingham, UK). The waist-to-hip ratio was calculated as the circumference of the waist (cm) to that of the hips (cm), and abdominal obesity was defined as waist-to-hip ratio ≥ 0.9 for men and ≥ 0.85 for women.[21]

Blood pressure was measured on the right arm with the automatic sphygmomanometer OMRON M6 Comfort (OMRON Healthcare Europe BV, Hoofddorp, The Netherlands), with the individual seated, and using an appropriate cuff size. Three readings were done at three-minute intervals. The mean value of the last two measurements was used to determine the blood pressure. Hypertension was defined as systolic blood pressure of ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg and/ or use of antihypertensive drugs during the previous two weeks.[22]

Blood sugar was measured using a blood glucose meter ACCU-CHEK Aviva (Roche Diagnostic, Indianapolis, IN, USA) with ACCU-CHEK Aviva glucose reactive strips (Roche Diagnostic, Indianapolis, IN, USA). The definition of diabetes followed WHO diagnostic criteria of 126 mg/dl (6.9 mmol/l) glucose in a fasting blood sample,[23] and/or use of antidiabetic drugs during the previous two weeks.

Total cholesterol in the blood was measured using a point-of- care device ACCUTREND Plus (Roche Diagnostic, Indianapolis, IN, USA) with ACCUTREND cholesterol reactive strips (Roche Diagnostic, Indianapolis, IN, USA). Hypercholesterolaemia was defined according to WHO diagnostic criteria for STEPS, with cholesterol ≥ 240 mg/dl (6.2 mmol/l) in a fasting blood sample,[2,11] and/or use of anticholesterol drugs during the previous two weeks.

All procedures performed in this study were in accordance with the standards of the ethics committee of the Angolan Ministry of Health and with the 1964 Helsinki declaration and its later amendments. Written informed consent was obtained from all individual participants included in the study (in the case of those under 18 years old, from their parent or legal guardian).

A copy of the signed consent form, as well as instructions regarding the fasting period and contact information, were delivered to each participant.

Statistical analysis

Data were double entered into a PostgreSQL® database and SPSS® version 22 (IBM Corp, Armonk, NY, USA) was used for statistical analysis. Post-stratification survey weights were calculated using the known gender and categorical age distribution of the Dande-HDSS population,[17] and these were used in all further calculations. Descriptive data are reported as absolute frequencies and percentages or means and standard deviations (SD), as appropriate.

To facilitate comparisons with other studies, the prevalence of the three conditions under study was determined for three age groups: 15 to 64, 18 to 64 and 25 to 64 years. Logistic regression models were fitted to the categorical variable of age because of its known effect on hypertension, diabetes and hypercholesterolaemia. Gender-specific adjusted odds ratios (OR) were estimated for each variable (age, residence, education, BMI, abdominal obesity, tobacco and alcohol consumption) related to the conditions studied. A 95%

Table 1. Socio-demographic, anthropometric and behavioural characteristics of the population (Caxito, 2016)

Parameters	All participants (*n* = 2 354) % (95% CI)*	Female (*n* = 1 222) % (95% CI)*	Male (*n* = 1 132) % (95% CI)*
Age (years) (*n* = 2 354)			
15–24	36.2 (34.3–38.1)	30.1 (27.6–32.7)	42.7 (39.9–45.6)
25–34	25.9 (24.2–27.7)	25.4 (23.0–27.9)	26.5 (24.0–29.1)
35–45	16.1 (14.7–17.6)	18.7 (16.6–20.9)	13.3 (11.5–15.4)
45–54	12.6 (11.3–14.0)	15.3 (13.4–17.4)	9.7 (8.1–11.6)
55–64	9.2 (8.1–10.4)	10.6 (9.0–12.4)	7.8 (6.3–9.5)
Residence (*n* = 2 354)			
Urban	81.0 (79.4–82.5)	81.2 (78.9–83.3)	80.8 (78.4–83.0)
Rural	19.0 (17.5–20.6)	18.8 (16.7–21.1)	19.2 (17.0–21.6)
Education (years completed) (*n* = 2 348)			
None	9.3 (8.2–10.5)	16.6 (14.6–18.8)	1.4 (0.9–2.3)
1–4	23.1 (21.5–24.9)	34.5 (31.9–37.2)	10.9 (9.2–12.8)
5–9	42.2 (40.2–44.2)	35.7 (33.1–38.5)	49.2 (46.3–52.1)
> 10	25.4 (23.7–27.2)	13.1 (11.4–15.2)	38.5 (35.7–41.4)
BMI class (kg/m²) (*n* = 2 354)			
Underweight (< 18.5)	11.3 (10.1–12.6)	10.2 (8.7–12.1)	12.5 (10.7–14.5)
Normal (18.5–24.9)	66.1 (64.1–67.9)	58.7 (55.9–61.4)	74.0 (71.4–76.5)
Overweight (25.0–29.9)	15.8 (14.4–17.3)	20.5 (18.4–22.9)	10.7 (9.0–12.6)
Obese (≥ 30)	6.8 (5.9–7.9)	10.6 (9.0–12.4)	2.8 (2.0–4.0)
Abdominal obesity (*n* = 2 354)			
No	75.1 (73.3–76.8)	63.5 (60.8–66.2)	87.6 (85.6–89.4)
Yes	24.9 (23.2–26.7)	36.5 (33.8–39.2)	12.4 (10.6–14.4)
Tobacco smoking (*n* = 2 342)			
Non-current	93.8 (92.7–94.7)	97.3 (96.2–98.1)	90.0 (88.1–91.6)
Current	6.2 (5.3–7.3)	2.7 (1.9–3.8)	10.0 (8.4–11.9)
Alcohol consumption (*n* = 2 335)			
No consumption	63.8 (61.8–65.7)	69.5 (66.9–72.0)	57.6 (54.7–60.4)
Occasional (< 3 days per week)	18.8 (17.2–20.4)	19.6 (17.5–21.9)	17.8 (15.7–20.2)
Frequent (≥ 3 days per week)	17.5 (16.0–19.1)	10.9 (9.2–12.7)	24.6 (22.2–27.2)

*Post-stratification weights used as described in the methods section.

confidence interval (95% CI) and a significance level of $p < 0.05$ were set for all applicable determinations.

Results

The mean age of this population was 32.5 years (SD 13.6) with 63.0% (*n* = 1 482) women and the majority (81.0%) living in urban settings. Nearly 10% had never received any formal education, with men having completed more school years. Overall, almost a quarter of participants had abdominal obesity (36.5% of women and 12.4% of men), 6.8% were obese (10.6% of women and 2.8% of men), 6.2% were smokers (2.7% of women and 10.0% of men) and approximately two-fifths consumed alcohol occasionally or frequently, with a higher proportion of frequent drinkers among men (24.6 vs 10.9%) (Table 1).

The prevalence of hypertension in the general population was 18.0%, reaching 20.0% in those over 18 years of age, and 26.6% in those aged 25 to 64 years (Table 2). This prevalence was always higher among women than men, but with no statistically significant relationship (data not shown).

The overall prevalence of diabetes among participants aged 15 to 64 years was 9.2%; the prevalence among those over 18 years old was 9.8%, and 11.9% in those aged over 25 years (Table 2). Men had a higher OR than women for diabetes of 1.4 (95% CI: 1.0–1.8, data not shown).

Similar to that of hypertension and diabetes, the prevalence of hypercholesterolaemia was higher in the older age groups, with an estimated 5.5% in participants aged 25 to 64 years, and a lower prevalence of 4.0% in the overall population (Table 2). Women had an OR of 2.3 (95% CI: 1.3–4.0, data not show) for hypercholesterolaemia.

Only five participants (0.2%; 95% CI: 0.1–0.4, data not shown) presented all three conditions, but 22.0% (95% CI: 18.4–26.2, data not shown) of hypertensive participants had an associated condition, as did 37.2% (95% CI: 31.1–43.7, data not shown) of participants with diabetes and 47.9% (95% CI: 36.7–59.3, data not shown) of those with hypercholesterolaemia. The most common associations were hypertension and diabetes, present in 71 individuals (3.0%; 95% CI: 2.4–3.7, data not shown).

The prevalence of hypertension was higher in rural areas (26.9 vs 15.9% in urban areas) for both genders. Individuals with lower levels of education had a higher prevalence of hypertension, with women with no formal education presenting an OR for hypertension of 4.3 (Table 3).

Hypertension was higher among the obese (34.9% of women and 48.5% of men) and individuals with abdominal obesity (32.5% of women and 45.7% of men), with a higher OR in men for both conditions (Table 3). Hypertension prevalence was also higher among current smokers (50.0% in women and 20.4% in men) and frequent alcohol drinkers (28.0% in women and 24.3% in men). Men presented a higher OR for hypertension than women, related to the consumption of alcohol (Table 3).

Residents in urban areas presented a higher prevalence of diabetes, with a significantly higher OR for diabetes in men. Participants with lower education levels had a higher prevalence of diabetes, but without statistical significance (Table 4).

With regard to anthropometric variables, there was a higher

Table 2. Prevalence of hypertension, diabetes and hypercholesterolaemia by gender and age (Caxito, 2016)

Parameters	All Participants			Female			Male		
	15–64 years (*n* = 2 354)	18–64 years (*n* = 2 100)	25–64 years (*n* = 1 503)	15–64 years (*n* = 1 222)	18–64 years (*n* = 1 116)	25–64 years (*n* = 854)	15–64 years (*n* = 1 132)	18–64 years (*n* = 984)	25–64 years (*n* = 649)
Hypertension, %	18.0	20.0	26.6	20.0	21.8	27.8	15.9	18.1	25.1
(95% CI)	(16.5–19.6)	(18.4–21.8)	(24.4–28.9)	(17.8–22.3)	(19.5–24.3)	(24.9–30.8)	(13.9–18.1)	(15.8–20.6)	(21.9–28.6)
Diabetes, %	9.2	9.8	11.9	8.9	9.3	10.8	9.6	10.4	13.5
(95% CI)	(8.1–10.4)	(8.6–11.2)	(10.3–13.6)	(7.4–10.6)	(7.8–11.2)	(8.9–13.0)	(8.0–11.4)	(8.7–12.5)	(11.0–16.3)
Hypercholesterolaemia, %	4.0	4.4	5.5	5.6	6.0	7.4	2.0	2.4	2.9
(95% CI)	(3.2–5.0)	(3.5–5.5)	(4.4–6.9)	(4.3–7.2)	(4.7–7.8)	(5.7–9.5)	(1.2–3.2)	(1.5–3.8)	(1.8–4.8)

Table 3. Prevalence of hypertension and relationship with other factors by gender (Caxito, 2016)

	All Participants (*n* = 2 354)	Female (*n* = 1 222)		Male (*n* = 1 132)	
Associated factor	**Prevalence % (95% CI)***	**Prevalence % (95% CI)***	**Adjusted OR[a, b] (95% CI)***	**Prevalence % (95% CI)***	**Adjusted OR[a, b] (95% CI)***
Total	18.0 (16.5–19.6)	20.0 (17.8–22.3)	–	15.9 (13.9–18.1)	–
Age (years)					
15–24	2.8 (1.9–4.2)	1.9 (0.9–3.9)	1	3.5 (2.2–5.6)	1
25–34	12.3 (9.9–15.2)	10.6 (7.7–14.6)	6.6 (2.8–15.4)	14.3 (10.8–18.8)	4.6 (2.6–8.2)
35–44	25.6 (21.5–72.0)	26.8 (21.4–32.9)	20.3 (8.9–46.5)	23.8 (17.7-31.2)	8.7 (4.7-16.0)
45–54	38.7 (33.4–44.4)	39.6 (32.8–39.6)	36.6 (16.0–83.8)	37.3 (28.8–46.6)	16.2 (8.7–30.0)
55–64	51.6 (45.0–58.2)	53.5 (44.9–61.9)	63.4 (27.1–147.9)	48.9 (38.7–59.1)	26.4 (13.9–50.0)
Residence					
Urban	15.9 (14.3–17.6)	17.6 (15.3–20.1)	–	14.0 (11.9–16.4)	–
Rural	26.9 (23.0–31.2)	30.0 (24.4–36.2)	–	23.5 (18.4–29.6)	–
Education (years completed)					
None	45.4 (38.9–52.0)	45.5 (38.8–52.4)	4.3 (1.8–10.2)	46.7 (24.8–69.9)	2.0 (0.6–6.5)
1–4	24.9 (21.4–28.7)	23.3 (19.5–27.6)	2.4 (1.0–5.4)	29.8 (22.5–38.4)	0.8 (0.5–1.5)
5–9	12.7 (10.8–14.9)	10.3 (7.8–13.6)	2.2 (0.9–5.1)	14.5 (11.8–17.7)	0.9 (0.6–1.4)
> 10	10.4 (8.2–13.1)	4.4 (2.1–8.8)	1	12.6 (9.8–16.1)	1
BMI class (kg/m^2)					
Underweight (< 18.5)	11.0 (7.8-15.3)	12.9 (8.1-19.0)	1	9.3 (5.5-15.2)	1
Normal (18.5–24.9)	15.2 (13.5–17.1)	17.0 (14.4–19.9)	1.1 (0.6–2.1)	13.7 (11.5–16.2)	1.3 (0.7–2.5)
Overweight (25.0–29.9)	25.8 (21.6–30.5)	23.9 (19.0–29.5)	1.2 (0.6–2.3)	29.2 (21.8–37.8)	2.2 (1.1–4.7)
Obese (≥ 30)	37.3 (30.2–45.0)	34.9 (27.2–43.4)	2.0 (1.0–4.1)	48.5 (32.5–64.8)	5.1 (1.9–13.4)
Abdominal obesity					
No	12.1 (10.6–13.7)	12.6 (10.5–15.2)	1	11.6 (9.7–13.7)	1
Yes	35.7 (31.9–39.6)	32.5 (28.3–37.0)	1.6 (1.2-2.3)	45.7 (37.7–54.0)	2.8 (1.8–4.3)
Tobacco smoking					
Non-current	17.3 (15.8–18.9)	18.9 (16.7–21.2)	–	15.5 (13.4–17.8)	–
Current	26.7 (20.2–34.4)	50.0 (34.1–65.9)	–	20.4 (14.0–28.7)	–
Alcohol consumption					
No consumpion	14.2 (12.6–16.1)	18.1 (15.7–20.9)	1	9.1 (7.2–11.6)	1
Occasional (< 3 days per week)	23.5 (19.8–23.5)	21.4 (16.7–27.1)	0.9 (0.6–1.4)	26.0 (20.4–32.5)	2.5 (1.6–4.0)
Frequent (≥ 3 days per week)	25.5 (21.5–25.5)	28.0 (21.1–36.2)	1.7 (1.1–2.7)	24.3 (19.6–29.7)	2.5 (1.7–3.9)

*Post-stratification weights used as described in the methods section.
[a]Adjusted for age (categorical: 15–23, 25–34, 35–44, 45–54, and 55–64).
[b]Only variables with relations with statistical significance shown.

prevalence of diabetes among obese participants (17.1% in women and 24.2% in men) and those with abdominal obesity (8.8% in women and 24.3% in men). Men with obesity (2.4 vs underweight) and abdominal obesity (2.3 vs no abdominal obesity) presented higher ORs for diabetes than women (2.1 for obese vs underweight and 1.5 for abdominal obesity) (Table 4).

For current smokers and occasional consumers of alcohol the prevalence of diabetes was higher, but with no significant relationship (Table 4). No significant relationships were found with education, residence, BMI, abdominal obesity, tobacco smoking and alcohol consumption; however, the prevalence of hypercholesterolaemia was higher among less educated individuals, the obese, smokers and frequent alcohol drinkers (Table 5).

The majority of the population (61.5%; *n* = 1 460) reported previous measures of blood pressure, and nearly half (48.5%) of the hypertensive participants were aware of their condition. Only 32.5% of the aware hypertensive participants were on treatment and 57.7% of them had their blood pressure controlled. This represented only 9.1% of all hypertensive participants (Fig. 1).

Only 7.3% (*n* = 172) of the population reported previous measurement of glycaemia, with a low awareness rate of 10.8% among participants with diabetes in this study. Of the aware participants, 41.7% were receiving treatment (4.5% of all hyperglycaemic participants) and 60.0% had a controlled blood sugar level (Fig. 1). Only 2.9% (*n* = 68) of participants reported previous measures of cholesterolaemia and only 4.2% of individuals with hypercholesterolaemia were aware of their condition (Fig. 1).

The hypertension awareness rate was higher among women (62.7%; 95% CI: 55.9–69.0) and older participants, without a difference regarding education level (Table 6). The diabetes awareness rate was higher among men (58.3%; 95% CI: 38.8–75.5), older participants and those with higher education levels (Table 7). The hypercholesterolaemia awareness rate was higher among women (66.7%; 95% CI: 20.8–93.9), older age groups and higher education levels (Table 8). The treatment rate of all conditions was more prevalent in the older age groups and higher education levels, but the control rate was more frequent in younger participants.

Among the individuals who were aware of any of the three conditions, the advice most often given by healthcare professionals to follow non-pharmacological approaches for the management of cardiovascular risk factors was a change in dietary habits, with a decrease in salt and fat intake, and increased fruit and vegetable intake (Table 9).

Table 4. Prevalence of diabetes and relationship with other factors by gender (Caxito, 2016)

	All Participants (*n* = 2 348)	Female (*n* = 1 220)		Male (*n* = 1 128)	
Associated factor	**Prevalence % (95% CI)***	**Prevalence % (95% CI)***	**Adjusted OR[a, b] (95% CI)***	**Prevalence % (95% CI)***	**Adjusted OR[a, b] (95% CI)***
Total	9.2 (8.1–10.4)	8.9 (7.4–10.6)	1	9.6 (8.0–11.4)	1.4 (1.0–1.8)
Age (years)					
15–24	4.4 (3.2–6.0)	4.4 (2.7–7.0)	1	4.4 (2.9–6.6)	1
25–34	5.6 (4.0–7.7)	3.2 (1.8–5.9)	0.8 (0.3–1.7)	8.0 (5.4–11.6)	1.9 (1.0–3.5)
35–44	13.2 (10.2–17.0)	12.7 (9.0–17.7)	3.3 (1.7–6.2)	13.9 (9.3–20.3)	3.4 (1.8–6.5)
45–54	19.3 (15.2–24.2)	17.6 (12.9–23.7)	4.8 (2.6–9.0)	22.2 (15.4–30.9)	6.2 (3.3–11.6)
55–64	17.2 (12.8–22.8)	15.5 (10.3–22.7)	4.0 (2.0–8.0)	20.7 (13.5–30.4)	5.6 (2.8–11.0)
Residence					
Urban	9.8 (8.5–11.2)	9.2 (7.5–11.1)	1.6 (0.9–2.8)	10.4 (8.6–12.6)	2.6 (1.4–4.9)
Rural	6.8 (4.8–9.5)	7.4 (4.7–11.6)	1	6.0 (3.6–10.1)	1
Education (years completed)					
None	11.5 (7.9–16.5)	11.9 (8.1-17.1)	–	6.7 (1.2-29.8)	–
1–4	11.7 (9.2–14.6)	10.0 (7.5-13.3)	–	17.2 (11.5-24.9)	–
5–9	8.3 (6.7–10.1)	7.1 (5.1–9.9)	–	9.0 (6.9–11.6)	–
> 10	7.7 (5.9–10.2)	6.2 (3.4–11.1)	–	8.3 (6.1–11.3)	–
BMI class (kg/m^2)					
Underweight (< 18.5)	7.5 (4.9–11.4)	4.0 (1.7–9.0)	1	10.7 (6.6–16.9)	1
Normal (18.5–24.9)	7.8 (6.6–9.2)	7.7 (5.9–9.9)	2.0 (0.7–5.1)	7.9 (6.3–9.9)	0.7 (0.4–1.2)
Overweight (25.0–29.9)	12.4 (9.4–16.1)	10.4 (7.2–14.7)	2.4 (0.9–6.5)	16.5 (11.0–24.2)	1.1 (0.5–2.3)
Obese (≥ 30)	18.6 (13.4–25.4)	17.1 (11.5–24.5)	3.9 (1.4–11.1)	24.2 (12.8–41.0)	1.7 (0.6–4.5)
Abdominal obesity					
No	7.0 (5.9–8.3)	3.5 (2.3–5.2)	1	7.5 (6.0–9.3)	1
Yes	15.9 (13.1–19.0)	8.8 (6.4–12.2)	1.5 (1.0–2.3)	24.3 (17.9–32.0)	2.3 (1.4–3.8)
Tobacco smoking					
Non-current	8.8 (7.6–10.0)	8.6 (7.2–10.4)	–	8.9 (7.3–10.8)	–
Current	14.4 (9.6–21.0)	17.6 (8.3–33.5)	–	13.3 (8.2–20.8)	–
Alcohol consumption					
No consumption	8.9 (7.6–10.5)	8.7 (6.9–10.8)	–	9.2 (7.2–11.7)	–
Occasional (< 3 days per week)	10.5 (8.0–13.7)	10.1 (6.9–14.6)	–	11.0 (7.4–16.1)	–
Frequent (≥ 3 days per week)	8.8 (6.4–12.0)	8.3 (4.7–14.3)	–	9.1 (6.2–13.0)	–

*Post-stratification weights used as described in the methods section.
[a]Adjusted for age (categorical: 15–23, 25–34, 35–44, 45–54, and 55–64).
[b]Only variables with relations with statistical significance shown.

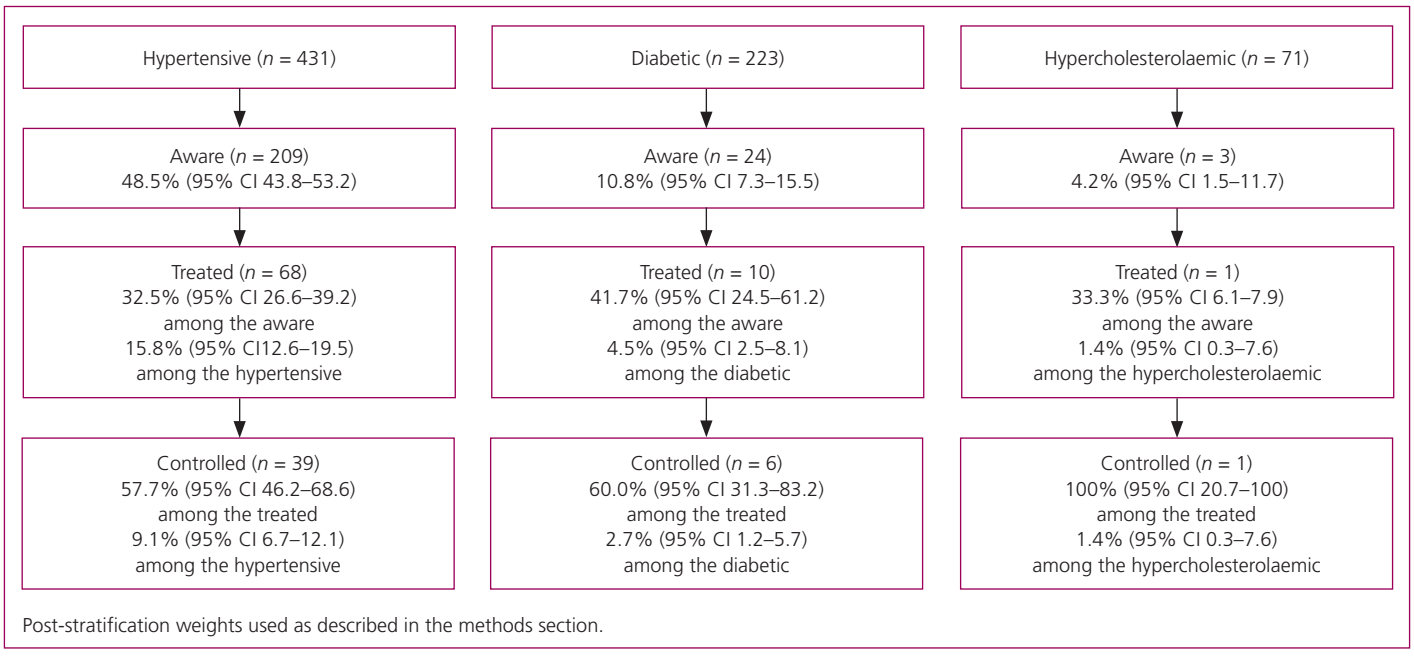

Fig. 1. Frequencies, awareness, treatment and control of hypertension, diabetes and hypercholesterolaemia.

Table 5. Prevalence of hypercholesterolaemia and relationship with other factors by gender (Caxito, 2016)

	All Participants (*n* = 1 781)	Female (*n* = 978)		Male (*n* = 803)	
Associated factor	**Prevalence % (95% CI)***	**Prevalence % (95% CI)***	**Adjusted OR[a, b] (95% CI)***	**Prevalence % (95% CI)***	**Adjusted OR[a, b] (95% CI)***
Total	4.0 (3.2–5.0)	5.6 (4.3–7.2)	2.3 (1.3–4.0)	2.0 (1.2–3.2)	1
Age (years)					
15–24	0.7 (0.3–1.8)	1.1 (0.4–3.2)	1	0.3 (0.1–1.9)	1
25–34	2.5 (1.4–4.3)	2.8 (1.4–5.7)	2.6 (0.6–10.8)	2.5 (1.1–5.3)	5.0 (0.8–31.6)
35–44	3.6 (2.0–6.4)	5.4 (2.9–9.6)	5.2 (1.4–20.0)	0.9 (0.2–4.7)	2.1 (0.2–24.4)
45–54	9.4 (6.3–13.7)	10.8 (6.9–16.7)	11.9 (3.30–42.7)	5.7 (2.5–12.8)	13.7 (2.1–88.1)
55–64	11.4 (7.6–16.8)	15.4 (10.0–23.0)	17.2 (4.8–61.9)	4.5 (1.6–12.5)	9.0 (1.2–69.5)
Residence					
Urban	3.9 (3.0–5.0)	5.6 (4.2–7.4)	–	1.8 (1.0–3.2)	–
Rural	4.2 (2.5–7.0)	5.3 (2.8–9.8)	–	3.5 (1.5–7.9)	–
Education (years completed)					
None	10.8 (7.0–16.2)	10.7 (6.9–16.3)	–	11.1 (2.0–43.5)	–
1–4	5.7 (3.9–8.3)	6.4 (4.3–9.5)	–	2.5 (0.7–8.8)	–
5–9	2.6 (1.7–4.1)	3.3 (1.9–5.9)	–	2.0 (1.0–3.9)	–
>10	2.0 (1.0–3.7)	2.3 (0.8–6.5)	–	1.9 (0.9–4.0)	–
BMI class (kg/m^2)					
Underweight (< 18.5)	2.3 (0.9–5.7)	3.2 (1.1–9.1)	–	1.2 (0.2–6.5)	–
Normal (18.5–24.9)	3.5 (2.6–4.7)	5.1 (3.6–7.3)	–	1.9 (1.1–3.3)	–
Overweight (25.0–29.9)	5.3 (3.3–8.3)	6.0 (3.6–10.1)	–	3.8 (1.5–9.3)	–
Obese (≥ 30)	6.7 (3.5–12.2)	8.6 (4.6–15.5)	–	–[a]	–
Abdominal obesity					
No	2.4 (1.7–3.4)	3.5 (2.3–5.2)	–	1.5 (0.8–2.7)	–
Yes	8.1 (6.0–10.9)	8.8 (6.4–12.2)	–	5.9 (2.9–11.6)	–
Tobacco smoking					
Non-current	3.7 (2.9–4.8)	5.1 (3.9–6.7)	–	2.0 (1.2–3.3)	–
Current	6.4 (3.1–12.6)	17.9 (7.9–35.6)	–	2.5 (0.7–8.6)	–
Alcohol consumption					
No consumption	4.3 (3.2–5.6)	5.7 (4.2–7.7)	–	2.2 (1.2–4.1)	–
Occasional (< 3 days per week)	2.7 (1.4–5.0)	4.6 (2.5–8.6)	–	–[c]	–
Frequent (≥ 3 days per week)	3.9 (2.2–6.7)	5.6 (2.6–11.6)	–	2.5 (1.1–5.7)	–

*Post-stratification weights used as described in the methods section.
[a]Adjusted for age (categorical: 15–23, 25–34, 35–44, 45–54, and 55–64).
[b]Only variables with relations with statistical significance shown.
[c]No cases in this category.

Discussion

The prevalence of hypertension among participants in the range of 15 to 64 years old was 18.0%. This value rose to 26.6% among participants aged 25 to 64 years, which is slightly higher than those previously described for Angola over the last eight years,[14-15] particularly a study conducted in the same region in 2010,[16] and the WHO age-standardised (25 to 64 years old) estimated hypertension prevalence for 2014 in Angola of 23.9% (95% CI: 16.3–31.1).[1] More recently, a cross-sectional study conducted in Uganda, South Africa, Tanzania and Nigeria encountered an overall age-standardised prevalence of hypertension of 25.9%.[24]

The estimated 9.2% prevalence of diabetes (9.8% in urban and 6.8% in rural areas) was higher than previous reports from Angola of 5.7% among an urban population (aged 20 to 72 years) in 2010,[15] and 2.8% for a rural community (aged 30 to 69 years) in 2009.[17] The value of 9.8% estimated in individuals older than 18 years is in the middle range of prevalence levels encountered in STEPS surveys, with values from 3.0% in Benin to 22.5% in Niger.[25,26] This value also falls within the confidence intervals of the WHO estimate of 12.1% (95% CI: 5.6–18.9) for increased blood glucose levels in those over 18 years in Angola for 2014.[1]

This rise in diabetes is aligned with the global tendency for this disease, which has increased faster in LMIC than in highincome countries since 1980.[27] Since the end of the Angolan civil war in 2002, the population has been increasing and ageing. This, together with changes in food habits and the urbanisation process, may have led to the increased prevalence of diabetes in this region.

The prevalence of hypercholesterolaemia (5.3% among participants 25 and 64 years old) in this study was lower than that found in a previous study in Luanda among an older urban population.[15] However, this value falls within a wide range of values from several STEPS surveys measuring the prevalence of total cholesterol, from 2.1% in Mozambique to 26.0% in Tanzania.[25,26] This prevalence may also be tied to the ageing population and changes in dietary habits that most African countries are currently facing.[28] There is a lack of solid knowledge regarding the prevalence levels of hypercholesterolaemia in Africa, mainly owing to the difficulties in determining values of blood cholesterol in African communities because of the high cost of laboratory tests. This situation presents a challenge when comparing research results.

As described in other studies worldwide, the clustering of risk factors helps to explain the known impacts of age, education

Table 6. Awareness, treatment and control rates of hypertension by gender (Caxito, 2016)

	Awareness			Treatment			Control		
	All (*n* = 209) % (95% CI)	Female (*n* = 131) % (95% CI)	Male (*n* = 78) % (95% CI)	All (*n* = 68) % (95% CI)	Female (*n* = 41) % (95% CI)	Male (*n* = 27) % (95% CI)	All (*n* = 39) % (95% CI)	Female (*n* = 25) % (95% CI)	Male (*n* = 14) % (95% CI)
Education (years completed)									
None	21.5 (16.5–27.6)	34.4 (26.8–42.8)	0	17.6 (10.4–28.4)	26.8 (15.7–41.9)	3.7 (0.7–18.3)	10.3 (4.1–23.6)	16.0 (6.4–34.7)	0
1–4	31.1 (25.2–37.7)	40.5 (32.4–49.0)	15.4 (9.0–25.0)	27.9 (18.7–39.6)	39.0 (25.7–54.3)	11.1 (3.9–28.1)	25.6 (14.6–41.1)	40.0 (23.4–59.3)	0
5–9	28.2 (22.6–34.7)	22.1 (15.9–30.0)	38.5 (28.4–49.6)	29.4 (19.9–41.1)	26.8 (15.7–41.9)	33.3 (18.6–52.2)	33.3 (20.6–49.0)	36.0 (20.2–55.5)	28.6 (11.7–54.6)
> 10	19.1 (14.4–25.0)	3.1 (1.2–7.6)	46.2 (35.5–57.1)	25.0 (16.2–36.4)	7.3 (2.5–19.4)	51.9 (34.0–69.3)	30.8 (18.6–46.4)	8.0 (2.2–25.0)	71.4 (45.4–88.3)
Age (years)									
15–24	2.9 (1.3–6.1)	0.8 (0.1–4.2)	6.4 (2.8–14.1)	1.5 (0.3–7.9)	2.4 (0.4–12.6)	0	2.6 (0.5–13.2)	4.0 (0.7–19.5)	0
25–34	16.7 (12.3–22.4)	12.2 (7.7–18.9)	24.4 (16.2–34.9)	26.5 (17.4–38.0)	24.4 (13.8–39.3)	29.6 (15.9–48.5)	33.3 (20.6–49.0)	32.0 (17.2–51.6)	35.7 (16.3–61.2)
35–44	19.6 (14.8–25.5)	19.1 (13.3–26.7)	20.5 (13.0–30.8)	20.6 (12.7–31.6)	19.5 (10.2–34.0)	22.2 (10.6–40.8)	25.6 (14.6–41.1)	24.0 (11.5–43.4)	28.6 (11.7–54.6)
45–54	31.1 (25.2–37.7)	37.4 (29.6–45.9)	20.5 (13.0–30.8)	23.5 (15.0–34.9)	26.8 (15.7–41.9)	18.5 (8.2–36.7)	17.9 (9.0–32.7)	20.0 (8.9–39.1)	14.3 (4.0–39.9)
55–64	29.7 (23.9–36.2)	30.5 (23.3–38.9)	19.4 (19.4–39.0)	27.9 (18.7–39.6)	26.8 (15.7–41.9)	29.6 (15.9–48.5)	20.5 (10.8–35.5)	20.0 (8.9–39.1)	21.4 (7.6–47.6)

and obesity on the occurrence of hypertension, diabetes and hypercholesterolaemia. The prevalence of these three conditions was higher among individuals with less education, and increased with age and BMI.

Obesity represents a major concern as a risk factor for CVD and NCDs in general, and is connected with the current nutritional transition in Africa, with a shift in the composition and structure of diets traditionally low in fat and high in unrefined carbohydrates toward higher intakes of refined carbohydrates, added sugars, fats and animal-source foods.[28] This shift may have had an impact on the rise in incidence of diabetes over the past decades, revealed in recent literature reviews,[29-31] as well as a WHO estimation of the rise in median prevalence of elevated total cholesterol for this region.[2]

Similar to this nutritional transition, the process of urbanisation underway in the region must be taken into consideration for future interventions. Living in an urban area has been associated with a two-fold increase in the prevalence of diabetes among this population, as described in other studies.[1,29-31]

Information regarding the awareness, treatment and control rates for the three conditions investigated is scarce for the African continent, except for hypertension; there are also some available data with regard to diabetes. Our findings for awareness of hypertension were higher than those calculated in 2010 for Africa, with an estimated 33.7% pooled awareness rate.[32] Current values for awareness, treatment and control of hypertension are higher than in 2011 in the same population; results for awareness were 21.6% (95% CI: 17.0–26.9) in 2011 and 48.5% in the present study. Values for participants who were aware of their condition and on pharmacological treatment (13.9%, 95% CI: 5.9–29.1) increased to 32.5%; approximately one-third of participants were controlled in 2011 and more than half were controlled in our study. This may have resulted from the positive effect of identification of

Table 7. Awareness, treatment and control rates of diabetes by gender (Caxito, 2016)

	Awareness			Treatment			Control		
	All (*n* = 24) %	Female (*n* = 10) %	Male (*n* = 14) %	All (*n* = 10) %	Female (*n* = 6) %	Male (*n* = 4) %	All (*n* = 6) %	Female (*n* = 5) %	Male (*n* = 1) %
Education (years completed)									
None	12.5	30.0	0.0	20.0	33.3	0	16.7	20.0	0
1–4	4.2	10.0	0.0	10.0	16.7	0	16.7	20.0	0
5–9	33.3	30.0	35.7	50.0	33.3	75.0	50.0	40.0	100.0
> 10	50.0	30.0	64.3	20.0	16.7	25.5	16.7	20.0	0
Age (years)									
15–24	8.3	20.0	0.0	20.0	33.3	0	33.3	40.0	0
25–34	12.5	10.0	14.3	10.0	16.7	0	16.7	20.0	0
35–44	20.8	10.0	28.6	20.0	16.7	25.5	16.7	20.0	0
45–54	25.0	20.0	28.6	10.0	16.7	0	0	0	0
55–64	33.3	40.0	28.6	40.0	16.7	75.0	33.3	20.0	100.0

Table 8. Awareness, treatment and control rates of hypercholesterolemia by gender (Caxito, 2016)

	Awareness			Treatment			Control		
	All (*n* = 3) %	Female (*n* = 2) %	Male (*n* = 1) %	All (*n* = 1) %	Female (*n* = 1) %	Male (*n* = 0) %	All (*n* = 1) %	Female (*n* = 1) %	Male (*n* = 0) %
Education (years completed)									
None	0	0	0	0	0	0	0	0	0
1–4	33.3	50.0	0	0	0	0	0	0	0
5–9	0	0	0	0	0	0	0	0	0
> 10	66.6	50.0	100.0	100.0	100.0	0	100.0	100.0	0
Age (years)									
15–24	0	0	0	0	0	0	0	0	0
25–34	0	0	0	0	0	0	0	0	0
35–44	33.3	50.0	0	100.0	100.0	0	100.0	100.0	0
45–54	66.6	50.0	100.0	0	0	0	0	0	0
55–64	0	0	0	0	0	0	0	0	0

hypertensive individuals and medical follow up after the first survey in 2011.

Nonetheless, the levels of awareness about hypertensive status are still low, a situation common in Africa,[33] with levels much lower than those in North America and Europe.[34] A similar framework exists for diabetes awareness in Africa, with fewer than 50% of participants in one study aware of their condition.[29] No data were found for awareness of total cholesterol levels.

The lack of primary healthcare facilities in this region, especially in rural areas, makes the low levels of previous measurements plausible. Furthermore, the current training of Angolan health professionals and the availability of clinical equipment are still focused on infectious diseases, not considering CVD a priority. Therefore initiatives promoting the awareness of CVD are lacking in the region, and proper monitoring of patients' conditions does not occur.

Moreover, the information available to the population is not enough to convince patients to take lifelong medication in order to treat a condition, which is usually asymptomatic. Only one-third of participants with any of these conditions had access to treatment, which demonstrates the inadequacy of the region's health system to help patients manage risk factors. Economic difficulties and the lack of drugs to address CVD may also help explain the low levels of treatment and control found.

Nevertheless, a positive note should be made as to the number of patients who had controlled levels of blood pressure, blood sugar and cholesterolaemia in this specific population.

Considering that they were younger and better educated, they could have had easier access to drugs and health facilities. Also noteworthy, in the absence of access to drugs, physicians' advice in most cases is to adopt non-pharmacological approaches to reducing modifiable risk factors, mainly associated with diet.

Table 9. Non-pharmacological advice by health professionals to aware participants (Caxito, 2016)

Advice	Hypertension (*n* = 209) % (95% CI)	Diabetes (*n* = 24) % (95% CI)*	Hypercholesterolaemia (*n* = 3) % (95% CI)*
Reduce salt in your diet	78.5 (72.4–83.5)	100.0	100.0
Reduce fat in your diet	61.7 (55.0–68.0)	91.7	66.7
Eat at least five servings of fruit and/or vegetables each day	58.4 (51.6–64.8)	70.8	66.7
Reduce or stop alchool consumption	51.2 (44.5–57.9)	83.3	33.3
Start or do more physical activity	34.4 (28.3–41.1)	75.0	66.7
Quit using tobacco or don't start	31.1 (25.2–37.7)	45.8	0
Maintain a healthy body weight or lose weight	30.1 (24.3-36.7)	75.0	66.7

*Due to the small sample size, the 95% CI was not determined.

Strengths and limitations of the study

Our study findings should be interpreted cautiously because the Dande-HDSS was developed as a district-level surveillance system in an urban and rural setting and is therefore not representative of the demographic structure of the country. In addition, age groups over 65 years old (known for higher rates of the conditions studied) were not considered owing to their low representation in the general structure of the population (3.6% of the Dande-HDSS population),[18] which is a common practice for surveys conducted in sub-Saharan Africa.

Internal migration and the geographical isolation of some hamlets within the Dande-HDSS, together with the fact that working individuals were unavailable during the daytime,[17] were reflected in the sampling definition, with a 30% non-participation rate. The distribution of non-respondents was uneven, with a higher proportion of younger people and men (data not shown). This may have caused instability in the estimates in some strata.

Participants were requested not to eat anything eight hours before participating in the study; however, it was difficult to measure adherence to this request, which adds uncertainty to the measures of blood glucose and cholesterol. We used dry chemistry devices to measure glycaemia and cholesterolaemia, but owing to high temperatures and humidity during field surveys, data collection was not possible in some cases, causing a higher number of missing data than expected.

Due to the many variables covered in the survey and to avoid drop-out of participants in future rounds, additional questions relating to awareness, pharmacological treatments and non-pharmacological

approaches were conducted in a more detailed form in individual follow-up visitations. These are not dealt with extensively in this article. Also the low number of aware individuals and consequently under-treatment limited the statistical analysis of data regarding these aspects.

It is therefore not possible to extrapolate our findings to a larger population at country level. However, this study reveals new data about the prevalence, awareness, treatment and control of diabetes and hypercholesterolaemia, and it is the most comprehensive community-based study conducted to date in Angola.

Future direction

The inclusion of younger participants (15 to 24 years) allows a better representation of the demographic structure of the country and creates a baseline for future surveys. The emphasis for future interventions should be aimed at younger populations in which the prevalence of major risk factors is still low, so as to make a difference in the long term.

In all LMIC, NCDs are the leading cause of death and disability, killing nearly eight million people under 60 years old in 2013.[25] Over the past decade, the focus of assistance in these countries has primarily addressed maternal and child health and infectious diseases. Without setting these aside, there is an opportunity to use structures that are already in place, to maximise resources. The international community should consider expanding the mandate of current programmes to include outcome-orientated measures for improving general health and lifestyles.

Many of the methods of NCD prevention, management and treatment, which are responsible for the decline in some of these diseases in high-income countries, are inexpensive but are not widely used in LMIC. These methods could be implemented through established global health strategies, such as increased use of low-cost drugs,[35] and improved access to NCD services for young adults and people with low educational attainment.[36]

Conclusions

This report reinforces the available data for the main CVD risk factors in Angola and helps to build the basis for further prospective studies, especially among the younger group in this region. We provide the first evidence that hypertension prevalence is rising, together with diabetes, when compared with previous studies in the region.

Despite being a growing economy, Angola's primary health system may not be currently able to provide an adequate answer to the changing health needs of this population. A gradual shift from infectious diseases to NCDs is underway and this puts additional stress on the reinforcement of primary care intervention in the region.

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Assessment of left atrial function in patients with type 2 diabetes mellitus with a disease duration of six months

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Abstract

Introduction: **Changes in left atrial (LA) size and function are associated with adverse clinical events. Recently, duration of diabetes mellitus (DM2) has been found to be positively associated with increased LA volume and impaired LA function. This study was performed, using two-dimensional echocardiograpy, to evaluate the changes in LA volume and function in patients with DM2 with a disease duration of six months, and to assess the parameters that affect LA volume and function.**

Methods: **Fifty-six patients (28 male, age: 52.6 ± 6.5 years) with DM2 and 56 controls (24 male; age: 50.1 ± 7.0 years) were enrolled in the study. Each subject underwent conventional two-dimensional echocardiography to assess LA volume (indexed maximal LA volume: Vmax, pre-atrial contraction volume: Volp, minimal LA volume: Vmin) and LA function [passive emptying volume – passive emptying fraction (PEV – PEF), active emptying volume – active emptying fraction (AEV – AEF), total emptying volume – total emptying fraction (TEV – TEF)].**

Results: **LA diameter, indexed Vmax, Volp, Vmin, AEV and TEV were found to be significantly higher in the DM2 group compared with the controls ($p < 0.05$). Indexed Vmax, Volp and Vmin were significantly correlated with HbA_{1c} level, body mass index (BMI), high-sensitivity C-reactive protein and uric acid levels, mitral A wave, E/E' ratio and A' wave. According to multivariate analysis, age and BMI had a statistically significant effect on LA volume.**

Conclusion: **Impaired LA function may be present in patients with newly diagnosed DM2. BMI and increasing age caused LA enlargement and LA volumes that were independent of the effects of hypertension and DM2.**

Keywords: left atrial volume, left atrial function, diabetes mellitus, transthoracic echocardiography

The prevalence of type 2 diabetes mellitus (DM2) increases over a person's lifetime due to aging, the epidemic of obesity and sedentary lifestyles. Moreover, the incidence of cardiovascular disease (CVD), and morbidity and mortality due to CVD increase in patients with DM2.[1,2]

Early changes in left ventricular (LV) function in patients with DM2 have been extensively investigated, however, assessment of left atrial (LA) function is of growing interest.[2-8] The left atrium serves as a reservoir during ventricular systole, as a conduit during early diastole, and as an active contractile chamber that augments LV filling in late diastole.

Total emptying volume (TEV) describes LA reservoir function, passive emptying volume (PEV) describes LA conduit function, and active emptying volume (AEV) describes LA booster pump function.[7,9] Two-dimentional (2D) echocardiography is a non-invasive, easy-to-use and accessible method to evaluate LA volume and function.

Several studies have shown that changes in LA size and function were associated with adverse clinical events such as atrial fibrillation, stroke, diastolic dysfunction and LV failure.[10-13]

Moreover, studies that evaluated LA volume and function in patients with DM2 showed that LA volume and function were independent predictors of cardiovascular events.[4-8] Recently, the duration of DM2 disease has been found to be strongly and positively associated with larger LA volume and impaired LA function measured by echocardiography.[14]

The aims of our study were to evaluate the change in LA volume and function, and assess the parameters that affect LA volume and function in patients with DM2 with a disease duration of six months, using 2D echocardiograpy.

Methods

Fifty-six patients (28 male, mean age 52.6 ± 6.5 years) with DM2, according to the American Diabetes Association (ADA) 2013 criteria, with a disease duration of a maximum of six months (recruited from the endocrinology and metabolism departments) and 56 age-matched healthy volunteers (24 male, mean age 50.1 ± 7.0 years) (recruited from the cardiology department) were included in the study.[15] A detailed medical history, physical examination and 12-lead electrocardiography were obtained from the study population.

All subjects underwent a treadmill exercise test according to the Bruce protocol, or myocardial perfusion scintigrapyh to rule out latent ischaemia. Patients with evidence of ischaemia, arrhythmia on an electrocardiogram (ECG), LV dysfunction with an ejection fraction (EF) of < 50%, significant valvular disease, history of coronary artery disease, suspicion of secondary hypertension, uncontrolled hypertension, thyroid disorder, pulmonary disease and renal failure (defined as decreased glomerular filtration rate of < 60 ml/min/1.73 m^2 for at least three months), type 1 DM, electrolyte imbalance, and technically insufficient echocardiographic and electrocardiographic data were excluded.

The local ethics committee approved the study. All participants provided written, informed consent prior to participation in the study.

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Transthoracic echocardiographic examinations were performed using a commercially available cardiac ultrasound scanner (Acuson Sequoia 512 system with 2.5–4.0 MHz transducer, Siemens Mountain View, California, USA) in the left lateral position, according to the criteria of the American Society of Echocardiography.[16] During echocardiography a continuous one-lead ECG recording was done.

Left ventricular end-diastolic and end-systolic volumes were determined in the apical view, and stroke volume and EF were measured using the modified Simpson's equation.[16] LV mass (LVM) was calculated with the Devereux formula as:

$$LVM\ (g) = 1.04\ [(LVID + PWT + IVST)^3 - LVID^3] - 14$$

Where LVID = LV internal dimension; PWT = posterior wall thickness; IVST = interventricular septum thickness. LVM was indexed to body surface area (BSA) by dividing LVM by BSA.

Peak early diastolic (E) velocity, atrial contraction (A) velocity and E-wave deceleration time (DT) were measured from the transmitral pulsed-wave Doppler spectra, and the E/A ratio was calculated. Pulsed-wave tissue Doppler imaging (TDI) was performed in an apical four-chamber window with a sample volume of 5 mm and the monitor sweep speed was set at 100 mm/s to optimise the spectral display of myocardial velocities. All Doppler spectral velocities were averaged over three consecutive beats. The average pulsed-wave TDI-derived early (E') diastolic myocardial velocity was obtained from the lateral and septal sides of the mitral annulus. Then the E/E' ratio was calculated to provide an estimation of LV filling pressures.[17]

The TDI-derived late-diastolic wave (A') was obtained from the mitral lateral annulus.

LA diameter was measured from the parasternal long axis with M-mode echocardiography. LA volumes were traced and calculated by means of the modified Simpson's method from apical four- and two-chamber views, according to the guidelines of the American Society of Echocardiography and European Association of Cardiovascular Imaging.[16] LA volumes were measured as: (1) just before the mitral valve opening, at end-systole (maximal LA volume or V_{max}); (2) at the onset of the P wave on electrocardiography (pre-atrial contraction volume or Volp); and (3) at mitral valve closure, at end-diastole (minimal LA volume or Vmin). From these, the following measurements were calculated:

- LA passive emptying volume (PEV) = $V_{max} - V_{olp}$
- LA passive emptying fraction (PEF) = PEV/V_{max} x 100
- LA active emptying volume (AEV) = $V_{olp} - V_{min}$
- LA active emptying fraction (AEF) = AEV/V_{olp} x 100
- LA total emptying volume (TEV) = $V_{max} - V_{min}$
- LA total emptying fraction (TEF) = TEV/V_{max} x 100

Left atrial volumes were indexed to BSA in all patients.[18]

Statistical analysis

Statistical analyses were performed with the MedCalc Statistical Software version 12.7.7 (MedCal Software bvbv, Ostend, Belgium; 2013). All continuous variables are expressed as mean ± standard deviation and median (minimum–maximum). All categorical variables are defined as frequency and percentage. All continuous variables were checked with the Kolmogorov– Smirnov normality test to show their distributions. Continuous variables with normal distributions were compared using the unpaired Student's *t*-test, while continuous variables with abnormal distributions were compared using the Mann–Whitney *U*-test. For categorical variables, the chi-squared test was used.

Pearson or Spearman's correlation analyses were used to determine the associations between LA volume and function, and various laboratory parameters and 2D echocardiographic diastolic parameters. Multivariate evaluations were performed using linear regression analysis. The confounders that were found to have a statistically significant impact on the dependent variable on univariate analysis were described as the independent variables in a multivariate linear regression analysis model. The p-values less than 0.05 were considered significant.

Sample size justification: according to the article 'Effects of diabetes mellitus on left atrial volume and functions in normotensive patients without symptomatic cardiovascular disease',8 the V value for DM2 patients was 40.9 ± 11.9 ml, and for the control group, 34.6 ± 9.3 ml. The mean difference was assumed as 6.3 ml; the standard deviation of the DM2 group was 11.9 ml and of the control group, 9.3 ml. With the assumption of 5% of type 1 error (a) and 80% power (1b), the sample size was calculated at 46 patients for each group. With a 20% drop-out rate, a minimum of 56 patients (112 in total) would have to be enrolled in the study.

Results

The study population consisted of 112 subjects (52 male, mean age 51.7 ± 7.0 years). Patient characteristics, analysed according to the two groups, are shown in Table 1. The groups were similar regarding age and gender. In the DM2 group, 44 (78.6%) patients were hypertensive and 33 (58.9%) were receiving insulin and oral antidiabetic agents. Patients in the DM2 group were also taking more medications, such as acetylsalicylic acid, angiotensin converting enzyme inhibitors, beta-blockers and statins than the control group.

Body mass index (BMI) and levels of triglycerides (TG), high-sensitivity C-reactive protein (hsCRP), uric acid, fasting glucose and HbA_{1c} were significantly higher in the DM2 group compared with the control group ($p < 0.05$). There were no significant differences regarding total cholesterol and low- (LDL) and high-density lipoprotein (HDL) cholesterol levels between the groups ($p > 0.05$) (Table 1).

Table 2 reports the results of 2D echocardiographic parameters reflecting diastolic function with preserved systolic function. Twelve (21.4%) subjects in the control group and 29 (51.8%) patients in the DM2 group had some degree of diastolic dysfunction. Mitral A wave, E/E' ratio and mitral A' wave were significantly higher, and mitral E' wave was significantly lower in the DM2 group compared with the controls ($p < 0.05$).

There were no significant differences between the groups regarding EF, mitral E wave and E/A ratio ($p > 0.05$). LA diameter, and indexed Vmax, Volp, Vmin, AEV and TEV were found to be significantly higher in the DM2 group compared with the controls ($p < 0.05$). PEF was significantly lower in the DM2 group compared with the controls ($p < 0.05$). Between the two groups, there were no significant differences in indexed PEV, AEF and TEF ($p > 0.05$) (Table 3).

Patients in the DM2 group were divided according to presence of diastolic dysfunction. There were no significant differences within the DM2 group regarding LA volume and function ($p > 0.05$) (Table 4).

Table 1. Demographic characteristics and laboratory parameters of the groups

Characteristics	Control group (*n* = 56)	DM2 group (*n* = 56)	*p*-value
Age, years	50.1 ± 7.0	52.6 ± 6.5	0.06
Male, *n* (%)	24 (42.9)	28 (50)	0.55
BMI (kg/m²)	22.5 ± 2.0	28.0 ± 4.9	< 0.001
Tobacco use, *n* (%)	9 (16.1)	8 (14.3)	1.00
Hypertension, *n* (%)	6 (10.7)	44 (78.6)	< 0.001
Hyperlipidaemia, *n* (%)	11 (19.6)	47 (83.9)	< 0.001
Medication, *n* (%)			
ACE inhibitors	5 (8.9)	40 (71.4)	
Beta-blockers	1 (1.8)	16 (28.6)	
Statins	5 (8.9)	36 (64.3)	
ASA	37 (66.1)	3 (5.4)	
Insulin and OAD		33 (58.9)	
Fasting glucose (mg/dl) (mmol/l)	93.9 ± 6.4 (5.21 ± 0.36)	153.0 ± 67.0 (8.49 ± 3.72)	< 0.001
HbA_{1c} (%)	4.8 ± 0.6	8.1 ± 1.9	< 0.001
Total cholesterol (mg/dl) (mmol/l)	211.4 ± 39.7 (5.48 ± 1.03)	225.3 ± 50.6 (5.84 ± 1.31)	0.11
HDL-C (mg/dl) (mmol/l)	48.2 ± 12.5 (1.25 ± 0.32)	45.4 ± 8.5 (1.18 ± 0.22)	0.16
LDL-C (mg/dl) (mmol/l)	132.9 ± 38.2 (3.44 ± 0.99)	140.1 ± 40.7 (3.63 ± 1.05)	0.34
TG (mg/dl) (mmol/l)	141.0 ± 84.7 (1.59 ± 0.96)	190.4 ± 105.0 (2.15 ± 1.19)	0.01
hsCRP (mg/l)	1.9 ± 1.2	5.3 ± 2.9	< 0.001
Uric acid (mg/dl)	4.6 ± 1.0	6.2 ± 1.6	< 0.001

DM: diabetes mellitus, BMI: body mass index, ACE: angiotensin converting enzyme, ASA: acetylsalisilic asid, OAD: oral antidiabetics, HbA_{1c}: glycosylated haemoglobin, HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, TG: triglycerides, hsCRP: high-sensitivity C-reactive protein.

To determine the influential factors for LA volume, we examined the potential variables that we thought to be echocardiographically and clinically relevant: mitral A wave, E' wave, A' wave, E/E' ratio, BMI, and fasting glucose, HbA_{1c}, hsCRP and uric acid levels. There were weak positive correlations between all indexed LA volumetric parameters and all the variables except for indexed PEV and BMI, fasting glucose, HbA_{1c}, hsCRP and uric acid levels, mitral A wave, E/E' ratio and mitral A' wave. There was a weak negative correlation between all indexed LA volumetric parameters and all the variables except indexed PEV and mitral E' wave (Table 5).

Univariate analysis showed that DM2, hypertension, age, BMI, and hsCRP and uric acid levels had a statistically significant impact on LA diameter, and indexed Vmax, Volp, Vmin, AEV and TEV. According to multivariate analysis when adjusted with other confounders, hypertension, age and BMI had a statistically significant effect on LA diameter; age and BMI had a statistically significant effect on indexed Vmax; age, BMI and uric acid level had a statistically significant effect on indexed Volp; uric acid level had a statistically significant effect on indexed Vmin; age had a statistically significant effect on indexed AEV; and age and BMI had a statistically significant effect on indexed TEV (Table 6).

Table 2. Echocardiographic parameters of the study groups

Parameters	Control group (*n* = 56)	DM2 group (*n* = 56)	*p*-value
EF (%)	61.9 ± 5.0	60.6 ± 4.4	0.14
Left ventricular mass (g/m²)	93.2 ± 8.4	102.3 ± 8.0	< 0.001
Mitral E (cm/s)	79.1 ± 14.1	81.2 ± 16.7	0.47
Mitral A (cm/s)	66.4 ± 13.2	80.8 ± 18.8	< 0.001
E/A ratio (cm/s)	1.2 ± 0.3	1.2 ± 0.9	0.68
Deceleration time (s)	199.0 ± 17.9	222.8 ± 19.7	< 0.001
Mitral E' (cm/s)	18.5 ± 4.3	15.3 ± 3.3	< 0.001
Mitral A' (cm/s)	14.0 ± 3.2	16.1 ± 5.0	0.011
E/E' ratio (cm/s)	4.4 ± 1.0	5.5 ± 1.7	< 0.001
Diastolic dysfunction, *n* (%)	12 (21.4)	29 (51.8)	0.002

DM: diabetes mellitus; EF: ejection fraction.

Table 3. The echocardiographic parameters for the LA function of the study groups

Parameter	Hypertensives (*n* = 140)	Controls (*n* = 70)	*p*-value
Mean sodium (mmol/l)	135.9 ± 4.7	133.7 ± 2.4	> 0.05
Mean potassium (mmol/l)	3.8 ± 0.5	3.1 ± 0.4	< 0.05*
Mean urea (mmol/l)	5.8 ± 2.2	3.2 ± 1.7	> 0.05
Mean creatinine (µmol/l)	84.2 ± 12.6	68.4 ± 10.8	> 0.05
Mean FBS (mmol/l)	5.6 ± 1.9	4.0 ± 1.3	< 0.005*
Mean LDL-C (mmol/l)	2.49 ± 1.41	2.35 ± 0.63	> 0.05
Mean HDL-C (mmol/l)	1.06 ± 0.36	1.29 ± 0.46	< 0.05*
Mean TG (mmol/l)	1.33 ± 0.59	1.18 ± 0.41	> 0.05
Mean TC (mmol/l)	4.84 ± 1.69	4.23 ± 1.29	> 0.05

DM: diabetes mellitus, LA: left atrium, PEV: passive emptying volume, AEV: active emptying volume, TEV: total emptying volume.

Discussion

Diabetes mellitus can lead to changes in LA volume and function. In most studies, LA function is determined by performing real-time three-dimensional (3D) echocardiography, cardiac magnetic resonance imaging (CMRI), and strain and strain rate tests. However, in general practice, LA function can be easily and non-invasively determined by performing 2D echocardiography. In our study, we showed that even if LA size and volume were within normal limits, LA dysfunction may be present in patients with DM2 who was diagnosed in the preceding six months, and this finding was mainly due to BMI and age.

Table 4. Comparison of echocardiographic parameters regarding diastolic dysfunction for the LA function in the DM2 group

Parameters	Diastolic dysfunction (+) (*n* = 29)	Diastolic dysfunction (–) (*n* = 27)	*p*-value
LA diameter (mm)	37.4 ± 5.1	36.5 ± 5.8	0.548
Indexed V_{max} (ml/m²)	25.8 ± 6.9	23.5 ± 6.2	0.196
Indexed V_{olp} (ml/m²)	18.1 ± 5.8	16.1 ± 4.7	0.168
Indexed V_{min} (ml/m²)	10.8 ± 4.6	9.2 ± 3.7	0.168
Indexed PEV (ml/m²)	7.6 ± 3.2	7.3 ± 3.4	0.735
Indexed AEV (ml/m²)	7.3 ± 2.8	6.8 ± 2.6	0.555
Indexed TEV (ml/m²)	14.9 ± 4.1	14.2 ± 4.0	0.505
LA passive emptying fraction (%)	29.5 ± 10.9	30.5 ± 11.5	0.751
LA active emptying fraction (%)	41.1 ± 11.1	43.0 ± 12.7	0.541
LA total emptying fraction (%)	58.7 ± 9.8	60.9 ± 9.4	0.402

DM: diabetes mellitus, LA: left atrium, PEV: passive emptying volume, AEV: active emptying volume, TEV: total emptying volume.

Table 5. Correlation analysis of LA volume and function with 2D echocardiographic parameters and laboratory findings

		Indexed V_{max} (ml/m²)	Indexed V_{olp} (ml/m²)	Indexed V_{min} (ml/m²)	Indexed PEV (ml/m²)	Indexed AEV (ml/m²)	Indexed TEV (ml/m²)
Glucose (mg/dl)	*r*	0.153	0.252	0.182	–0.034	0.204	0.075
	P	0.108	0.007	0.055	0.725	0.031	0.429
HbA_{1c} (%)	*r*	0.288	0.367	0.294	0.006	0.301	0.192
	P	0.002	< 0.001	0.002	0.954	0.001	0.043
BMI (kg/m²)	*r*	0.430	0.441	0.368	0.135	0.340	0.325
	P	< 0.001	< 0.001	< 0.001	0.154	< 0.001	< 0.001
TG (mg/dl)	*r*	0.152	0.248	0.136	–0.047	0.239	0.089
	p	0.110	0.008	0.153	0.625	0.011	0.350
hsCRP (mg/l)	*r*	0.412	0.420	0.320	0.103	0.371	0.308
	p	< 0.001	< 0.001	0.001	0.281	< 0.001	0.001
Uric acid (mg/dl)	*r*	0.362	0.378	0.297	0.125	0.283	0.253
	p	< 0.001	< 0.001	0.001	0.190	0.002	0.007
Mitral A (cm/s)	*r*	0.328	0.380	0.292	–0.002	0.321	0.232
	p	< 0.001	< 0.001	0.002	0.981	0.001	0.014
Mitral E' (cm/s)	*r*	–0.274	–0.258	–0.211	–0.094	–0.202	–0.226
	p	0.003	0.006	0.026	0.323	0.033	0.017
Mitral A' (cm/s)	*r*	0.278	0.281	0.310	0.064	0.117	0.138
	p	0.003	0.003	0.001	0.504	0.220	0.147
E/E' ratio (cm/s)	*r*	0.279	0.286	0.255	0.059	0.197	0.192
	p	0.003	0.002	0.007	0.539	0.037	0.028
E/A ratio (cm/s)	*r*	0.085	0.129	0.288	–0.050	–0.135	–0.140
	p	0.374	0.177	0.002	0.604	0.154	0.142
	p	0.003	0.006	0.026	0.323	0.033	0.017
Mitral A' (cm/s)	*r*	0.278	0.281	0.310	0.064	0.117	0.138
	p	0.003	0.003	0.001	0.504	0.220	0.147
E/E' ratio (cm/s)	*r*	0.279	0.286	0.255	0.059	0.197	0.192
	p	0.003	0.002	0.007	0.539	0.037	0.028
E/A ratio (cm/s)	*r*	0.085	0.129	0.288	–0.050	–0.135	–0.140
	p	0.374	0.177	0.002	0.604	0.154	0.142

LA: left atrium, BMI: body mass index, TG: triglycerides, hsCRP: high-sensitivity C-reactive protein, PEV: passive emptying volume, AEV: active emptying volume, TEV: total emptying volume.

Recent studies have shown that LA enlargement, obtained from 2D echocardiography, is a good predictor of cardiovascular outcomes.[7] However, there are several limitations to estimating LA size because of the irregular geometry of the left atrium. Additionally, the left atrium often enlarges asymmetrically, which causes underestimation of its size. Therefore, it has been suggested that LA volume may be a superior measure of LA size.[7] Moreover, changes in LA volume are increasingly becoming a parameter of interest as a marker of overall cardiac function.

Several studies have shown that changes in LA size and mechanical function may be associated with adverse clinical events such as atrial fibrillation, stroke, diastolic dysfunction and LV failure, both in the general and the diabetic population.[6,8,10-14,19,20]

Moreover, it has been reported that indexed V ≥ 32 ml/m² predicts cardiovascular mortality and morbidity independently of myocardial perfusion sintigraphy-detected myocardial ischaemia with a six-year follow-up period.[21]

Cardiovascular imaging modalities for the determination of LA function, such as computed tomography (CT), CMRI, 2D and 3D echocardiography, are evolving. Although the main advantage of CMRI and CT over echocardiography is the determination of all parts of the left atrium, including the LA appendage, the use of iodine and radiation during CT and the usefulness of CMRI in patients with pacemakers limit their usage.[7] Therefore, we preferred to use 2D echocardiography, which is a non-invasive, easy-to-use and accessible method to evaluate LA volume and function. Moreover, similar to our findings, the mean indexed V value was 23.6 ± 5.8 ml/m² in max a newly diagnosed diabetes group in the study population of Zoppini.[14]

The incidence of diastolic dysfunction in patients with DM2 is reported to be 43 to 75%.[4] Recent evidence suggests that LA dilatation and dysfunction may be a co-existing marker of diastolic dysfunction in patients with DM2.[4] However, Kadappu *et al.* demonstrated LA dilatation may be present in patients with DM2 independent of diastolic dysfunction and associated hypertension.[4] Recently, another study by Zoppini *et al*. reported that diabetes itself might cause LA enlargement.[14] These findings suggest that co-existing diabetic atrial cardiomyopathy may independently alter the LA size and function.[4,14]

In our study, 51.8% of the diabetic patients had some degree of diastolic dysfunction with no difference regarding LA volume and function, compared with the diabetic patients without diastolic dysfunction. This finding and a weak correlation between 2D echocardiographic diastolic parameters and LA volume in our

Table 6. Univariate and multivariate analysis for predictors of LA volume and function of the study population

	Univariate analysis							Multivariate analysis						
Parameters	**DM2**	**HT**	**HL**	**Age**	**BMI**	**hsCRP**	**Uric acid**	**DM**	**HT**	**HL**	**Age**	**BMI**	**hsCRP**	**Uric acid**
LA diameter (mm)	< 0.001	< 0.001	0.0281	< 0.001	< 0.001	0.003	0.001	0.227	0.001	0.005	0.002	< 0.001	0.879	0.194
Indexed V_{max} (ml/m²)	< 0.001	< 0.001	0.003	< 0.001	< 0.001	< 0.001	< 0.001	0.438	0.056	0.100	0.001	0.004	0.191	0.064
Indexed V_{olp} (ml/m²)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	0.991	0.181	0.244	0.003	0.016	0.226	0.042
Indexed V_{min} (ml/m²)	< 0.001	< 0.001	0.007	< 0.001	< 0.001	0.001	0.001	0.869	0.171	0.334	0.069	0.099	0.371	0.034
Indexed PEV (ml/m²)	0.66	0.268	0.971	0.171	0.164	0.281	0.190	–	–	–	–	–	–	–
Indexed AEV (ml/m²)	< 0.001	< 0.001	0.001	0.001	< 0.001	< 0.001	0.002	0.822	0.623	0.476	0.010	0.064	0.383	0.486
Indexed TEV (ml/m²)	0.004	0.001	0.051	< 0.001	< 0.001	0.001	0.007	0.189	0.259	–	0.003	0.020	0.443	0.418
LA passive emptying fraction (%)	0.003	0.052	0.011	0.169	0.044	0.065	0.338	0.150	–	0.438	–	0.897	–	–
LA active emptying fraction (%)	0.386	0.769	0.499	0.393	0.718	0.430	0.968	–	–	–	–	–	–	–
LA total emptying fraction (%)	0.05	0.117	0.162	0.293	0.148	0.395	0.363	–	–	–	–	–	–	–

DM: diabetes mellitus, HT: hypertension, HL: hyperlipidaemia, BMI: body mass index, hsCRP: high-sensitivity C-reactive protein, LA: left atrium, PEV: passive emptying volume, AEV: active emptying volume, TEV: total emptying volume.

study may have been due to the duration of DM2, normal LV filling pressures determined by E/E' ratio, and normal LV mass.

We demonstrated that increasing age and BMI had a significant effect on LA volume. The main difference of our study from previous ones was the duration of DM2, which was strongy and positively associated with larger LA diameter and impaired LA function. CARDIA investigators showed a 20-year follow-up period of diabetes was associated with indexed LA diameters.[19] On the other hand, Zoppini *et al*. showed a possible 65% LA enlargement (defined as indexed Vmax ≥ 34 ml/m) for each 10 years' duration of diabetes.[14] On the basis of these findings, we speculate that although diabetes was an independent predictor of LA volume in univariate analysis, in multivariate analysis, age and BMI were the independent predictors of LA volume in the early stages of diabetes.

LA function is evaluated and indexed to BSA by calculating PEV, AEV, TEV and PEF, AEF and TEF from Vmax, Vmin and Volp. TEV describes the reservoir, PEV describes the conduit, and AEV describes the pump function of the left atrium. Contrary to current knowledge, Vmin increases, even in mild LV diastolic dysfunction, whereas Vmax increases in the later stages, suggesting that Vmin may be a more sensitive marker of LV diastolic dysfunction. Moreover, this finding underlines the importance of evaluation of LA function.[22]

Based on current knowledge, LA reservoir function is associated with worsening LV diastolic function.[7] Graca *et al*. showed that LA reservoir and conduit function were reduced in asymptomatic DM2 patients.[23] The same study also demonstrated that DM2 was independently associated with LA reservoir function, but not with conduit function.[23]

Mondillo *et al*. investigated only diabetic patients with norma LA size and did not find any difference in conduit and pump function. However, they showed LA deformation was impaired in diabetics even if LA volumes were similar between the groups.[24] Murakana *et al*. showed decreased LA reservoir and conduit functions in patients with DM2 even in the absence of LA dilatation.[5] Huang *et al*. demonstrated, with 2D echocardiographic evaluation, increased reservoir and pump function and reduced conduit function in patients with DM2.[6]

Recently, Atas *et al*. reported depressed reservoir and pump function with similar conduit function in patients with DM2 compared to the control group.[8]

In our study, in accordance with the study of Huang *et al*., we found reduced conduit, and increased pump and reservoir function in diabetic patients compared with the controls. The possibly inconsistent results with previous studies may have been due to different cardiovascular imaging techiques used for the determination of LA function, small sample sizes, different baseline characteristics, and different diabetes durations of the study populations.

There are some limitations to our study. As this was a cross-sectional study, follow up of the patients for clinical endpoints such as AF and heart failure could not be done. Therefore, our study results cannot be used to direct standard clinical care. Moreover, as the population size was relatively small, our study does not permit any causal inferences and analysis on the effect of medications on LA volume and function. For this reason, long-term follow up and large-scale prospective studies are needed to determine the clinical predictive value of early LA functional impairment in this population. Evaluation of LA volume and function with 2D echocardiography was an additional limitation of our study.

Conclusion

The results of our study showed impaired LA function may be present in patients with DM2 with a disease duration of a maximum of six months. BMI and increased age caused LA enlargement and LA volumes that were independent of the effects of hypertension and DM2. Further studies with larger sample sizes are needed to better define the underlying mechanisms.

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Daily fasting helps control weight and lower blood pressure

Daily fasting is an effective tool to reduce weight and lower blood pressure, according to a study published by University of Illinois at Chicago researchers. The study is the first to examine the effect of time-restricted eating – a form of fasting that limits food consumption to select hours each day – on weight loss in obese individuals.

To study the effect of this type of diet, researchers worked with 23 obese volunteers who had an average age of 45 years and average body mass index, or BMI, of 35 kg/m^2. Between the hours of 10 am and 6 pm the dieters could eat any type and quantity of food they desired, but for the remaining 16 hours they could only drink water or calorie-free beverages. The study followed the participants for 12 weeks.

When compared to a matched historical control group from a previous weight loss trial on a different type of fasting, the researchers found that those who followed the time-restricted eating diet consumed fewer calories, lost weight and had improvements in blood pressure. On average, participants consumed about 350 fewer calories, lost about 3% of their body weight and saw their systolic blood pressure decreased by about 7 mmHg. All other measures, including fat mass, insulin resistance and cholesterol, were similar to the control group.

'The take-home message from this study is that there are options for weight loss that do not include calorie counting or eliminating certain foods,' said Krista Varady, associate professor of kinesiology and nutrition in the UIC College of Applied Health Sciences and corresponding author on the study.

While this is the first study to look at the 16:8 diet, named for its 16 hours of fasting and its 8 hours of 'feasting,' Varady says that the results align with previous research on other types of intermittent fasting diets.

'The results we saw in this study are similar to the results we've seen in other studies on alternate day fasting, another type of diet,' Varady said, 'but one of the benefits of the 16:8 diet may be that it is easier for people to maintain. We observed that fewer participants dropped out of this study when compared to studies on other fasting diets.'

Varady says that while the research indicates daily fasting works for weight loss, there have not yet been studies to determine if it works better than other diets, although the researchers observed the weight loss to be slightly less than what has been observed in other intermittent fasting diet studies.

'These preliminary data offer promise for the use of time-restricted feeding as a weight loss technique in obese adults, but longer-term, large-scale randomized controlled trials (are required),' Varady and her colleagues write.

'The 16:8 diet is another tool for weight loss that we now have preliminary scientific evidence to support,' Varady said. 'When it comes to weight loss, people need to find what works for them because even small amounts of success can lead to improvements in metabolic health.'

The Centres for Disease Control and Prevention estimates that more than one-third of adults in the USA have obesity, which greatly increases the risk of metabolic diseases such as coronary heart disease and type 2 diabetes, and that obesity is most prevalent among non-Hispanic black individuals and middle-aged adults.

Cerebrovascular disease in Sudan: a huge gap to be bridged

MUWADA BASHIR AWAD BASHIR, SAMUEL NAMBILE CUMBER

Abstract

Organised national structural and research efforts are crucial to minimising the high morbidity and mortality burdens attributed to cerebrovascular disease in Sudan. The dearth of quality research evidence to guide decision making in neurological services, and the lack of political will and resources have accounted for the uncertainty regarding this major health problem in Sudan. This article reviews the research efforts on cerebrovascular diseases in Sudan from an epidemiological and health-service point of view, highlighting areas of information deficiency and recommending health-system and research-based interventions to improve cerebrovascular disease status in Sudan.

Keywords: cerebrovascular diseases, Sudan

Introduction

Cerebrovascular disease is defined by the World Health Organisation as 'rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin'.[1] Cerebrovascular diseases have contributed to 5.5 million deaths globally in 2000, two-thirds of which were recorded in low- and middle-income countries, and 40% of the subjects were less than 70 years of age.[1] Results from recent studies in Africa indicate the increasing burden from various types of cerebrovascular disease and their risk factors.[2]

Sudan is an African country with a population of 37 million inhabitants. The majority of this population lives in the rural areas, with only one-third living in urban areas. Sudan has a young population, 29.1% of subjects are 30 to 70 years of age, of whom 16.4% are estimated to be younger than five years old and 42% under 15 years. In Sudan, life expectancy at birth is 64.1 years and its age-standardised mortality rate for non-communicable diseases per 100 000 population is 551.[3] Such figures reflect the low health standards experienced in all parts of Sudan, which are expected to be worse in the poor and remote regions.

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This article aims at providing a glimpse at the current situation of cerebrovascular diseases in Sudan, based on relevant retrieved and reviewed data from studies and reports, highlighting areas of information deficiency and recommending health-system, service and research actions for improving the health status and outcomes of cerebrovascular diseases in Sudan.

Economic and social burden

Sudan is a low-income country with limited facilities and services devoted to neurological healthcare. Cerebrovascular diseases, with their consequent physical dependency and disability outcomes, inflict high social and economic costs on people in Sudan.[4]

A treatment requiring surgical intervention can be very expensive, costing $1 000–2 000 on average. In the capital city, Khartoum, where most secondary and tertiary services are located, admission costs for intensive medical care range from $50 to $450 per day, including private and public care options. Rehabilitative care is mainly provided by privately operated bodies who do not offer free services. Besides, the facilities are limited and difficult to access by those in the rural areas due to geographical challenges and political instability in Sudan.[5]

Disabilities caused by cerebrovascular diseases cause a serious psychosocial burden in patients and their families. In Sudan, families are large and all members shoulder the responsibilities when any member of the family is ill. If the father, who is the income earner, is ill, the family is more affected than if the mother is indisposed. Medical handicaps in the bread winner may have catastrophic consequences on the economic status of the family, not to mention the time and energy needed from other family members to care for the patient.[6]

Epidemiology

Stroke is the main cause of cardiovascular disability-adjusted life years (DALYs) in sub-Saharan Africa, with figures increasing from 5 930 040 (39.5%) in 1990 to 7 824 920 (52.0%) in 2010.[2] In Sudan, cerebrovascular diseases contribute to one-third (31%) of the medical admissions of elderly adults, with a DALY of 1 143.2 for ischaemic stroke.[4,7] Most of the studies aimed at identifying risk factors among stroke patients report mortality rates that are higher than in Western and wealthier countries.[4] Males are more affected than females,[4,7] and the peak frequency of stroke is 45.8% in the age group from 61 to 80 years and above.[4]

Despite the absence of statistics and studies on the prevalence of cerebrovascular accidents (CVAs) in young Sudanese adult patients, a systematic review on stroke in Arab countries, including Sudan, revealed that six to 20% of patients with stroke are young.[8] Another study from Sudan's western state, Darfur, reported 8% of stroke cases among study subjects, including young patients, were not fully investigated and diagnosed.[6]

Considering the different types of CVAs, ischaemic stroke is

more prevalent than haemorrhagic stroke, as stated by two studies; 66.4% for ischaemic stroke and 33.6% for haemorrhagic stroke,[7] with the highest mortality rates (57%) occurring in the haemorrhagic stroke type.[4,8] There is a significant absence of any reference to sub-arachnoid haemorrhage in the information that has been reported in the Sudanese studies on CVAs.[4,8]

Risk factors of cerebrovascular diseases in Sudan

Hypertension is the most frequently cited risk factor, with a prevalence of 61%, and found in 46% of the cases in two different studies.[8] Interestingly, 26% of the stroke patients in one study were newly diagnosed cases of hypertension, detected after the occurrence of stroke.[4,7] Other reported risk factors were heart diseases in 16% of the cases, diabetes mellitus in 14%, syphilis in 4.2% and previous transient ischaemic attacks in 2.1%.[4,8] Smoking and hypercholesterolaemia were also reported as risk factors, but without specific figures.

Females are more affected than males when it comes to this type (thrombotic type) of stroke and the most prevalent risk factor is the use of combined oral contraceptive pills. Haematological profiles of the study subjects were indicative of natural anticoagulant (protein C, protein S and antithrombin III) levels at the lower range of normal in all patients ($p = 0.04$), but significantly lower in those of the age- ($p = 0.04$) and gender-matched controls ($p = 0.02$).[9]

Neurological services and cerebrovascular diseases in Sudan

Modern medicine was introduced to Sudan in the early nineteen-hundreds by the British government, which colonised Sudan from 1898 until 1956. Since then, health services and systems in Sudan have been quantitatively and qualitatively evolving, but not as fast as required. Proof of this is the high mortality and morbidity rates in the country and the poor development of certain components of the health system, including neurological services.[10]

Despite the high numbers of hypertension cases reported, very little research in the literature has addressed the situation of neurological services in Sudan and none has approached it with regard to the problem of healthcare for cerebrovascular disease in Sudan. There are no recent and accurate published figures on the actual size of the services devoted to the problem.[11]

A recent study estimated the number of neurologists per million populating to be 0.530, which means 18 neurologists for the whole Sudanese population.[11] Also, the ratio of neurologists in academic institutions to neurologists in training is 3:21.[11] The national centre for specialised neurological care in Sudan is located in Khartoum, and it has to meet the needs of the entire population.[5,10] However, it lacks key equipment and facilities that are crucial for the adequate provision of services, for example, intensive care needs, with serious deficiencies in the number of beds in intensive care and ventilation support for patients.[5] The centre provides both neuromedical and neurosurgical services but no neurophysiology or neuro-rehabilitation activities.[5,10]

Neuro-imaging techniques, such as computed tomography (CT) scanning and magnetic resonance imaging (MRI) are the key diagnostic measures for CVA. However, the centres are located in the capital city only, and are mainly operated by the private sector, which reflects a deficiency in the services devoted to such needs.[10] This increases the difficulty of service utilisation by the patients due to financial, geographical or social barriers. There is also a complete lack of diagnostic modalities, even in the national governmental centre for neurology in Khartoum.[5]

Interventional radiological procedures for CVA are carried out in only one centre, Khartoum.[5,10] However, such procedures are rarely done as they are too expensive for the majority of the population, with an estimated average cost of $5 000 per procedure.[5,6] Such an intensive medical care centre was expensive to set up, however, and employment of the required number of specialists is also costly.[6]

Neuro-rehabilitation is neglected in Sudan, with no governmental bodies assigned to providing such services for needy patients. The few available centres offering such services are privately operated with high average costs, and the working personnel are limited to trained nurses and physiotherapists.[5,10]

Recommendations

- National, systematic and wide-based epidemiological research on the incidence of, and morbidity and mortality caused by CVA is desperately needed to guide decision making and service improvement.
- Research on clinical profiling, presentation and outcomes of cerebrovascular diseases are of great importance in instituting the neglected aspects of neurological services in Sudan, such as neuro-rehabilitation, neuropsychology and neurophysiology.
- Primary care neurological services in Sudan need to be identified, established and organised, with appropriate clinical identification and interventional protocols for CVA, and guidelines directed through national programmes that cover both rural and urban areas. There is also a need for systematic research efforts.
- Neurological service centres for CVAs in Sudan need to be adjusted to population needs and characteristics, quantitatively by increasing the number of services and imaging facilities both in urban and rural cities, and qualitatively through free or affordable and accessible provision of crucial diagnostic and treatment measures.
- Statistics are deficient for the utilisation of health services, as well as on the quality of services and patient satisfaction with regard to cerebrovascular diseases in Sudan. This needs to be improved by broad research action.

Conclusion

Cerebrovascular diseases account for the majority of the morbidity and disability experienced in Sudan, with hypertension being the number one risk factor. Insufficient research action has resulted in lack of knowledge about the epidemiological, clinical and socio-demographic characteristics of cerebrovascular diseases.

The absence of nationally organised, wide-based, quantitative research using valid and reliable indicators for measuring disability, morbidity and mortality burdens caused by cerebrovascular diseases, as well as the lack of qualitative research has left a gap in the knowledge on the state of affairs regarding cerebrovascular disease in Sudan. This explains the deficit in neurological services for cerebrovascular diseases, which are not able to meet the needs of the population in terms of quality or quantity of neurological health services. The lack of political will and dedication of resources, as well as the socio-cultural characteristics of the Sudanese population have exacerbated the problem.

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Benefits from at least two servings of cow's milk a day

Obese children who consume at least two servings of any type of cow's milk daily are more likely to have lower fasting insulin, indicating better blood sugar control, according to researchers at The University of Texas Health Science Center at Houston (UTHealth). The findings of the study, presented at the European Congress on Obesity in Vienna, reiterate the importance of milk in the child's diet despite its declining consumption.

'Our findings indicate that obese children who consume at least the daily recommended amount of milk may have more favourable sugar handling and this could help guard against metabolic syndrome,' said Dr Michael Yafi, the study's first author and professor of paediatrics at McGovern Medical School at UTHealth. 'Worryingly, only one in 10 young people in our study were consuming the recommended amount of milk.'

Milk consumption in the US has consistently fallen over the past few decades, according to the US Department of Agriculture, especially among adolescents where it has dropped by nearly half – to less than a cup daily – between 1977 and 2006. 'Parents have started to look at milk not as a good thing and they are wary of it. The message to them is not to be scared of milk, or to limit its consumption, and to encourage children of all ages to keep drinking it freely,' said Dr Mona Eissa, the study's principal investigator and professor of paediatrics and adolescent medicine at McGovern Medical School at UTHealth.

The metabolic syndrome is defined as the presence of at least three of five conditions that increase the risk of diabetes, heart disease, and stroke – high levels of blood sugar or triglycerides, high blood pressure, excess belly fat, and low 'good' cholesterol levels. A third of American children and teens are overweight or obese, which is closely linked to the development of metabolic syndrome.

Previous studies have shown that milk protects against the metabolic syndrome and diabetes in adults, but this is the first to explore these factors among obese children. 'The findings that milk has a healthy effect on high insulin level, which may lead to type 2 diabetes, are significant, particularly given the growing prevalence of this condition among children nowadays,' said Eissa, corresponding author.

The investigators assessed daily milk intake and its association with fasting levels of insulin – the hormone that stabilises blood sugar and a biomarker for metabolic syndrome risk – in obese children and adolescents attending a paediatric weight management clinic. They carried out a retrospective chart review of 353 obese children and adolescents over a two-year period (between December 2008 and December 2010). Information on fasting serum insulin was available for nearly half of the participants at their first visit. The research team also recorded information on daily milk intake, milk types, daily fruit juice and other sugary drinks intake, fasting blood glucose and insulin sensitivity.

More than half of the participants, all between the ages of three and 18, were male; three-quarters were Hispanics; and the average age was 11.3 years. On average, only 23 of 171 children reported drinking the daily recommended intake of two to three cups. Girls reported drinking less milk than boys, but no difference in intake was noted by ethnicity.

The study also found that under half (44%) of children who reported drinking less than one cup a day had below the upper normal levels of fasting insulin, compared to almost three-quarters (72%) of children who reported drinking more than two cups a day. Overall, children who drank less than one cup of milk each day had significantly higher levels of fasting insulin than those who drank at least two cups a day.

After adjusting for other aspects that might affect insulin levels, including race, ethnicity, gender, level of physical activity, sugary drinks intake, glucose levels and type of milk based on fat content, the researchers found lower fasting insulin levels among children who drank at least two cups of milk a day. No association was noted between milk intake and blood glucose or lipid levels.

'The link between sugary drinks and childhood obesity is well documented. Vitamin D deficiency has also been connected to this. By contrast, from a preventive perspective, our pilot study suggests that milk intake is not only safe but also may protect against development of metabolic syndrome,' Eissa said. 'Yet fewer children are drinking enough, especially with growing concerns over fat content and dairy intolerance. Only a small percentage of children are actually intolerant to milk so parents shouldn't be afraid of milk or cut back on it.'

Eissa said since the sample size was relatively small and included mostly Hispanic children, future studies should be done to confirm the findings.

"Nonetheless this still presents reasonable grounds to stick with the recommended daily amount and to make friends again with milk," Eissa added.

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Risk factors for diabetic foot ulceration

SIMISO NTULI, CRAIG VINCENT LAMBERT, ANDRÉ SWART

Abstract

Objective: **The main purpose of the study was to investigate the need for podiatrists as members of the primary healthcare team. One of the objectives of the study was to determine the percentage of patients presenting at the two primary healthcare clinics who are at risk of developing foot complications as a result of an underlying concomitant systemic disease.**

Methods: **This was a descriptive, cross-sectional study in which data were collected from patients presenting at two homogeneously selected primary healthcare clinics in Johannesburg. Nursing staff assisted by a final-year podiatry student collected data using a self-constructed data-collection form from each consenting patient as part of their routine patient consultation. Simple descriptive statistics were used for data analysis.**

Results: **Data were collected and analysed from 1 077 patients and showed that 29% of the patients had diabetes. Diabetic foot ulceration risk factors that were recorded included peripheral neuropathy in 74% of the diabetic patients, structural foot deformities in 47%, peripheral vascular symptoms in 39% and foot ulcer in 28% of the diabetic patients.**

Conclusion: **Early identification of diabetic patients who are at high risk of diabetic foot ulceration is important and can be achieved via mandatory diabetic foot screening with subsequent multi-disciplinary foot-care interventions. Understanding the factors that place patients with diabetes at high risk of ulceration, together with an appreciation of the links between different aspects of the disease process and foot function, is essential for the prevention and management of diabetic foot complications.**

Keywords: diabetic foot ulceration, diabetic foot risk factors, primary healthcare, podiatry services, diabetic foot assessment

Introduction

Diabetes mellitus is a disease affecting many systems and tissues, and foot problems, including foot ulcerations, are common in patients with diabetes. In 2015, there were 2.8 million diabetics in South Africa.[1] The majority of diabetic patients in South Africa (SA) are most likely seen at primary healthcare clinics (PHC). These clinics bring healthcare as close as possible to where people live and work, are the first line of access for people needing healthcare services, and in some cases are the only available platform for delivery of healthcare for most of the population.[2,3] In Gauteng province where this study was done, 740 118 diabetic patients presented at various PHC clinics for routine diabetic follow-up visits in 2012/13.[4]

Foot problems are an associated complication and are an increasing problem among individuals with diabetes. Risk factors such as peripheral neuropathy, peripheral arterial disease and structural foot deformities put the foot at risk of ulceration. Healthcare professionals at PHC level are mandated and are accountable for screening, early identification, and referral to more advanced levels of sophisticated care and/or treatment if the need arises.[5-7] However, with regard to patients at risk of diabetic foot ulcerations, it remains unclear if this is done as there are no data on the diabetic risk factors recorded in patients presenting at various PHC clinics in SA.

Diabetic foot ulceration (DFU) develops as a result of a combination of factors that together lead to tissue breakdown. The most frequently occurring causal pathways to the development of foot ulcers include peripheral neuropathy, vascular disease, foot deformity and trauma.

Early identification of patients with diabetes mellitus who are at high risk of DFU is important, as between 10 and 25% of diabetic patients are likely to develop DFUs at some stage of their lives, which may lead to foot or leg amputations in 25 to 50% of these patients.[8,9] Available data in SA suggest that 60.2% of all non-traumatic lower-limb amputations in public hospitals in SA are accountable to diabetes, with unpublished data from two separate public hospitals showing an amputation rate of 78.5%, with 85% of these beginning with a foot ulcer.[10,11] In most cases, by the time patients with diabetic foot ulcerations are referred, it is often too late to save the foot.[12]

Currently, the PHC clinics provide an ideal setting for early diabetic foot risk identification, as these facilities are primarily focused on preventative care and early risk identification rather than a curative approach.[13-15] However, nurses who are at the coalface of primary healthcare delivery are overworked and do not have time to provide comprehensive care in all consultations.[16] This may lead to diabetic foot assessment being omitted as part of the diabetic patient routine assessment. This assertion is supported by the lack of data on diabetic foot risk factors emanating from PHC clinics.

There is, therefore, a need to look at including other healthcare cadres to ensure essential delivery of foot health services, including to the diabetic patients. A multi-disciplinary approach underscoring a comprehensive preventative strategy, including early risk detection via mandatory foot assessment, patient and staff education, and multi-factorial treatment of diabetic foot ulcers is needed. The literature shows that in some cases, such approaches have reduced amputations by more than 50%.[17-20] Such interventions will ensure good outcomes for diabetic patients, as well as prompt treatment and or referral where needed. This may be difficult to realise immediately as currently, foot health service guidelines or

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policies are unclear. In fact, the current PHC package of services available at PHC level and the Human Resources for Health plans do not mention foot health services or integration of (podiatric) such services as part of services to be offered at PHC level of care.[21,22]

There is, however, a need to understand and document the factors that predispose diabetic patients to the risk of ulceration, together with an appreciation of the links between different aspects of the disease processes and foot function. This is necessary for the prevention and management of diabetic foot complications. Therefore, this article focuses on the risk factors for diabetic foot ulceration recorded in patients presenting at two PHC clinics.

Methods

A descriptive, cross-sectional study was conducted over a period of 14 weeks between June and September 2013 at two PHCs in Johannesburg. The participating clinics were selected using homogeneous sampling methods with one clinic located in the inner city and the other in a township. Patients presenting at the participating clinics were asked to participate in the study and 1 077 patients consented to taking part in the study. Those patients who agreed to participate had their medical data recorded and their feet inspected by a clinic nurse, assisted by a final-year podiatry student. Data were collected as part of routine patient consultation and captured on a self-constructed data-collection form (DCF).

The DCF had four sections, which dealt with demographics, the presence of foot-related complaints, presenting systemic or joint condition, and current management of patients with foot complaints presenting at PHCs. The form was pre-tested at another PHC in Johannesburg before being used for data collection in the study. Simple descriptive statistics were undertaken to analyse data, which included performing basic frequencies, an inferential method for comparing groups, and a comparative analysis of demographics was completed using comparative inferential statistics.

Ethical clearance for the study was obtained from the University of Johannesburg, Faculty of Health Sciences, research ethics committees (REC-241112-035). Permission to access the selected clinics for data-collection purposes was granted by the executive director of the City of Johannesburg Health Department.

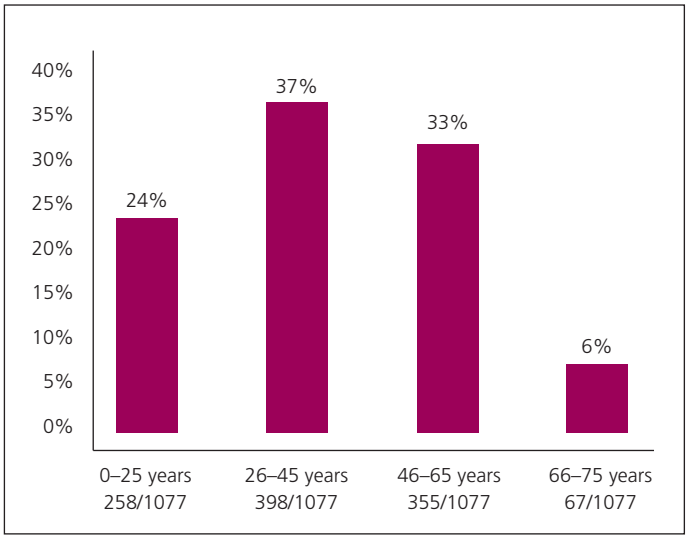

Fig. 1. Age spread of patients.

Table 1. Diabetic foot risk factors

Risk factor	Prevalence, *n* (%)
Neuropathy	236 (75)
Structural deformities	147 (47)
Peripheral vascular disease symptoms	124 (39)
Foot ulcers	87 (28)

Results

Data were analysed from the 1 077 completed DCFs, 442 from one clinic and 635 from the other. No patient-identifying data were collected as part of the study, only gender, population group and age were collected as part of the demographic data for this study. Three hundred and fourteen patients were confirmed as having diabetes, based on their medical records.

Overall analysis of the 1 077 DCFs gathered showed that 33% (n = 356) were male and 62% (n = 672) were female patients. The gender of the remaining 5% (n = 49) could not be decided as the forms were not properly completed concerning this question. The mean age was between 46 and 49 years. The age spread of patients in is presented in Fig. 1.

Black Africans were the majority population group in this study at 51%, followed by coloureds (mixed ancestry) at 25%. Whites and Indians made up 3 and 9%, respectively and in 12% of the DCFs, the population group was not documented.

In total, 54% (n = 583) of patients presenting at the two PHCs had a systemic disease or joint condition. Diabetes was recorded in 29% (n = 314) of the patients whose data were collected in this study. Systemic conditions recorded are presented in Fig. 2.

The risk factors for diabetic foot ulcerations recorded in this study are presented in Table 1. Foot pathologies and or symptoms that were recorded in diabetic patients are presented Table 2.

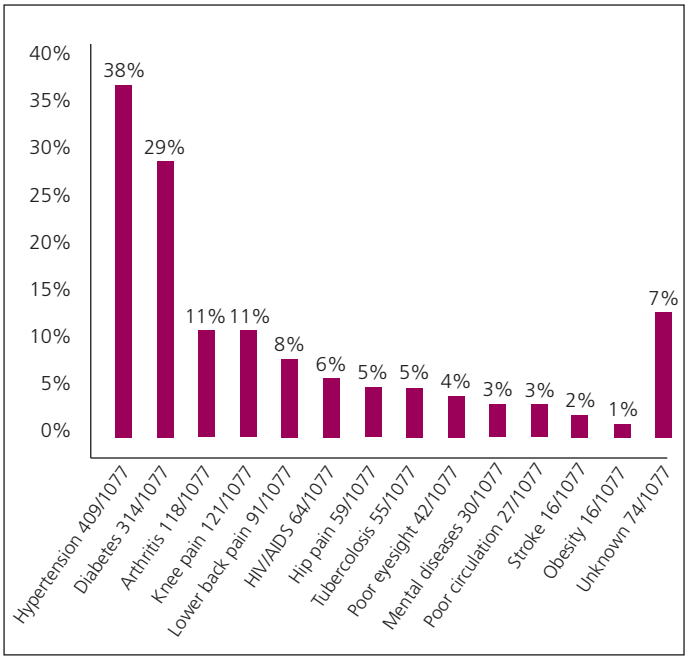

Fig. 2. Systemic disease or joint condition.

Table 2. Foot pathologies and symptoms recorded in diabetic patients

Foot pathology/complaint	Prevalence, *n* (%)
Corns	82 (26)
Calluses	125 (40)
Ulcers/wounds	87 (28)
Infections	79 (25)
Thick nails	13 (4)
Ingrown nail	66 (21)
Fissures/cracks	102 (32)
Interdigital maceration	67 (21)
Burning feet	50 (16)
Tingling	97 (31)
Numbness	89 (28)
Cold feet	70 (22)
Intermittent claudication	54 (17)
Pes planus (flat feet)	98 (31)
Hammer toes	7 (2)
Bunions	22 (7)
Overlapping toes	5 (1)
Pes cavus (high arches)	15 (5)

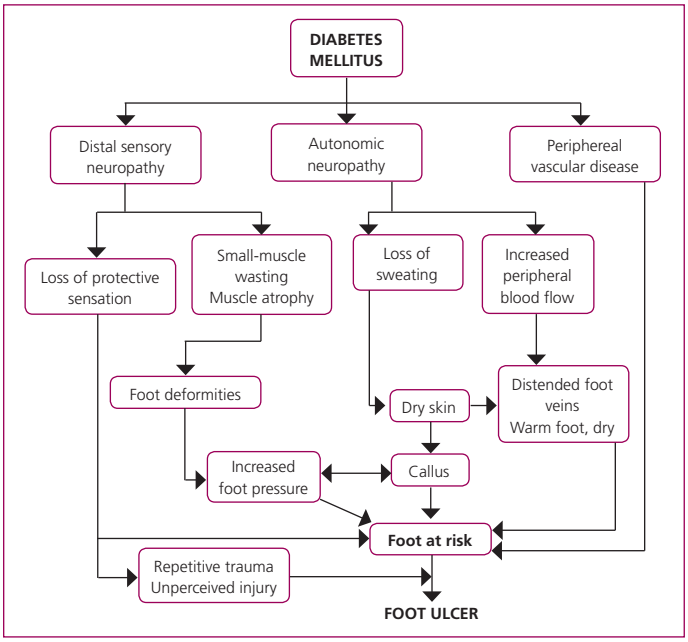

Fig. 3. The pathway to foot ulceration in diabetes. From Boulton *et al*.[38]

Discussion

Primary healthcare facilities may in most cases be the only available or accessible form of healthcare for the majority of the population.[2,3] This can be see in the 128 million people who were seen or visited a PHC clinic in 2013/2014.[23] It is very likely that a significant number of these patients were diabetic. We know that in Gauteng alone, 740 118 diabetic patients were seen at various PHC clinics for routine diabetic follow-up visits in 2012/13.[4] However, to date, there are no data available on the number of diabetic patients who had a diabetic foot assessment as part of their routine diabetes care coming from PHC clinics.

Our study has provided evidence of diabetic patients presenting at PHCs who are at real risk for developing DFU. This develops as a consequence of a combination of risk factors, most commonly peripheral neuropathy, peripheral vascular disease, foot deformity and (unperceived) trauma. In our study, we recorded all these risk factors in the diabetic patients.

The life-time risk of a diabetic patient developing a DFU is estimated to be as high as 25%.[24] Therefore early identification of risk factors that may lead to tissue breakdown is important, as potential DFU sites are often not diagnosed in diabetic patients until tissue loss is evident, usually in the form of a non-healing ulcer. Although the DFU pathway (Fig. 3) is a complex multi-factorial process involving interactions between numerous risk factors leading to skin breakdown, up to 85% of amputations could be prevented via routine diabetic foot assessment and early identification of risk factors.[25,26]

Foot assessment and the resultant early identification of those patients who are at risk for foot ulceration is therefore paramount in the prevention of DFUs. Early risk identification and regular inspection of the feet (by podiatrists) has been identified as the cornerstone in the prevention and management of diabetic foot complications.[27]

The annual diabetic foot inspection has been identified as probably the single most important tool available in the prevention of DFUs.[28] The aim of such assessment is to identify those with early signs of complications and institute appropriate interventions, such as determining the frequency of clinic visits and actions to be taken to prevent the progression of risk factors into DFUs. The

Table 3. Components of the diabetic foot examination (adapted from Boulton *et al*.[38])

Inspection	Neurological	Vascular
Evidence of past/present ulcers	10-g monofilament at four sites on each foot + one of the following:	Foot pulses
Foot shape	Vibration using 128-Hz tuning fork	Ankle–brachial index, if indicated
Prominent metatarsal heads/claw toes	Pinprick sensation	Doppler wave forms, if indicated
Hallux valgus	Ankle reflexes	
Muscle wasting	Vibration perception threshold	
Charcot deformity		
Dermatological		
Skin status: colour, thickness, dryness, cracking		
Sweating		
Infection: check between toes for fungal infection		
Ulceration		
Calluses/blistering: haemorrhage into callus		
Erythema		
Dystrophic nails		

characteristics of such foot assessment to be undertaken would include the removal of shoes and socks for a careful inspection of both feet, including between the toes (Table 3). Ideally, every diabetic patient should be screened for evidence of DFU risk factors at least annually at their PHC clinic.

For example, diabetic peripheral neuropathy risk factors, which are associated with a seven-fold increase in risk of ulceration,[29,30] and was recorded in patients in this study, can be identified by a simple clinical observation. Such an observation would including looking for features such as small-muscle wasting, clawing of the toes, prominence of the metatarsal heads, distended dorsal foot pains (a sign of sympathetic autonomic neuropathy), dry skin and callus formation. Additional tests may include a vibrating 128-Hz tuning fork, and the 10-g monofilament to be used at specific sites of the foot.

Assessment of the actual foot structure for deformity should also be undertaken. Structural foot deformities, when combined with neuropathy and ensuing altered biomechanics, may lead to abnormal loading of the foot or abnormal plantar pressure, leading to ulcer formation.[24] Foot deformities were noted on patients in this study as well as actual foot ulcers in diabetic patients. Patients in this study were at an increased risk of amputation as 28% had foot ulcers and 39% had symptoms of peripheral arterial disease.[31,32]

Studies done on the diabetic population in SA suggest that foot health at PHC level ranges from non-existent, to mostly ignored, or disorganised, at best. One study done at an out-patient department of a district hospital found that 67.5% of diabetic patients had never had their feet examined by either a doctor or a nurse at a PHC.[33] Other studies have found that primary and secondary prevention were not prioritised in routine diabetic patient clinical care and that foot screening is often neglected at PHC level.[34,35]

Although our findings are suggestive of the need for preventative measures, including having diabetic foot assessment included as a mandatory item of routine diabetic patient care at PHCs, poor diabetic foot care at PHC level is understandable. Nurses at PHCs have a heavy patient load, which may limit patient consultation times and getting through their patient load may lead to a situation where possibly, feet assessment may be the last thing on both the nurses' and patients' minds during consultation.[16,36] Therefore, there is a need to consider the involvement of podiatrists at PHCs to undertake diabetic foot assessment and risk stratify patients as well as provide treatment for some of the foot pathologies at this level of care.[37]

Podiatrists play a key role in the prevention (includes regular foot examinations, risk stratification and appropriate footwear recommendations) and treatment of foot deformities and complications related to diabetes at PHC level. A podiatric approach to diabetic foot ulceration is distinctive in that the diabetic foot ulceration is not viewed in isolation but rather in the perspective of the overall structure and function of the foot, ankle and lower limb. Therefore, podiatric treatment of DFUs includes a focus on biomechanical anomalies that often precede ulcer formation. Further, simple interventions such as regular callus debridement to prevent increases in focal pressures can reduce the likelihood of ulcer formation.

Conclusions

We have provided some evidence of patients presenting at PHCs with risk factors for DFU. Our findings should be used as an indicator of a silent but imminent public health problem that is likely to impose significant challenges on the South African healthcare systems in the near future. This is indicative of a need for effective, early preventative approaches, primarily the early identification of at-risk patients at PHC level.

In our healthcare structures, a substantial number of diabetic patients are most likely seen at PHC facilities across SA and a considerable number may be at risk of DFUs. Early identification of at-risk patients could prevent or delay development of DFUs, and in cases where patients already have DFUs, prompt management or referral with subsequent multi-disciplinary foot-care intervention could be assured. Therefore, there is a need for diabetic foot assessment to be mandated as a part of routine diabetic patients care at PHC level.

Significance of the study

- There are limited data available on diabetic foot risk factors across all levels of care in South Africa.
- The study found that up to 74% of patients presenting at PHC facilities in this study had symptoms of diabetic peripheral neuropathy and 28% had foot ulcers.
- The findings are suggestive of a need for diabetic foot assessment to be mandated at PHC level as part of the routine diabetic patient assessment and for podiatrists to be involved at this level of care.

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2017 SEMDSA diabetes management guidelines

DAVID WEBB

The updated 2017 South African guidelines for the management of type 2 diabetes mellitus were launched on 5 May at the 52nd congress of the Society of Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) in Johannesburg. This is the fourth edition of the guidelines, which were last updated in 2012. The 2017 edition has been completely revised and updated using the most recent clinical science, with contributions from more than 45 local experts in various aspects of diabetes management. It is a comprehensive document, consisting of 29 chapters covering epidemiology; definitions; diagnosis; screening and organisation; lifestyle interventions; glucose management; co-morbidities and complications (weight management, cardiovascular risk, hypertension, diabetic kidney disease, diabetic eye disease and diabetic foot); along with type 2 diabetes management in special patient populations (pregnant women, children and adolescents, the elderly, those with HIV, those observing Ramadan, drivers and men with sexual dysfunction).

The guideline has been written with the clinician in mind and is practical and easy to use. Recommendations are summarised in table form at the beginning of each chapter and information relating to support for the recommendations is included in appendices at the end of the document.

The following is a brief summary of general recommendations and highlights information that is new or where recommendations from past editions of the guideline have been updated.

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KEY MESSAGES

- It is estimated that as many as one in four South African adults older than 45 years may have type 2 diabetes
- More than half of those with type 2 diabetes remain undiagnosed
- The diabetes epidemic is largely driven by modifiable risk factors, in particular overweight and obesity
- Type 2 diabetes mellitus is a diagnosis of exclusion following careful investigation for an aetiology
- In symptomatic patients, diagnosis is confirmed by random plasma glucose ≥ 11 mmol/l, fasting plasma glucose ≥ 7 mmol/l, or HbA_{1c} ≥ 6.5%
- All patients should receive ongoing diabetes education and support to enable self-management and lifestyle change
- The target HbA_{1c} for most treated patients is ≤ 7%
- If it is not contra-indicated and if it is tolerated, the initial pharmacotherapeutic choice is metformin, titrated to an appropriate dose for the individual
- In patients with diabetes that is inadequately controlled with monotherapy, the choice of add-on therapy should be individualised, with particular attention paid to glycaemic target, risks of hypoglycaemia and weight gain, co-morbidities and patient preferences and capabilities
- Statins are recommended for all patients with cardiovascular risk factors
- Low-dose aspirin is not recommended for primary cardiovascular protection (in those who have not yet had a cardiovascular event).

Epidemiology of type 2 diabetes

Based on the 2015 statistics from the International Diabetes Federation (IDF), there are approximately 2.3 million adults aged between 20 and 79 years with type 2 diabetes in South Africa, of whom approximately 60% remain undiagnosed. According to the 2012 South African National Health and Nutrition Examination Survey (SANHANES), the estimated prevalence of type 2 diabetes in South Africans older than 15 years was 9.5%, with a further 9% having impaired glucose regulation (HbA_{1c} 6.0–6.4%). However, in individuals older than 45 years, the prevalence of type 2 diabetes may be as high as 25%. Type 2 diabetes is most common among the Asian (30%) and coloured (13%) populations, with equal prevalence in blacks and whites (8%). It occurs in all sectors of society, with a similar prevalence in rural informal dwellers and urban formal dwellers.

Worldwide, the number of people who die annually from type 2 diabetes exceeds the combined mortality from HIV/AIDS, tuberculosis and malaria, and that is expected to rise. For example, by 2040, it is anticipated that the number of people in Africa with type 2 diabetes will have increased by 140%.

The diabetes epidemic is driven by interrelated risk factors, including positive family history, psychosocial factors, overweight and obesity, and insufficient physical exercise. Nevertheless, the rising prevalence of type 2 diabetes is predominantly associated with modifiable risk factors. The most important of these, and one that demands urgent attention, is the increasing prevalence of obesity. According to SANHANES, half of all South African males and three-quarters of females between the ages of 45 and 54 years are overweight or obese [body mass index (BMI) ≥ 25 kg/m^2].

Definition and classification of diabetes

Diabetes mellitus is defined as 'a metabolic disorder with heterogeneous aetiologies, which is characterised by chronic hyperglycaemia and disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both'.

Table 1. Aetiological classification of diabetes mellitus

Type I diabetes
Type II diabetes
Specific aetiologies
- Genetic defects of β-cell function
- Genetic defects in insulin action
- Diseases of the exocrine pancreas (e.g. pancreatitis, trauma, neoplasia, haemochromatosis)
- Endocrinopathies (e.g. acromegaly, Cushing's syndrome, hyperthyroidism)
- Drug or chemical induced (e.g. glucocorticoids, nicotinic acid, thiazides, atypical antipsychotics, antiretroviral therapy)
- Infections
- Uncommon forms of immune-mediated diabetes
- Other genetic syndromes sometimes associated with diabetes (e.g. Down's syndrome)

From SEMDSA 2017 Guidelines

Type 2 diabetes is associated with specific long-term adverse health consequences, including retinopathy, nephropathy, neuropathy and cardio-, cerebro- and peripheral vascular diseases.

The clinical stages of hyperglycaemia include intermediate hyperglycaemia (impaired fasting glucose and impaired glucose tolerance), which represents a high-risk state for development of future diabetes and cardiovascular disease.

When assessing a patient with diabetes, a wide array of potential aetiologies needs to be considered. Type 2 diabetes is a diagnosis of exclusion after careful investigation for and exclusion of other causes (Table 1).

Screening and diagnosis

In patients with symptoms of type 2 diabetes (polyuria, polydipsia, blurred vision, weight loss) or metabolic decompensation (diabetic keto-acidosis or hyperosmolar non-ketotic state), the diagnosis is confirmed if one or more of the following are present:

- Random plasma glucose ≥ 11 mmol/l or fasting plasma glucose (FPG) ≥ 7 mmol/l
- HbA_{1c} ≥ 6.5%

Type 2 diabetes is diagnosed in asymptomatic patients by any one of the following tests, which must be confirmed on separate days within a two-week period:

- FPG ≥ 7 mmol/l
- Two-hour post-load plasma glucose [oral glucose tolerance test (OGTT)] ≥ 11 mmol/l
- HbA_{1c} ≥ 6.5%

Bedside or point-of-care devices (HbA_{1c} or glucose) should not be used to make the diagnosis.

Impaired fasting glucose and impaired glucose tolerance (prediabetes) are present when two consecutive tests on different days confirm FPG 6.1–6.9 mmol/l or two-hour post-load plasma glucose 7.8–11.0 mmol/l, respectively.

Asymptomatic individuals at high risk for diabetes should be screened using FPG, OGTT (preferred) or HbA_{1c} at least every three years, or more frequently if initial screening results are abnormal, or if they are at very high risk. This includes all adults who are overweight (BMI > 25 kg/m^2 or > 23 kg/m^2 in Asians), and have one or more of the following risk factors: physical inactivity, hypertension, a first-degree relative with diabetes, dyslipidaemia, polycystic ovarian syndrome, high-risk race/ethnicity, history of cardiovascular disease, gestational diabetes or baby > 4 kg, previous impaired FPG or OGTT, or other conditions associated with insulin resistance (severe obesity, acanthosis nigricans).

Management

Diabetes self-management education and support (DSME)

All people with diabetes and their families should be provided with the education and support for self-management so that they can effectively manage the disease at home themselves. DSME has been shown to be associated with better glycaemic control and is one of the strongest predictors of disease progression and development of diabetes complications.

Lifestyle change and medical nutrition therapy (MNT)

Behaviour change, physical activity (aerobic and resistance exercise) and healthy nutritional choices can achieve modest weight loss and improve outcomes in overweight and obese individuals with type 2 diabetes and prediabetes, and are the essential foundation of every patient's management programme. MNT can reduce HbA_{1c} by up to 2%. Nutritional recommendations should be individualised, aiming at a high-quality diet consistent with metabolic goals and sensitive to ethnic, cultural and socio-economic needs, so that it is sustainable. There is no one recommended diet that is considered superior, or ideal in respect of which percentage of calories should come from carbohydrates, fat or protein. Macronutrient distribution should be individualised to suit the patient. Refined carbohydrates high in sugar, fats and sodium should be replaced with whole grains, legumes, milk, vegetables and fruit. Mono-unsaturated fats are preferred to saturated fats and foods rich in long-chain omega-3 fatty acids, such as fatty fish, nuts and seeds, are recommended for cardiovascular risk prevention. Processed and fatty red meats should be limited. The long-term health risks associated with high-fat, low-carbohydrate and very-low-calorie diets are uncertain and these diets are not recommended. Whole foods are the best source of micronutrients and unless there are specific clinical indications, vitamins and supplements are not recommended.

Glycaemic targets

In most patients, management should aim to achieve and maintain HbA_{1c} ≤ 7% (self-monitored plasma glucose (SMPG) fasting or preprandial 4–7 mmol/l and postprandial 5–10 mmol/l). In newly diagnosed patients who are in good health, as long as it can be achieved safely, target HbA_{1c} ≤ 6.5% can prevent further retinopathy and nephropathy. In elderly patients and those with limited life expectancy, multiple co-morbidities, severe vascular disease, advanced chronic kidney disease, recurrent severe hypoglycaemia or hypoglycaemia unawareness, HbA_{1c} 7.1–8.5% is acceptable.

Pharmacotherapy for type 2 diabetes

When added to metformin, most drug options for type 2 diabetes are equally efficacious at lowering blood glucose with reductions in HbA_{1c} of approximately 0.8–1.2%. However, in clinical practice the response to individual drugs varies widely between patients, with some responding well and others not at all. Implementation and intensification of lifestyle modifications also affect drug efficacy. Therefore, drug selection should be individualised, based not only on glycaemic targets, but also taking into consideration hypoglycaemia risk, risk of treatment-associated weight gain and other side effects, individual patient characteristics, treatment complexity and cost. Maximum glucose lowering is usually evident by six months.

Guidelines for step-wise pharmacotherapy for stable patients with type 2 diabetes with suboptimal glycaemic control, who are being managed at primary care facilities, are shown in Table 2. Intensification (step-up) of treatment may be considered if the HbA_{1c} target is not achieved after three months or if HbA_{1c} rises after initiating new therapy. Patients with metabolic decompensation who have severe symptomatic hyperglycaemia and those with severe micro- or macrovascular complications should be managed under specialist supervision.

Unless it is contra-indicated, metformin is the drug of first choice and, as long as it is tolerated, should be continued indefinitely. Most patients will require titration to 1 000–2 550 mg in two or three divided doses and the optimal dose for cardiovascular benefit in obese patients is 2 550 mg/day (850 mg TDS). If tolerability is poor, consideration should be given to switching to the extended-release (XR) formulation.

Table 2. Guidelines for management of type 2 diabetes in non-pregnant adults without metabolic decompensation or cardiovascular disease

	Preferred	Alternative options without motivation*	Not recommended if HbA_{1c} target is attainable with other agents
Monotherapy	Metformin XR	DPP4i Gliclazide MR Pioglitazone	GLP-1a Insulin SGLT2i
Dual therapy	Metformin XR DPP4i Gliclazide MR	Pioglitazone SGLT2i	GLP-1a Insulin
Triple therapy	Metformin XR DPP4i Gliclazide MR Pioglitazone	GLP1a Insulin (basal) SGLT2i	
Complex therapy	Metformin XR + insulin (pre-mix or basal)	Oral therapy + basal insulin + GLP1a	

DPP4i: dipeptidyl peptidase-4 inhibitor; SGLT2i: sodium glucose cotransporter-2 inhibitor; GLP-1a: glucagon-like peptide-1 receptor agonist
*These alternatives do not require motivation to funders as they offer similar benefits and are selected for the individual circumstances based on clinical judgement.
From SEMDSA 2017 Guidelines

Because of its low rate of hypoglycaemia and cardiovascular safety relative to other sulphonylureas, and its proven benefits in terms of microvascular outcomes, the sulphonylurea of choice is gliclazide modified release (MR). Glibenclamide should not be used.

In patients with symptomatic hyperglycaemia and HbA_{1c} > 9% at diagnosis, initial dual therapy with metformin plus gliclazide MR should be considered. After optimisation of metformin dose and lifestyle modification it may be appropriate to discontinue the sulphonylurea.

Fig. 1 provides additional advice for triple therapy and initiating insulin. When selecting additional therapies, consideration should be given to patient preference, co-morbidities, the individual properties of each of the pharmacological options and access to medicines. Expected HbA_{1c} reductions are similar when adding a glucagon-like peptide-1 (GLP-1) receptor agonist or titrated basal insulin, which are both slightly superior to triple oral therapy. Insulin initiation must be accompanied by ongoing patient education, appropriate SMBG, self-titration of insulin doses, frequent review (initially) and counselling regarding hypoglycaemia. In the absence of appropriate support for insulin therapy, a third oral agent is preferred.

A GLP-1 receptor agonist may be preferred to other options under the following circumstances:

- For overweight and obese patients
- Weight gain or hypoglycaemia has been or is likely to be problematic with other treatment options (see Hypoglycaemia)
- HbA_{1c} is very high
- Patients with established cardiovascular disease (liraglutide benefit) who are to be managed with specialist-level participation or responsibility.

Equally, these agents should not be the preferred option:

- In patients in whom weight loss is not desirable
- In patients with chronic gastrointestinal disorders
- In patients with a history of pancreatitis or pancreatic tumours.

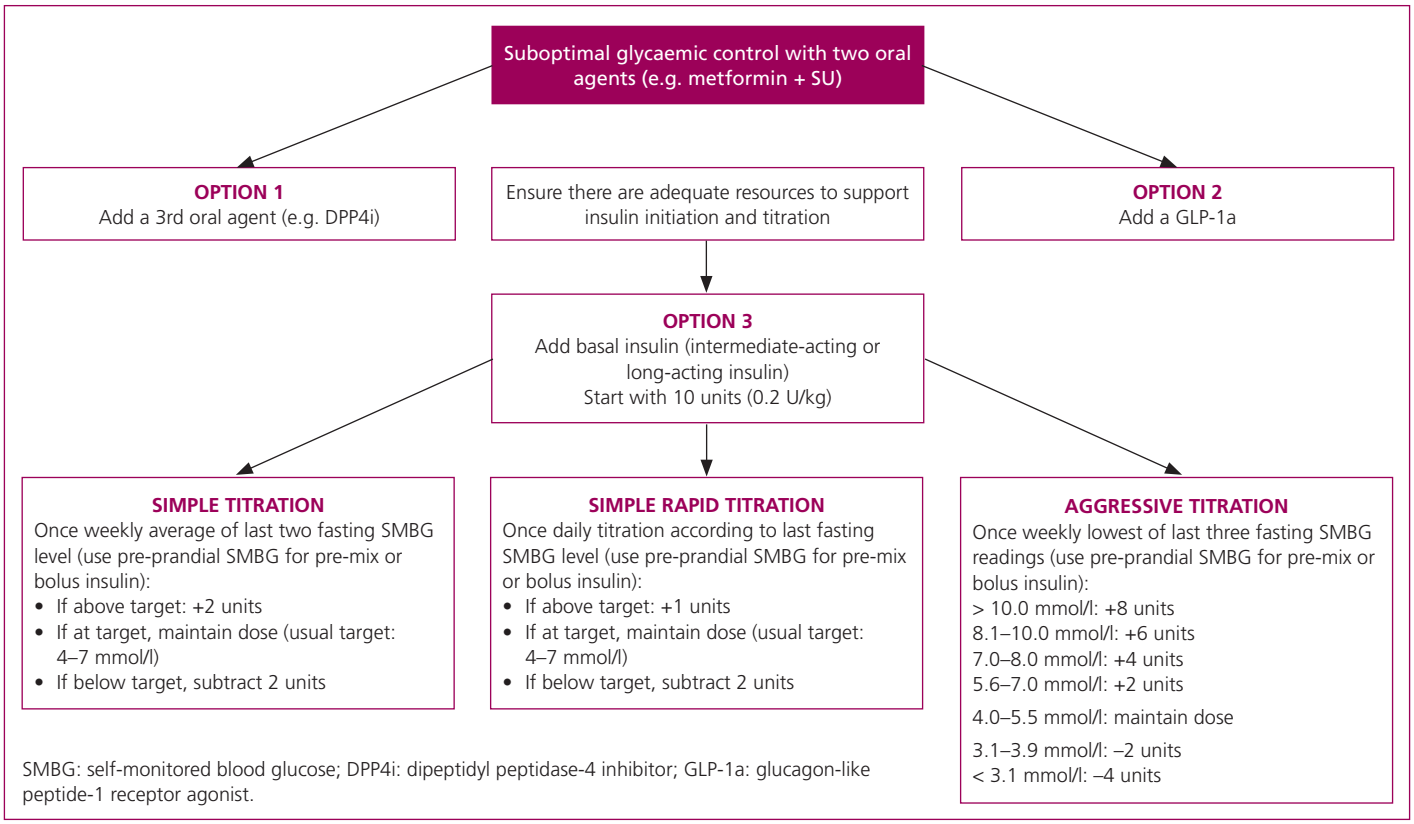

Fig. 1. Initiating and titrating basal insulin therapy.

Equally, the guidelines provide detailed considerations for use of the other agents, including pioglitazone, DPP-4 inhibitors and SGLT-2 inhibitors.

Hypoglycaemia

Hypoglycaemia is an important limitation in achieving optimal glycaemic control and is a significant risk factor for cardiovascular mortality and morbidity, especially in those with pre-existing cardiovascular disease. It is defined as SMBG < 3.9 mmol/l, with significant hypoglycaemia < 3 mmol/l. Severe hypoglycaemia is any low blood glucose value accompanied by cognitive dysfunction and the need for external assistance to correct the hypoglycaemia. Patients at risk of hypoglycaemia (Table 3) require education to recognise and treat hypoglycaemic episodes (with confirmation of hypoglycaemia with SMBG wherever possible). Oral glucose (15–20 g) is the preferred treatment for non-severe episodes and intravenous (IV) 50% dextrose water for severe hypoglycaemia. In the event of no IV access, 1 mg subcutaneous or intramuscular glucagon may be administered.

Any episode of severe hypoglycaemia or hypoglycaemia unawareness requires re-evaluation of the treatment regimen and patients. Patients with recurrent episodes should be referred to specialist care.

Cardiovascular risk management

- Statins are the first-line agents for lowering LDL cholesterol in patients with type 2 diabetes. They should be added to lifestyle therapy regardless of baseline lipid levels in all patients with pre-existing cardiovascular disease, chronic kidney disease (eGFR < 60 ml/min/1.72 m^2) and in those aged ≥ 40 years or with diabetes duration ≥ 10 years and with ≥ one additional cardiovascular risk factors.
- Low-dose aspirin therapy is strongly recommended for secondary prevention of cardiovascular disease in patients with type 2 diabetes, but is not recommended for primary prevention in those who have not yet had a cardiovascular event.
- Blood pressure (BP) should be measured at every routine visit to the healthcare professional. The threshold for treatment initiation is > 140/90 mmHg. The treatment targets for most patients are systolic BP 130–140 mmHg and diastolic BP 80–90 mmHg. Suitable initial choices in patients without albuminuria include an angiotensin converting enzyme (ACE) inhibitor, angiotensin receptor blocker (ARB), thiazide-like diuretic (due to its widespread availability and low cost, indapamide is the preferred diuretic) or calcium channel blocker (CCB). Diuretics or CCBs are preferred in black patients. ACE inhibitors, ARBs, thiazide-like diuretics and non-dihydropyridine CCBs have been shown to be of benefit in diabetic kidney disease. CCBs should be avoided in patients with heart failure, and beta-blockers should be avoided in patients at high risk of stroke. ACE inhibitors and ARBs should not be used in combination.

Table 3. Characteristics of patients at high risk of hypoglycaemia

- Treatment with insulin and/or insulin secretagogues (sulphonylurea and meglitinides)
- Intensive glucose control
- Use of more than two glucose-lowering drugs
- Older age
- Longer duration of diabetes
- Hypoglycaemia unawareness
- Impaired cognitive function
- Low body mass index
- Renal or hepatic impairment
- Microvascular complications
- Patients who exercise or skip meals
- Excessive alcohol intake

Additional information

The following practical tools and patient support aids are included in the appendices of the 2017 SEMDSA diabetes management guidelines:

Appendix 13a: Algorithm for the management of hyperglycaemic emergencies.

Appendix 13b: Diabetic coma chart.

Appendix 14: Treatment algorithm for in-hospital management of diabetes.

Appendix 21: Diabetes foot-care patient checklist; diabetic foot-screening assessment form; foot abnormalities and footwear illustrations; practical guide to neuropathy assessment; care pathway for people with diabetic foot problems.

Appendix 26: Examples of Ramadan-specific meal plans for South Africans.

Appendix 29: Assessment and treatment algorithm for sexual dysfunction in men with type 2 diabetes.

Acknowledgement

This article is based on a presentation by Dr A Amod at the 52nd congress of the Society of Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) in Johannesburg in May 2017 and the SEMDSA 2017 guidelines for the management of type 2 diabetes mellitus. The article was written for deNovo Medica by Dr David Webb.

The latest complete pdf version of the guideline is available at http://www.jemdsa.co.za/index.php/JEMDSA/issue/view/42/showToc

Reference

The Society of Endocrinology, Metabolism and Diabetes of South Africa Type 2 Diabetes Guidelines Expert Committee. The SEMDSA 2017 guidelines for the management of type 2 diabetes mellitus. *J Endocrinol, Metab Diabetes S Afr* 2017; **22**(1): S1–S182.

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