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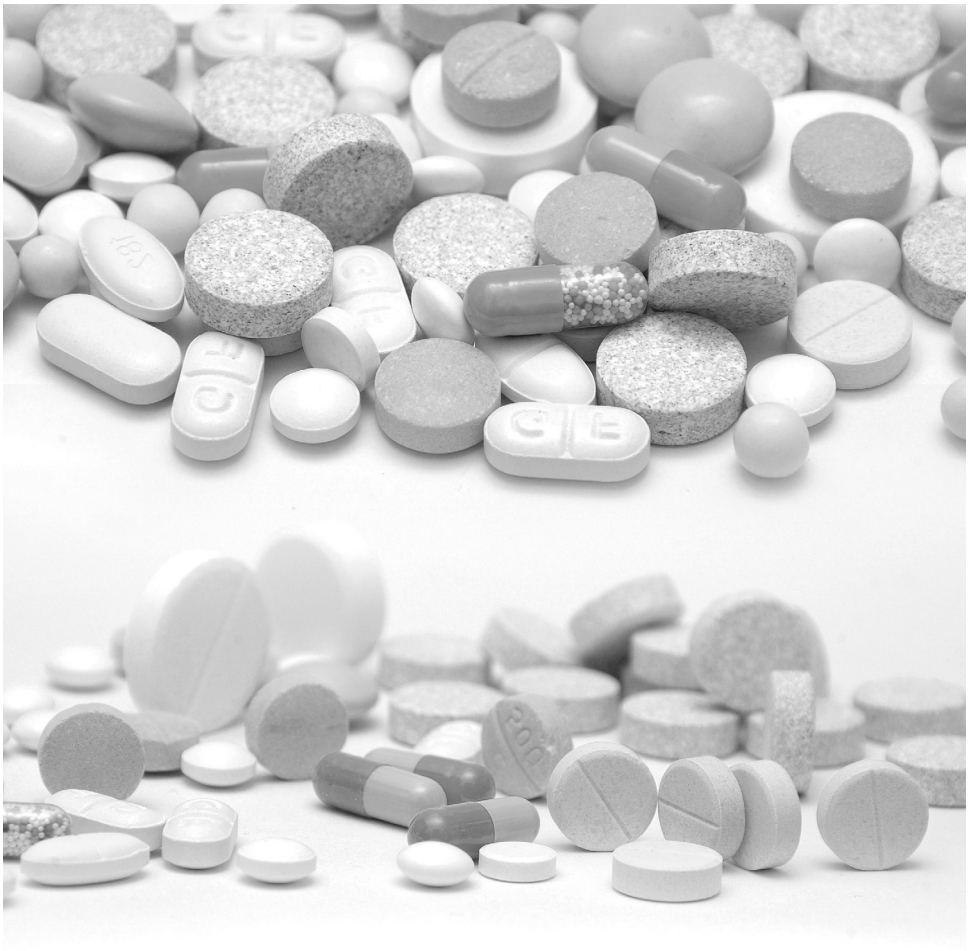

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From the Editor's Desk

In this issue of the journal, a wide range of topics is covered.

Phiri and co-workers (page 4) studied gestational diabetes mellitus (GDM) in Malawi and compare World Health Organisation (WHO) and International Association of Diabetes in Pregnancy study group (IADPSG) criteria. They show a marked difference in prevalence between the two sets of criteria and also show a poor correlation with the cheaper screening tool, finger-prick glucose test. Apart from adding to much-needed data on GDM in Africa, they also highlight the problem of cost of screening for GDM on a population level versus the unknown impact on improvement of health outcomes in a poorly resourced setting. This demonstrates the ongoing problem of achieving consensus on the definition of GDM.[1]

Olamoyegun *et al.* (page 10) discuss diabetic neuropathy in a tertiary-hospital setting in Nigeria. They show the usefulness of clinical examination in detecting foot pathology in diabetes, even where nerve-conduction testing is not accessible or feasible. This is reassuring for clinicians working in this setting. It would be interesting to see this study repeated in a primary-care setting. For example, in Chile,[2] a much higher prevalence of neuropathy was found. A study in a primary-care setting in South Africa showed a low rate of assessment for complications.[3] Another option is to consider the development of podiatrist-run evaluation centres.[4]

Muluvhu and colleagues (page 15) assessed obesity and hypertension in a group of government employees in South Africa. They found high levels of obesity and hypertension and females were more prone to this. This indicates possible areas for lifestyle and health interventions. Basic interventions could yield important benefits, such as a reduction in cardiovascular risk by an estimated 80%,[5] and are worth investing in on a population level.

Mokgwathi and Mwita (page 23) examined some cardiovascular risk factors in a group of adolescents in Botswana and picked up an early signal of obesity and hypertension. Females seemed to be more affected. The burden of cardiovascular disease in older adults may therefore have its seeds in this young group, and again, this represents a great opportunity for intervention in lifestyle and health education.

An American study[6] studying youth obesity gives an example of an intervention such as mindful eating in the family setting. We need to look at creative ways to engage the youth in participating in healthier lifestyles.

Wang and co-workers (page 29) describe an interesting case of cardiac arrest and prolonged cardiac dysfunction after accidental insulin-induced hypokalaemia. Their heroic, high-tech efforts ensure a favourable outcome for the young patient.

Rossing and Patel (page 33) report on diabetes and thrombo-embolic risk, with a special focus on risk reduction with non-vitamin K antagonist oral anticoagulants (NOACs). These produce benefit and fewer side effects compared to warfarin. This report is followed by an instructive case by Dalby (page 36).

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Drug trends looks at diabetes risk associated with statin use (page 38). Much is written about this topic and good summaries are published.[7-9] The risk of developing diabetes increases with dose of statin and level of preceding risk for diabetes. Overall, the consensus seems to be that the cardiovascular benefits of statins still outweigh the risk of diabetes.[7-9] Alternatives to statins, such as PSK9 inhibitors, can be considered where there is a very high risk of diabetes or in patient preference.

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Prevalence of gestational diabetes mellitus in urban women in Blantyre, Malawi: a cross sectional study evaluating diagnostic criteria and traditional risk factors

TAMARA J PHIRI, MARIANNE KASIYA, THERESA J ALLAIN

Abstract

Background: **Gestational diabetes mellitus (GDM) is associated with maternal and neonatal complications. The application of appropriate diagnostic criteria is essential. There is a paucity of GDM prevalence data for African countries, including Malawi.**

Objectives: **This study aimed to establish the prevalence of GDM in Blantyre, Malawi and assess the implications of applying different cut-off points for diagnosis as defined by WHO criteria and the recently established International Association of Diabetes in Pregnancy Study Group (IADPSG) criteria. It evaluated the relevance of internationally defined risk factors for GDM and compared the risk factors and prevalence between women accessing antenatal care in private hospitals to those accessing antenatal care at government hospitals. Patients at private hospitals are generally of a higher socio-economic status, have better access to care and are more likely to have a sedentary lifestyle and Westernised diet.**

Methods: **In this cross-sectional study, 2 274 consecutive women presenting at five antenatal clinic sites in Blantyre were screened for GDM, employing a random blood glucose (RBG) test. Of these, 250 women were randomly selected for an oral glucose tolerance test (OGTT). Logistic regression was used to quantify the association between various exposure variables and prevalence of GDM. Characteristics of patients attending government and private antenatal clinics were compared.**

Results: **The study population was predominantly urban, with a mean age of 25 years (range 14–43) with 66% being in the third trimester. The mean RBG level was 5.1 mmol/l (range 2.4–10.6) and overall prevalence of GDM based on the OGTT was 1.6 and 24% using the WHO and IADPSG criteria, respectively. GDM, diagnosed using WHO criteria, was associated with older maternal age, high parity, and attendance at government antenatal clinics but not with mid upper-arm circumference, a positive family history of diabetes mellitus (DM) or previous poor neonatal outcome. There was no correlation between RBG level and GDM diagnosed on the OGGT.**

Conclusions: **The prevalence of GDM in Blantyre using WHO criteria was low in the predominantly young population that was screened. A much higher proportion had GDM based on the IADPSG criteria and these may warrant long-term follow up. GDM was not associated with some previously described risk factors for GDM, suggesting a different risk-factor profile compared to the high-income countries.**

Keywords: gestational diabetes mellitus, diabetes mellitus, non-communicable diseases, pregnancy, sub-Saharan Africa, Malawi

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Background

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy.[1] It is associated with an increased risk of pre-eclampsia, macrosomia and risk of the mother developing type 2 diabetes mellitus after pregnancy. Infants born to mothers with GDM are at an increased risk of birth trauma and neonatal metabolic complications, including hypoglycaemia, hypocalcaemia and hyperbilirubinaemia.[2,3] Risk factors for GDM in developed countries include advanced maternal age, obesity and a family history of diabetes mellitus (DM).[4]

Few studies have been done in Africa on the prevalence of GDM. A 2013 systematic review on the prevalence of GDM in Africa found data for only six of the 54 African countries.[5] The review included 14 studies and estimated the average prevalence of GDM in Africa at 5% (range 0–14). While some studies in the review screened women with risk factors for GDM only, others screened all women regardless of risk factors. The study populations were predominantly rural and GDM was associated with macrosomia, maternal age over 30 years and prior history of diabetes mellitus.

Comparisons between the African studies are limited by heterogeneity of the study populations, small sample sizes and variable diagnostic criteria used. In seven African studies over the past three decades, using the WHO criteria, the prevalence was reported as 3.8% in South Africa (1989),[6] 0% in Tanzania (1990),[7] 11% in Nigeria (1997),[8] 3.7% in Ethiopia (1997),[9] 1.7% in Nigeria,[10] 3.8% in South Africa (2007),[11] and 14% in Nigeria (2012).[12] Among studies using WHO criteria, however, some used the 1985 diagnostic criteria while others used the 1999 diagnostic criteria.

In Malawi, the nationwide WHO STEPwise Approach to Surveillance (STEPS) survey in 2009 found that 5.6% of adult Malawians had DM, the majority of which was undiagnosed.[13] There are no studies on the prevalence of GDM in Malawi.

There has been a universal lack of consensus on screening and diagnosis of GDM with regard to the impact of screening on

outcomes, appropriate individuals to screen, optimal screening time, the appropriate screening tool and appropriate diagnostic criteria. This has resulted in several revisions of diagnostic criteria by various groups.

There are two large studies that have influenced the interpretation of diagnostic criteria. The 2005 Australian Carbohydrate Intolerance Study in Pregnancy (ACHOIS)[14] demonstrated that mild forms of hyperglycaemia, below those diagnostic of GDM, were associated with poor perinatal outcomes. The 2008 Hyperglycaemia and Pregnancy Outcomes (HAPO) study[14] showed a linear association between maternal hyperglycaemia and adverse events, including macrosomia, pre-eclampsia, caesarean section rates and neonatal hypoglycaemia with no clear cut-off above which these adverse events occurred.

Following the HAPO study, the IADPSG recommended new criteria for the diagnosis of GDM with a fasting plasma glucose cut-off level much lower than the WHO criteria.[15] This has resulted in up to a three-fold increase in the proportion of women diagnosed as having GDM using the IADPSG criteria compared to WHO criteria. There is varied opinion as to whether IADPSG criteria universally translate into improved outcomes, particularly when applied to a population that is different from that in the HAPO study.[16-18]

Some guidelines favour selective screening of women with known risk factors for GDM in order to avoid unnecessary screening of low-risk women. Whether the traditional risk factors, as described in studies in high-income countries, are applicable to and predict GDM in sub-Saharan Africa has not been explored.

Establishing a risk-factor profile for women with GDM to be prioritised for screening is essential, particularly in a low-resource setting such as Malawi where routine screening of all pregnant women is not feasible. Random blood glucose (RBG), fasting blood glucose and the 50-g oral glucose tolerance (OGTT) tests have all been used in studies as screening tests.[19] Finger-prick RBG, although inferior to formal laboratory glucose tests, is a feasible screening option in Malawi where the majority of the population has limited access to formal blood glucose tests.

This study aimed to establish the prevalence and risk factors for GDM among urban women in Blantyre, compare the differences in prevalence using the different cut-offs defined in the WHO and IADPSG criteria, and assess if the prevalence would differ in women seen at government antenatal clinics (ANCs) compared to those attending private ANCs.

Methods

Blantyre is the main commercial city in southern Malawi, with an estimated population of 1.1 million.[20] Queen Elizabeth Central Hospital (QECH) is the main government tertiary referral centre. Chilomoni and Limbe health centres are government primary-care facilities in Blantyre with an average ANC attendance of 100 women per day. Mwaiwathu and Blantyre Adventist hospitals are the two main private hospitals in Blantyre.

In this cross-sectional study, consecutive women presenting at any gestational age to QECH, Chilomoni and Limbe ANCs between 1 June and 30 September 2012 and at Mwaiwathu and Blantyre Adventist hospital private ANCs between February and April 2013 were asked to participate in the study. Recruitment was restricted to women of Malawian origin residing in Blantyre during the study period.

Ethical approval for the study was obtained from the Malawi College of Medicine Research and Ethics Committee (reference number P02 12 1170). Each participant provided written consent. For participants who could not read or write, the consent form was read out to them by a research assistant and the participant gave verbal consent and put her fingerprint on the consent form to acknowledge her voluntary participation in the study. The consent form was available in English and the vernacular and had been approved by the College of Medicine Research and Ethics Committee prior to commencement of the study.

Consenting women had a capillary RBG test done at the clinic site with a finger-prick test and a SDCheck® glucometer (SD Standard Diagnostics Inc, Hagal-dong, Korea). A sub-sample of 200 women from the government ANCs and 50 women from the private ANCs were randomly selected for an OGTT by selecting every fifth woman who was recruited. Gestational age was calculated from the last normal menstrual period.

For RBG, a sample size of 614 was initially calculated in order to detect hyperglycaemia at an estimated prevalence of 2–3% (suggested by local Blantyre obstetricians from observation) but the sample size was subsequently increased after detecting a high proportion of normal RBGs when recruitment began. Furthermore, the test could easily be administered to large numbers of women attending the facilities within a short period of time. The sample size of 250 for OGTTs was limited by available resources to perform OGTTs.

All OGTTs were done at QECH laboratory and plasma glucose level was determined using an automatic analyzer (KeyLab BPC BioSed®, Rome, Italy). OGTTs were done following the 1999 WHO guidelines, with each participant having a fasting plasma glucose test done and then being given 75 g of anhydrous glucose dissolved in 200 ml of water to drink. Plasma glucose level was re-checked two hours after taking the glucose solution.

Using the WHO criteria,[21] GDM was defined as a fasting plasma glucose of 7.0 mmol/l or a two-hour plasma glucose of 11.1 mmol/l. Using the modified IADPSG criteria,[15] GDM was defined as a fasting plasma glucose of ≥ 5.1 mmol/l or two-hour plasma glucose of 8.5 mmol/l.

Blood pressure (BP), weight, height and mid upper-arm circumference (MUAC) were recorded on recruitment. BP was measured with an Omron® digital BP machine (Omron Healthcare Worldwide, Kyoto, Japan). Weight was measured using a digital scale. Where previously documented in the woman's health records, the pre-pregnancy weight was noted. The majority of the women did not have a documented pre-pregnancy weight or height and pre-pregnancy body mass index (BMI) could not be calculated. MUAC was used to assess nutritional status as a single BMI in pregnancy is not an accurate measure because of the additional weight gain from pregnancy.[22,23]

Patients diagnosed with GDM or hypertension were referred to the QECH, Mwaiwathu and Blantyre Adventist specialist diabetes clinics for follow up and management.

Statistical analysis

Means and percentages were used to explore the distribution of risk factors between government and private ANCs. The relationship between GDM prevalence and risk factors was first explored through univariate analyses. The *t*-test comparing women with GDM to those without GDM was used to assess if any of the continuous risk factors were associated with prevalence. To

adjust for possible simultaneous confounding of the risk factors, a multivariate logistic regression was fitted.

The stepwise model selection method was employed to come up with the final model, which included the following risk factors: type of hospital, age, parity, MUAC and history of macrosomia for the WHO criteria. Similarly, a multivariate linear regression was used to assess the relationship between RBG and the risk factors. The final selected model included hospital type, BMI and history of macrosomia.

SAS software version 9.3 (SAS Institute, North Carolina State University) was used for analysis and all inferences were made at the 0.05 significance level.

Results

All participants were recruited from urban Blantyre. Fig. 1 shows a flow chart of participants recruited in the study.

The study population was predominantly young with an average age of 25.8 years (25th, 50th and 75th percentiles: 22, 25 and 30, respectively). Six per cent of the women were above 35 years of age, 66.4% were in the third trimester and 24% were between 24 and 28 weeks' gestational age. Table 1 compares the demographic characteristics of women in government and private ANCs.

Women at government-funded facilities were younger, of higher parity and gravidity, had a lower pregnancy BMI and were more likely to be HIV positive. Based on MUAC, 9% of the women were overweight (MUAC 28–31 cm) and 1% were obese (MUAC ≥ 32 cm). There was no difference in the average MUAC between government and private ANCs. When the BMI in pregnancy was calculated, half of the women had a normal BMI (average BMI 26 kg/m^2; 50th percentile 25).

Three per cent of the women had hypertension, but this was not explored further to determine whether this was pre-eclampsia or pre-existing hypertension. Eleven per cent of the women had HIV and of these, 61% had documented records of being on anti-retroviral therapy.

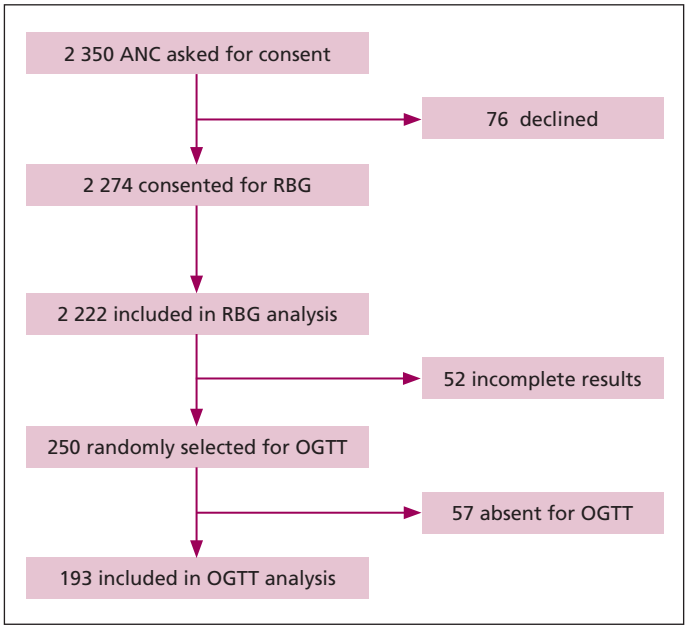

Fig. 1. Recruitment of participants. RBG, random blood glucose; OGTT, oral glucose tolerance test.

Table 1. Comparison of demographic characteristics between government and private ANCs

Characteristics	Government ANCs (*n* = 2044)	Private ANCs (*n* = 178)	*p*-value
Age (years), mean ± SD	25.8 ± 0.25	29.4 ± 0.6	< 0.0001
Gestational age (weeks), mean ± SD	26.9 ± 0.36	27.6 ± 3.2	0.68
Parity, mean ± SD	1.2 ± 0.05	0.76 ± 0.13	< 0.0001
Gravidity, mean ± SD	2.5 ± 0.05	2 ± 0.12	< 0.0001
BMI in pregnancy, mean ± SD	26.2 ± 0.3	27.7 ± 0.8	0.0003
MUAC (cm), mean ± SD	23.7 ± 0.15	23.5 ± 0.6	0.3646
Hypertension, *n* (%)	97 (4.7)	6 (3.3)	0.6574
HIV, *n* (%)	205 (10.0)	15 (8.4)	0.01
DM family history, *n* (%)	15 (0.7)	43 (24.1)	0.1573
Previous miscarriage, *n* (%)	361 (17.6)	41 (23.0)	0.308

ANC, antenatal clinic; BMI, body mass index; MUAC, mid upper-arm circumference; DM, diabetes mellitus.

Tables 2 and 3 show RBG and OGTT results. Only three women (0.1%) had an RBG level above 11.1 mmol/l. Twelve women (0.5%) were hypoglycaemic. There was a significant association between RBG level and attending government ANCs and BMI.

Based on the OGTTs, the overall prevalence of GDM was 1.6% (*n* = 5) and 24.8% (*n* = 65) by WHO and IADPSG criteria, respectively. The simple kappa coefficient was calculated to

Table 2. Risk factors associated with increasing RBG levels

Variable	Parameter estimate	Standard error	*t*-value	*p*-value
Government ANC	–15.50589	4.763	–3.26	0.0013
BMI	1.09278	0.37628	2.90	0.0041
Macrosomia	–22.14294	12.98251	–1.71	0.0898

RBG, random blood glucose; ANC, antenatal clinic; BMI, body mass index.

Table 3. Comparison of RBG and fasting glucose levels and GDM prevalence by OGTTs in government and private ANCs

Variable	Government ANCs	Private ANCs	Overall	OR (95% CI)
RBG (g/dl), mean ± SD	94.4 ± 20	107 ± 24	94 ± 21	
Fasting glucose (g/dl), mean ± SD	84 ± 16	70 ± 16	81 ± 19	
2-h glucose (g/dl), mean ± SD	84 ± 18	86 ± 53	84 ± 17	
GDM (WHO), % (95% CI)	1.4 (0.04–5.5)	0.04 (0–1)	1.6 (0.3–4)	3.5 (0.08–8.1)*
GDM (IADPSG), % (95% CI)	31.7 (24.6–39.8)	7.8 (3–19.1)	24.8 (19–32)	5.5 (1.9–16)*

*GDM prevalence odds ratio for government ANCs vs private ANCs.
RBG, random blood glucose; ANC, antenatal clinic; GDM, gestational diabetes mellitus; OGTT, oral glucose tolerance test.

Table 4. Risk factors associated with GDM by WHO criteria

Parameter	df	Estimate	Standard error	Wald chi-square	*p*-value
Government ANCs	1	2.0860	0.5959	12.2527	0.0005
Age	1	0.0973	0.0424	5.2690	0.0217
Parity	1	0.6160	0.2353	6.8541	0.0088
MUAC	1	–0.0744	0.0533	1.9534	0.1622
Previous macrosomia	1	–1.8416	0.9789	3.5391	0.059

df, degrees of freedom, ANC, antenatal clinic; GDM, gestational diabetes mellitus; MUAC, mid upper-arm circumference.

determine correlation between GDM diagnosed by the WHO and GDM diagnosed by IADPSG criteria, and it was found to be 0.597 (a coefficient of zero being no correlation and a coefficient of one being a strong correlation).

Table 4 shows risk factors associated with GDM. Five per cent of the women reported having previously had macrosomic babies (birth weight > 4 kg). This could not be confirmed as the majority did not have written records of birth weights from previous pregnancies and their responses were based on recall. Seven per cent reported having first-degree relatives with diabetes and 19% reported having had miscarriages or stillbirths in previous pregnancies.

Attending government ANCs, age and parity were associated with having GDM ($p < 0.05$). The risk of having GDM was higher in government compared to private ANCs and this increased with age and parity. A family history of diabetes mellitus, previous miscarriage/stillbirth, BMI, being HIV positive and having hypertension were not associated with GDM ($p > 0.05$).

Seventy-one per cent of the women diagnosed with GDM were lost to follow up post-delivery and complete outcome data were available for only 18 women. There were four miscarriages, four women who had a caesarean section and two babies with macrosomia. Data on follow up for diabetes at six weeks postpartum in particular were missing as this was collected telephonically and some of the women could not be reached.

Discussion

This study showed that the prevalence of gestational diabetes mellitus in Blantyre was low. It also showed a wide discrepancy in the prevalence when IADPSG criteria were used compared to WHO criteria, with a 12-fold increase in the prevalence when the IADPSG criteria were used. To our knowledge, this is the first description of the prevalence of gestational diabetes in the Malawian population.

The HAPO study, with an average BMI of 27 kg/m^2 among its participants, showed a direct correlation between obesity and poor outcomes.[24] Our study population, however, being largely young with few obese women (1% based on MUAC), was different from that described in other studies of risk factors for GDM.

In the nationwide WHO STEPS survey,[13] the prevalence of overweight and obesity among Malawian women was 16 and 2%, respectively. The age of the women screened was 25–64 years, but the majority of the women screened were young, as 46% of the women were between the ages of 25 and 34 years. Our GDM study similarly screened a young population of women and the prevalence of overweight and obesity was 9 and 1%, respectively. From both studies, obesity appears to be rare among Malawian women.

In another 2007 study of 620 patients attending the adult diabetes clinic at QECH, the average BMI in type 2 DM patients was 28.7 kg/m^2.[25] These observations suggest that obesity may not be the main driver for the DM epidemic in Malawi and that other factors such as genetics, low birth weight and stunting may play a larger role.

Advanced maternal age, high parity and attending government ANCs were associated with GDM, the older women being more likely to have high parity than the younger, consistent with traditional risk factors for GDM. Other known risk factors for GDM, such as a family history of DM, a history of macrosomia, previous miscarriages or stillbirths, or MUAC were not associated with GDM.

As observed in the STEPS survey, the majority of DM in the population is undiagnosed; as such a negative family history of DM may in part be a reflection of this. The overall picture however highlights the fact that risk factors for developing GDM may be population specific and there may be genetic variability inherent in the population to explain such differences. This raises a need for exploring population-specific risk factors other than those stated in the WHO guidelines or those from high-income countries.

Women attending private hospitals are generally perceived as having a higher socio-economic status and more likely to adopt a diet rich in refined foods and a sedentary lifestyle than their counterparts. By including private ANCs, we anticipated showing that this group would tend to be more obese and have a higher risk of developing GDM. Our findings though were contrary to this expectation as there was no difference in terms of nutritional status between women from government facilities and those from private hospitals. Furthermore, women at private ANCs were less likely to have GDM than those in government hospitals.

Dietary differences between the two groups were not explored in particular but it appears that the risk that may be conferred by sedentary habits or a Westernised diet may be balanced by better health-seeking behaviour and ready access to screening and diagnostic services in private hospitals.

RBG measurements were largely normal as only three women had RBG levels > 11.1 mmol/l and 75% of the study population had an RBG level below 5.5 mmol/l. Other than the RBG test being an insensitive screening tool, it was also observed on random questioning that many of the women at the health centres had not eaten for some time before the measurement, particularly those who had to leave their homes early in the morning to attend the clinic on time. Their results may reflect a fasting rather than RBG level and may explain the large proportion of women with normal RBG levels. There was no correlation between RBG level and GDM diagnosed by OGTT or risk factors for GDM. The RBG test may therefore not be a sensitive screening tool or used as a proxy for OGTTs in this population.

The prevalence of GDM of 1.6% using WHO criteria was lower than that described in other African studies using the 1999 WHO

diagnostic criteria (8.8% in South Africa and 13.9% in Nigeria),[11,12] but comparable with what was expected by local obstetricians who estimated prevalence between 2 and 3% among women attending ANCs (B Makanani pers commun). GDM was rare, even among those with traditional risk factors for GDM, suggesting there may be a unique environmental or genetic influence on risk factors for GDM in this population.

Using IADPSG criteria, the prevalence of GDM was 12 times higher compared to WHO criteria and, interestingly, showed a higher prevalence in government ANCs compared to private ANCs.

We anticipated finding a higher prevalence of GDM using IADPSG criteria compared to WHO criteria, as has been described in other studies. There are no other published studies from African populations for comparison. Many studies have compared prevalence using the two criteria, with some finding the two to be comparable.[19] The decision to change the criteria depends on performing careful cost analysis and weighing the risk–benefit ratio, particularly in a population that is different from the HAPO population; performance in a non-HAPO population is thought to be lower.[16,17] In a low-income setting, priority should probably be placed on treating those diagnosed with GDM based on WHO criteria.

There was a large loss to follow up among the women diagnosed with GDM, which precludes definitive conclusions on outcome. The causes of the four miscarriages among the women diagnosed with GDM were not explored further.

Limitations

The study had several limitations. The study population, being urban, may have been unrepresentative as it excluded older women in rural settings likely to have risk factors for GDM. Older and multiparous women are less likely to attend formal ANCs. Family history of DM was likely under-reported as most DM in Malawi is undiagnosed. Loss to follow up precluded making meaningful conclusions on outcomes on the already small population of women diagnosed with GDM. Digital instruments used for measuring anthropometric and biochemical data, including glucometers, BP machines and the weight scale, although readily accessible for use in the practical sense, are not always standardised and may be inappropriately calibrated, which could affect quality and reproducibility of data collected.

Being descriptive, definite causal relationships cannot be established. A larger prospective study with OGTTs performed on all women, exploring risk factors for GDM and comparing outcomes between the WHO and IADPSG criteria would reflect better on the usefulness of diagnosing GDM in this population.

Conclusion

Using the WHO criteria, GDM was relatively uncommon in women in Blantyre presenting to ANCs, even among those with traditional risk factors for GDM. This low prevalence has been demonstrated in other sub-Saharan countries and we anticipated that the prevalence would be similar in the Malawian population in general. The implication of the higher prevalence found when the IADPSG criteria were used remains to be explored.

Increasing age, parity and being at government hospitals were associated with GDM in this population. Alternative risk factors other than the traditional known risk factors need to be explored. Maintaining optimal weight should be encouraged as this is the single modifiable risk factor for GDM that was identified in this study. Should screening for GDM be performed, the RBG test is not a sensitive screening tool and risk factor-based screening may be more feasible and cost effective.

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Lower protein diet may lessen risk for cardiovascular disease

Amino acids are the building blocks of proteins. A subcategory, called sulphur amino acids, including methionine and cysteine, play various roles in metabolism and health. 'For decades it has been understood that diets restricting sulphur amino acids were beneficial for longevity in animals,' said John Richie, a professor of public health sciences at Penn State College of Medicine. 'This study provides the first epidemiological evidence that excessive dietary intake of sulphur amino acids may be related to chronic disease outcomes in humans.'

Richie led a team that examined the diets and blood biomarkers of more than 11 000 participants from a national study and found that participants who ate foods containing fewer sulphur amino acids tended to have a decreased risk for cardiometabolic disease based on their bloodwork.

The team evaluated data from the Third National Examination and Nutritional Health Survey. They compiled a composite cardiometabolic disease risk score based on the levels of certain biomarkers in participants' blood after a 10–16-hour fast including cholesterol, triglycerides, glucose and insulin.

'These biomarkers are indicative of an individual's risk for disease, just as high cholesterol levels are a risk factor for cardiovascular disease,' Richie said. 'Many of these levels can be impacted on by a person's longer-term dietary habits leading up to the test.'

Participants were excluded from the study if they reported having either congestive heart failure, heart attack or a reported change in diet due to a heart disease diagnosis. Individuals were also omitted if they reported a dietary intake of sulphur amino acids below the estimated average requirement of 15 mg/kg/day recommended by the Food and Nutrition Board of the National Academy of Medicine.

For a person weighing 132 pounds, food choices for a day that meet the requirement might include a medium slice of bread, a half an avocado, an egg, a half cup of raw cabbage, six cherry tomatoes, two ounces of chicken breast, a cup of brown rice, three quarters of a cup of zucchini, three tablespoons of butter, a cup of spinach, a medium apple, an eight-inch diameter pizza and a tablespoon of almonds. Nutritionists collected information about participants' diets by doing in-person 24-hour recalls. Nutrient intakes were then calculated using the US Department of Agriculture Survey Nutrient Database.

After accounting for body weight, the researchers found that average sulphur amino acid intake was almost two-and-a-half times higher than the estimated average requirement. Xiang Gao, associate professor and director of the nutritional epidemiology laboratory at the Penn State University and co-author of the study, suggested this may be due to trends in the average diet of a person living in the USA.

'Many people in the US consume a diet rich in meat and dairy products and the estimated average requirement is only expected to meet the needs of half of healthy individuals,' Gao said. 'Therefore, it is not surprising that many are surpassing the average requirement when considering these foods contain higher amounts of sulphur amino acids.'

The researchers found that higher sulphur amino acid intake was associated with a higher composite cardiometabolic risk score after accounting for potential confounders such as age, gender and history of diabetes and hypertension. They also found that high sulphur amino acid intake was associated with every type of food except grains, vegetables and fruit.

'Meats and other high-protein foods are generally higher in sulphur amino acid content,' said Zhen Dong, lead author on the study and College of Medicine graduate. 'People who eat lots of plant-based products like fruits and vegetables will consume lower amounts of sulphur amino acids. These results support some of the beneficial health effects observed in those who eat vegan or other plant-based diets.'

Dong said that while this study evaluated only dietary intake and cardiometabolic disease risk factors at one point in time, the association between increased sulphur amino acid intake and risk for cardiometabolic disease was strong. She said the data support the formation of a prospective, longitudinal study evaluating sulphur amino acid intake and health outcomes over time.

'Here we saw an observed association between certain dietary habits and higher levels of blood biomarkers that put a person at risk for cardiometabolic diseases,' Richie said. 'A longitudinal study would allow us to analyse whether people who eat a certain way do end up developing the diseases these biomarkers indicate a risk for.'

Source: Medical Brief 2020

Prevalence of diabetic neuropathy and risk factors for diabetic foot ulcers among patients in a tertiary health institution

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Abstract

Background: **Diabetic foot is one of the most devastating chronic complications of diabetes mellitus and is usually preceded by many risk factors, including peripheral neuropathy. An understanding of these potential risk factors enables early recognition and modification where possible. Hence this study aimed to assess prevalence of peripheral neuropathy and other risk factors for the development of diabetic foot.**

Methods: **This study involved adults diagnosed with type 2 diabetes who were consecutively recruited from the LAUTECH Teaching Hospital Diabetes Clinic, Ogbomoso, Nigeria. Participants were surveyed for the presence of foot ulcers, skin changes, deformities, dystrophic nails and sensory neuropathy, using a 10-g Semmes-Weinstein monofilament, 128-Hz tuning fork, diabetic neuropathy symptoms score and diabetic neuropathy examination score.**

Results: **The mean age was 62.08 ± 8.70 years and 47.5% were male. Diabetes duration was 4.97 ± 4.10 years. The prevalence of active foot ulceration among the study participants was 14.4%. Diabetic peripheral neuropathy (DPN) was diagnosed with monofilament insensitivity in 24.5% of patients, vibration insensitivity in 19.4%, no joint position sense in 12.2%, diabetic neuropathy examination in 15.1% and diabetic neuropathy symptoms score in 41.0%. We found dry skin in 24.5%, claw toes in 19.4%, dystrophic nails in 18.7%, calluses in 11.5% and gangrene in 4.3%.**

Conclusion: **There was a high prevalence of DPN in our patients, with a significant prevalence of diabetic foot ulcer in 14.4%. It is suggested that regular screening for DPN should be performed, with the aim of early recognition and prevention of factors predisposing to foot ulceration.**

Keywords: prevalence, diabetic foot, peripheral neuropathy, risk factors

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Introduction

Diabetic foot, according to the World Health Organisation (WHO) and the International Working Group on the Diabetic Foot, is defined as 'the foot of diabetic patients that has the potential risk of pathologic consequences including ulceration, infection, and/or destruction of deep tissues associated with neurologic abnormalities, various degrees of peripheral vascular disease, and/or metabolic complications of diabetes in the lower limb'.[1] In many developing countries it is a major debilitating complication with severe morbidity and possible amputations. Individuals with diabetes have a higher risk of amputation than non-diabetic subjects.[2-5]

Foot complications are one of the most frequent reasons for hospitalisation in diabetes, accounting for up to 25% of all admissions.[6,7] It has been estimated that 10 to 15% of diabetic patients will develop a foot ulcer at some point in their lifetimes,[8-10] and that the risk of lower-extremity amputation is 15 to 40 times higher in people with diabetes than in those without diabetes.[11] Up to 85% of foot amputations are preventable.[12] Foot ulcers have been reported in a Nigerian population to occur after a mean interval of 13 years from the diagnosis of diabetes.[13]

Hospital-based studies demonstrated that the prevalence of limb ulcerations in Nigeria was between 11.7 and 19.1%.[14,15] In Nigeria, no sufficient data exist to help recognise the magnitude of the risks for diabetic foot. A Nigerian study by Adigun and Olarinoye examined the characteristics of patients with diabetic foot ulcers attending an out-patient clinic at the University of Ilorin teaching hospital. The investigator examined 105 diabetic patients, with a mean age of 54 years, and found the prevalence of diabetic foot ulceration to be 29.5%, callus 5.7% and cracked skin 11.4%.[16]

Because of the high burden of diabetic foot ulceration and its sequelae, identification of patients at risk for foot ulceration is of paramount importance. This is because early detection with the initiation of effective treatment has been shown to reduce the prevalence of diabetic foot ulcerations and lesions by 44 to 85%.[17,18] Therefore, targeting patients at increased risk for developing foot ulcers is believed to constitute a cost-effective strategy to control progression to foot ulceration and amputation.

Diabetic peripheral neuropathy (DPN), which is defined as the presence of symptoms and/or signs of peripheral nerve dysfunction in patients with diabetes after exclusion of other causes,[19] is an independent risk factor for foot ulceration and lower-extremity amputation. It often presents with a loss of sensation on the foot (sensory deficit), which can cause a patient to sustain an injury without recognising any inciting trauma.[19]

While the gold standard for diagnosis of DPN continues to be a nerve conduction study (NCS), it is time consuming, requires a separate patient visit and is costly. This cumbersome procedure

cannot be recommended for screening in many of the hospitals in developing countries. A number of simple methods that are easy to use for regular screening are advocated, however, for early detection of DPN. This early recognition is essential to prevent foot ulceration in patients with diabetes.

Hence, in resource-constrained environments, the use of instruments such as neuropathy symptoms score, neuropathy examination score and the monofilament for detection of neuropathy among patients with diabetes is valuable. The monofilament is a non-invasive, inexpensive, easy-to-use and portable instrument for assessing the loss of protective sensation and it is recommended by several practise guidelines, including the American Diabetes Association,[20] to detect peripheral neuropathy in otherwise normal feet.

Early recognition of 'foot at risk' with the aim of arresting its progression to advanced foot ulcer is an important preventative measure to reduce the prevalence of amputation among individuals with diabetes, preserving quality of life and ameliorating the social and economic costs of diabetic foot disease. Hence this study aimed to determine the frequency and patterns of peripheral neuropathy and other risks that predispose to foot ulcerations among diabetic patients in south-west Nigeria.

Methods

This was a cross-sectional, descriptive study carried out at the diabetic clinic of LAUTECH teaching hospital, Ogbomoso, south-west, Nigeria. All adult diabetes mellitus patients who attended the diabetes clinic for follow-up visits during the study period, met the inclusion criteria and gave their consent, were included in this study. The purpose, nature and significance of the study were explained to each of the participants. The study was approved by the ethics and research committee of the hospital and informed consent was obtained from the study participants.

The main inclusion criteria for selection were being a known diabetic patient who had made at least three visits to the out-patient diabetes clinic, was aged 30 years or older, and with a confirmed diagnosis of type 2 diabetes mellitus based on WHO criteria of a fasting plasma glucose (FPG) level of ≥ 126 mg/dl (7 mmol/l).[21] Exclusion criteria included patients with gestational diabetes and those with amputation due to trauma, or conditions other than diabetes.

The age, gender, marital status, level of education, duration of diabetes, presence of hypertension and smoking history were obtained from the patients using a proforma questionnaire specifically designed for the study. Anthropometric measurements including body weight (kg), body height (m), and waist and hip circumferences (cm), measured with a non-stretchable measuring tape, were made. The height was measured, without shoes, to the nearest 0.1 cm on a stadiometer, and weight was measured, while wearing light clothing, to the nearest 0.1 kg using a standard bathroom scale.

The body mass index (BMI) was calculated as weight (in kg) divided by the square of the height (in m). The WHO classification was used to estimate the degree of obesity.[22] Waist circumference was used to assess central obesity, and was measured from midway between the lower border of the ribs and the iliac crest on the mid-axillary line, while hip circumference was taken as the widest diameter over the greater trochanters.

Blood pressure was measured in the left arm after participants had been seated for at least five minutes, using a digital sphygmomanometer (Omron M X2 Basic, Omron Health Care Co, Ltd, Kyoto Japan). Hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg and/or concomitant use of antihypertensive medications.[23]

The average of three most recent FPG values was used, as less than one-third of the study participants had had glycated haemoglobin (HbA_{1c}) tests. Good glycaemic control was assumed with a FPG level of ≤ 8.0 mmol/l.

The feet of each study participant were examined to identify diabetes-related lesions and other features on the foot that could predispose them to foot lesions in future. The appearance of the feet and inspection of the lower limbs for skin status (colour, thickness, dryness, cracking, trophic changes, loss of skin integuments), bony deformities (such as claws, hammer toes and callus), abnormal nails (colour, thickness, trophic changes), and other features (such as fissures, blistering, oedema, ulceration, gangrene and amputations) were then noted.

A peripheral neuropathy assessment was carried out with the use of the diabetes neuropathy symptoms score (DNS) as previously described.[24] The interviewer assessed five variables on both feet and counted the total points (0–10). A DNS score greater than two on the 10-point scale was considered neuropathic.[23] The diabetes neuropathy examination (DNE) score, which is a modification of the neuropathy disability score of Dyck, consists of eight items, two testing muscle strength, one a tendon reflex, and five sensations.[25] The maximum score is 16 but a score of more than three points is considered abnormal.

Light touch/pressure perception was assessed using the 5.07- or 10-g Semmes-Weinstein monofilament examination (SMWE), where the monofilament is applied perpendicularly to the test sites on each foot. The end of the filament is pressed on the plantar surface of the feet with enough pressure to cause the monofilament to buckle. A 'yes–no' method is used, meaning that the patient says yes each time he/she senses the application of the monofilament. The ability to correctly sense the monofilament on each site was defined as normal, whereas the inability to sense the monofilament correctly in one or more trials was defined as disturbed. Abnormality was assumed with insensitivity in at least four out of the 10 sites.

The 128-Hz tuning fork was struck against the palm of the tester's hand so that it would vibrate for approximately 40 seconds, and then applied to the base of the forehead so that participants could understand the concept of the vibration sensation. After asking the patient to close his/her eyes, the tuning fork was placed on the bony prominence at the dorsum of the first toe, which is just proximal to the nail bed. The participant was asked to report when the vibration stopped, and the tester dampened the tuning fork with the other hand. One point was assigned for each correct perception of vibration ('on' or 'off'). The procedure was performed twice on each foot in such a way that the participants could not anticipate the tester's actions. This is a rule-out test for the presence of neuropathy and does not indicate risks related to future onset.

Statistical analysis

The Statistical Package for Social Sciences version 17.0 (SPSS Inc, Chicago, IL, USA) was used for data analysis. The data were cross checked for data-entry errors. The results were initially analysed by descriptive statistical methods, including mean and standard deviation (SD). The independent *t*-test was used to ascertain the association between outcome variables of diabetic foot complications and their determinants (relevant clinical variables). Statistical significance was set at $p < 0.05$.

Results

A total of 139 participants were recruited for the study, comprising 66 (47.5%) male and 73 (52.5%) female subjects. The mean age was 62.0 ± 8.7 years (range 40–87 years), with males significantly older than females (65.24 ± 8.35 vs 59.07 ± 7.99 years) (p = 0.001). The mean duration of diabetes was 4.97 ± 4.10 years, and was similar in males and females (Tables 1, 2).

Foot lesions observed in this study are recorded as shown in Table 3. The foot symptom/lesion most commonly seen was numbness (n = 69, 49.6%). This was closely followed by a tingling sensation (n = 68, 48.1%), burning sensation (n = 51, 36.7%), previous ulcers (n = 28.1%), dryness (n = 34, 24.5%), skin discolouration in the form of hypo- or hyperpigmentation (n = 27, 19.1%), and previous amputation (n = 7.8%), among others. The presence of foot ulceration and calluses only were significantly higher in males compared to females (p = 0.026 and p = 0.048, respectively).

Table 4, shows the prevalence of neuropathy using both DNE and DNS in the study participants. Evaluation of the symptoms of neuropathy with the DNS questionnaire showed 82 (59%) patients had a score of zero, which indicated that they had no peripheral neuropathy, 21 (15.1%) had a score of one, 11 (7.9%) a score

Table 1. Sociodemographic and clinical characteristics of the study participants (n = 139)

Variable	Number	Percentage
Age group (years)		
40–55	33	23.8
56–70	84	60.4
> 70	22	15.8
Mean ± SD	62.0 ± 8.7	
Range	40–87	
Gender		
Female	73	52.5
Male	66	47.5
Systolic BP (mmHg)		
Normal	81	58.3
High	58	41.7
Mean ± SD	138.2 ± 20.8	
Range	90–190	
Diastolic BP (mmHg)		
Normal	97	69.8
High	42	30.2
Mean ± SD	83.1±11.5	
Range	50–114	
BMI (kg/m²)		
Underweight (< 18.5)	6	4.3
Normal (18.6–24.9)	44	31.7
Overweight (25.0–29.9)	54	38.8
Obese (≥ 30)	35	25.2
Mean ± SD	27.0 ± 5.2	
Range	17.1–60.2	

BP: blood pressure; BMI: body mass index

Table 2. Comparison of the clinical characteristics of the study participants by gender

Variable	Total (mean ± SD)	Male (mean ± SD)	Female (mean ± SD)	p-value
Age (years)	62.00 ± 8.70	65.24 ± 8.35	59.07 ± 7.99	< 0.001
Height (cm)	1.62 ± 0.08	1.68 ± 0.06	1.57 ± 0.05	< 0.001
Weight (kg)	70.77 ± 13.34	72.26 ± 10.15	69.42 ± 15.62	0.212
SBP (mmHg)	138.17 ± 20.85	139.21 ± 19.50	137.22 ± 22.08	0.575
DBP (mmHg)	83.06 ± 11.45	83.17 ± 11.56	82.96 ± 11.43	0.915
DM duration (years)	4.97 ± 4.10	5.23 ± 4.33	4.74 ± 3.90	0.485
FBS (mmol/l)	10.79 ± 4.73	10.86 ± 4.05	10.73 ± 5.30	0.875
BMI (kg/m²)	27.00 ± 5.20	26.35 ± 6.42	27.54 ± 5.64	0.082

SBP: systolic blood pressure; DBP: diastolic blood pressure; DM: diabetes mellitus; FBS: fasting blood sugar; BMI: body mass index.

Table 3. Frequencies of foot lesions/symptoms among the study participants by gender

Variable	Total, n (%)	Male, n (%)	Female, n (%)	p-value
Tingling	68 (48.9)	31 (47.0)	37 (50.7)	0.395
Numbness	69 (49.6)	32 (48.5)	37 (50.7)	0.464
Burning	51 (36.7)	26 (39.4)	25 (34.2)	0.325
Discoloration	27 (19.4)	12 (18.2)	15 (20.5)	0.446
Thinness	18 (12.9)	12 (18.2)	6 (8.2)	0.067
Dryness	34 (24.5)	18 (27.3)	16 (21.9)	0.296
Cracking	31 (22.3)	18 (27.3)	13 (17.8)	0.128
Trophic nail	26 (18.7)	13 (19.7)	13 (17.8)	0.472
Hair loss	23 (16.5)	11 (16.7)	12 (16.4)	0.575
Claw toes	27 (19.4)	15 (22.7)	12 (16.4)	0.235
Hammer toes	25 (18.0)	13 (19.7)	12 (16.4)	0.390
Oedema	7 (5.0)	4 (6.1)	3 (4.1)	0.444
Inter-digital infections	25 (18.0)	13 (19.7)	12 (16.4)	0.390
Ulceration	20 (14.4)	14 (21.2)	6 (8.2)	0.026
Callus	16 (11.5)	4 (6.1)	12 (16.4)	0.048
Blistering	9 (6.5)	4 (6.1)	5 (6.8)	0.564
Gangrene	6 (4.3)	2 (3.0)	4 (5.5)	0.389
Amputation	3 (2.2)	1 (1.5)	2 (2.7)	0.538
Light touch	34 (24.5)	12 (18.2)	22 (30.1)	0.074
Temperature	26 (18.7)	11 (16.7)	15 (20.5)	0.357
Vibration	27 (19.4)	15 (22.7)	12 (16.4)	0.235
Joint position sense	31 (22.3)	15 (22.7)	16 (21.9)	0.535

Table 4. Prevalence of peripheral neuropathy in the study participants according to gender using DNS and DNE scores

Scores	Male, n (%)	Female, n (%)	Total, n (%)
DNS			
0	37 (56.1)	45 (61.6)	82 (59.0)
1	12 (18.2)	9 (12.3)	21 (15.1)
2	6 (9.1)	5 (6.8)	11 (7.9)
3	5 (7.6)	9 (12.3)	14 (10.1)
4	6 (9.1)	5 (6.8)	11 (7.9)
DNE			
0	40 (60.6)	46 (63.0)	86 (61.9)
1	9 (13.6)	11 (15.1)	20 (14.4)
2	5 (7.6)	5 (6.8)	10 (7.2)
3	2 (3.0)	0 (0)	2 (1.4)
4	3 (4.5)	2 (2.7)	5 (3.6)
5	1 (1.5)	3 (4.1)	4 (2.9)
6	1 (1.5)	3 (4.1)	4 (2.9)
7	1 (1.5)	0 (0)	1 (0.7)
8	4 (6.1)	2 (2.7)	6 (4.3)
9	0(0)	1(1.4)	1(0.7)

DNS: diabetes neuropathy symptoms; DNE: diabetes neuropathy examination; n: number of participants.

Table 5. Relationship between neuropathy and the sociodemographic characteristics of the study participants

Scores	Male, *n* (%)	Female, *n* (%)	Total, *n* (%)
DNS			
0	37 (56.1)	45 (61.6)	82 (59.0)
1	12 (18.2)	9 (12.3)	21 (15.1)
2	6 (9.1)	5 (6.8)	11 (7.9)
3	5 (7.6)	9 (12.3)	14 (10.1)
4	6 (9.1)	5 (6.8)	11 (7.9)
DNE			
0	40 (60.6)	46 (63.0)	86 (61.9)
1	9 (13.6)	11 (15.1)	20 (14.4)
2	5 (7.6)	5 (6.8)	10 (7.2)
3	2 (3.0)	0 (0)	2 (1.4)
4	3 (4.5)	2 (2.7)	5 (3.6)
5	1 (1.5)	3 (4.1)	4 (2.9)
6	1 (1.5)	3 (4.1)	4 (2.9)
7	1 (1.5)	0 (0)	1 (0.7)
8	4 (6.1)	2 (2.7)	6 (4.3)
9	0(0)	1(1.4)	1(0.7)

DNS: diabetes neuropathy symptoms; DNE: diabetes neuropathy examination; *n*: number of participants.

of 14 (10.1%) and 11 (7.9%) had scores of two, three and four (maximum score), respectively. Therefore 57 (41.0%) patients had a high DNS score, which indicated that a significant proportion of patients with diabetic neuropathy were symptomatic. In addition, the DNS score was positively associated with duration of diabetes, age, blood glucose level and BMI. The DNE score was significant (> 3) in 21 (15.1%) patients. Using other neuropathy screening modalities, neuropathy was presumed to be present in 34 (24.5%) patients using the monofilament, 27 (19.4%) using the tuning fork, and impaired joint position sense was found in 31 (22.3%) patients.

As shown in Table 5, the risks of developing diabetic foot ulceration were significant with increasing height ($p = 0.041$) and BMI ($p = 0.006$) but were not related to age, blood pressure or level of glycaemic control.

Table 6 shows comparison of peripheral neuropathy as detected by the various screening modalities. Both the 10-g monofilament and impaired joint position sense, as defined by the presence/detection of DPN, had similar sensitivity (24.5 vs 22.3%), while the sensitivity or detection of DPN was highest with the DNS at 41.0% and lowest with the DNE at 15.1%.

Discussion

The most important reason for the evaluation of DPN is to assess the risk of neuropathic foot ulceration, which contributes to 50 to 70% of non-traumatic amputations.[26] The results of this study showed that the overall prevalence of DPN was 41% among diabetes patients in south-west Nigeria. This prevalence is higher than that reported in other populations[27,28] but similar to the 35 and 38% reported in the United Arab Emirates and Saudi Arabia, respectively,[29-31] who used a similar DNE questionnaire.

Table 6. Percentage of neuropathy as identified by different modalities

Modalities	Percentage of neuropathy *n* (%)
DNS	57 (41.0)
DNE	21 (15.1)
Monofilament	31 (24.5)
Tuning fork	27 (19.4)
Impaired joint position sense	31 (22.3)

DNS: diabetic neuropathy score; DNE: diabetic neuropathy examination.

The variation in the prevalence of DPN might be due to variation in the sensitivity and specificity of the various modalities of DPN diagnosis used in those referenced studies, since the sensitivity and specificity of the DNS score has been shown to be high when defined using other standard clinical methods.[6] The DNE questionnaire is a non-invasive screening test only, and not necessarily diagnostic, hence it may be less reliable due to its subjectivity.

The present study used the DNS score and DNE, which were designed by Meijer.[24,32] These scores are simple, reproducible, fast and easy to perform, and were modified from the widely used neuropathy symptoms score and neuropathy disability score of Dyck.[25] The construct validity of these scores in relation to the SWME and the vibration perception test (VPT) has been studied previously.[31,32] The correlation between the DNS score and DNE and NCS was significant ($r = 0.62$ for DNE and 0.51 for DNS).[33] The VPT is considered the gold standard for diagnosis of DPN and a significant correlation has been shown between the VPT score and DNE ($r = 0.532$, $p < 0.001$), DNS ($r = 0.546$, $p < 0.001$) score, absent tuning-fork sensation ($r = 0.590$; $p < 0.001$), monofilament sensation ($r = 0.573$; $p < 0.001$) and ankle reflex ($r = 0.377$, $p = 0.01$).[34] The DNS score and DNE are simple clinical scores that are useful to diagnose peripheral neuropathy in patients with diabetes.

As expected, the DNS, a symptoms score, gives the highest percentage of detection and diagnosis of DPN. This is not surprising as it comprises only symptoms, which could be quite subjective but probably less specific. Also, the DNE, which consists of both symptoms and examination findings, gave the least value (15.1%) of all the screening modalities in this study. It is relatively time consuming compared to the easy-to-use monofilament and tuning fork, both of which require a total of less than two minutes of inspection time per individual.

To improve on both the sensitivity and specificity of the screening methods for the diagnosis of DPN, it has been suggested that two screening methods, for example the SWME and the tuning fork, could be combined.[30] Combining the 10-g SWME and 128-Hz tuning fork makes a practical, highly efficient method suitable for screening of DPN in type 2 diabetes patients in many hospitals in developing countries, including primary health centres with limited diabetes care providers.

Our results show that foot lesions, such as deformity, fissure and dystrophic nails, frequently occurred among these individuals, and are features predisposing them to amputation in future if not detected early. A significant number of diabetic patients in this study (14.4%) had diabetic foot ulcers (DFUs). This is similar to the prevalence of DFUs reported from a hospital-based study conducted in Nigeria,[16] and the 14.3% prevalence reported at the SS Hospital, Banaras Hindu University, Varanasi, India.[35] This might be due to similar levels of healthcare management and socio-economic status of the subjects. Other studies have reported the prevalence of DFUs in the range of 5.3 to 10.5% among diabetic patients.[36,37]

The high prevalence of DPN in this study may have been due to the relatively older patients, poor diabetic foot self-care practices, poor health-seeking behaviour and poor diabetes-related knowledge. Also, the high prevalence of DPN may be related to the significant numbers of people who resided in the rural areas and the practice of walking bare foot.

Our study showed that increasing height of patients was associated with increased risk of diabetic foot. This finding agrees with that of Sosenko *et al.*,[38] who also found patient's height to be associated with diabetic foot. This may be related to increased demyelination in tall patients compared to shorter individuals, with shorter limb nerve fibres. Our study did not find duration of diabetes to be associated with diabetic foot ulceration, which is similar to other studies.[39,40]

The strength of this study was in using many screening instruments for the assessment of DPN. However, the study was limited because the screening instruments could not be compared with a more objective instrument for the diagnosis of DPN, such as nerve-conduction studies or VPT. Hence, the sensitivity and specificity of these screening instruments could not be established.

Conclusion

The aim of this study was to determine risk factors for diabetic foot ulcers among Nigerians. Health practitioners should extend beyond just treating the ulcers; attempts should be taken among diabetics to prevent ulcers in the first place. Screening to identify factors that could accurately predict those who are at risk of foot ulceration is practical in an out-patient setting in a low-resource country. Early identification of these factors, especially diabetic neuropathy, will prevent ulcers forming in patients with diabetes in this environment. Detection of these factors using a simple, less-expensive, easily available and less time-consuming tool could help reduce the incidence of diabetic foot ulcers.

These screenings and foot examinations may even be carried out by nurses and other health practitioners after minimal training. This is important because of a dearth across Nigeria (as in other parts of the world) of diabetes and foot-care specialists (podiatrists) who are key members of the diabetes team. The findings in this study will therefore be helpful in clinical practice to identify diabetic patients prone to developing diabetic foot. The establishment of specialised diabetic foot clinics to address foot problems in our environment and the combination of related health professionals (diabetologists, plastic surgeons, orthopaedic surgeons, diabetes nurses, dieticians and physiotherapists) in the management and preventions of diabetic foot problems will assist in early diagnosis and also reduce the prevalence of foot complications.

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Relationship between obesity and blood pressure among employees in the Vhembe district municipality of Limpopo Province, South Africa

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Abstract

Objective: **The aim of this study was to investigate the relationship between obesity and blood pressure among employees of the Vhembe district municipality of Limpopo province.**

Methods: **A cross-sectional study was conducted among 452 local government employees (207 males, 245 females) aged 24–65 years. Body mass index (BMI), blood pressure (BP) and waist circumference (WC) measurements, and waist-to-height ratio (WHtR) were assessed. Data were analysed using Statistical Package for Social Sciences (SPSS) statistics, version 21.**

Results: **The results showed that 27% of the participants were classified as overweight and 34% as obese, with females being more overweight and obese (29 and 48%, respectively) compared to males (24 and 17%, respectively). Twenty-five per cent of the participants were hypertensive, with females (27%) showing a higher prevalence compared to males (22%). Based on BMI categories, the obese group (35%) had a higher prevalence of hypertension in contrast to groups that were of normal weight (18%) and overweight (22%). The results also showed that systolic blood pressure (SBP) was positively ($p \leq 0.05$) correlated with BMI ($r = 0.15$), WC ($r = 0.26$) and WHtR ($r = 0.29$) in the normal and overweight groups (WC, $r = 0.23$ and WHtR, $r = 0.26$), and WHtR correlated with SBP ($r = 0.26$) and diastolic blood pressure (DBP) ($r = 0.19$).**

Conclusion: **The study showed a high prevalence of overweight, obesity and hypertension, with females more affected than their male counterparts. BMI, WC and WHtR were positively correlated with SBP in the normal and overweight groups, with WHtR positively correlated with both SBP and DBP in the overweight group. Therefore, it is recommended that intervention regimes designed to address obesity and hypertension should consider risk awareness for cardiovascular diseases, impaired quality of life and productivity among local government employees.**

Keywords: obesity, hypertension, employees, blood pressure, body mass index

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Obesity is one of the most important public health problems worldwide.[1] It is a major independent risk factor for chronic diseases, such as cardiovascular disease and diabetes mellitus, and is associated with high morbidity and mortality rates.[2] According to the World Health Organisation (WHO), up to 20% of the population in developed countries may suffer from obesity-associated hypertension, which may account for 78 and 65% of essential hypertension in males and females, respectively.[3,4] The WHO[4] reported that one in six adults is obese and one in three has elevated blood pressure (BP), with the highest prevalence recorded in Africa. Obesity and hypertension are among the preventable risk factors for cardiovascular disease that impose a considerable economic burden, particularly in developing countries.[5]

Hypertension is one of the 10 leading contributors to the global burden of disease and the most important risk factor for mortality worldwide,[4,6,7] and has been described as a silent killer due to its asymptomatic nature among sufferers.[8] Studies have reported that about nine million people die from hypertension annually.[9,10] The prevalence of hypertension in Africa has been reported in several previous studies.[9,11,12] Hypertension was once considered a disease of affluence but is now prevalent among the poor.[13] South Africa is facing a serious burden of hypertension.[14] More than 6.2 million South Africans are hypertensive, with 3.2 million having a BP of > 160 mmHg.[15]

Several studies have shown a clear association with BP increase and weight gain.[5,16,17] It has been reported that obese subjects have a 3.5 times increased likelihood of hypertension and that 60% of hypertension is attributable to an increase in adipose tissue stores.[2] Data from the National Health and Nutrition Examination Survey in 2004 indicated that the prevalence of hypertension among obese individuals with a body mass index (BMI) > 30 kg/m² was 42.5%, compared with 15.3% in lean individuals.[18] Visceral fat distribution is another genetic factor that contributes to the increase in BP levels among obese individuals.[19] In addition, environmental and behavioural factors, such as alcohol intake, cigarette smoking, timing of onset of childhood obesity, change in daily lifestyle habits

and alteration in lipid profile may be implicated in visceral fat distribution and increased BP values.[20-22] Most studies suggest that centrally located body fat is a stronger determinant of BP elevation than peripheral body fat in both men and women.[21,23]

A positive correlation between BMI and BP has been reported among Ghanaian adults aged 30 to 50 years old.[24] Certain occupations, especially white-collar jobs, are characterised by sitting for long periods of time, such as employees in financial institutions and administration offices, and this predisposes individuals to a sedentary lifestyle.[25] These individuals tend to spend the majority of their adult working lives less engaged in physical activity outside of working hours, thereby predisposing them to obesity and diseases.[26] A study in India reported a higher prevalence of hypertension, which was more positively correlated to obesity among employees than the general population of the country.[27]

A recent systematic review among workers in West Africa reported a prevalence of hypertension of 12 to 69% among employees.[28] The prevalence of obesity ranged from 2% among automobile garage employees in Kumasi, Ghana,[29] to 42.1% among healthcare workers in Umuahia, Nigeria.[30] The prevalence of hypertension ranged from 27.9 to 78.9% among obese workers compared with 7.3 to 65.4% among non-obese employees in West Africa.[31] Among healthcare workers in a university teaching hospital, there appeared an unusual ratio in the association between obesity and hypertension, which was 2.2 ($p = 0.004$).[32] In Kaduna, civil servants younger than 40 years old who were overweight or obese were five times as likely to have hypertension compared with healthy-weight workers.[33] Schutte *et al*.[34] reported a prevalence of 48% overweight and obesity among South African employees from 18 companies participating in healthscreening programmes. Cardiovascular risk factors, specifically diabetes and hypertension, were found to be associated with obesity among public service workers in Ondo State, Nigeria.[35]

This study will be first of its kind to study employees in the Vhembe district municipalities of the Limpopo Province to investigate the relationship between obesity and BP.

Methods

The research was based on a cross-sectional design on an available population sample of local government employees in the Vhembe district municipality of the Limpopo Province, South Africa. Participants voluntarily participated in the study.

There were 452 (men = 207; women = 245) participants from local government employees in the Vhembe district, which is one of the five districts of the Limpopo Province of South Africa (local government is a form of public administration in South Africa, which exists as the lowest tier of administration in the provinces). Vhembe district is located in the northern part of the country and shares its borders with the Beitbridge district in Matabeleland south, Zimbabwe. According to the 2001 census, 800 000 Vhembe district residents speak Tshivenda as their mother tongue, while 400 000 speak Tsonga and 27 000 speak Northern Sotho.[36] The majority of the participants in this study were employed as grounds maintenance workers, clerical workers, managers and councillors. The employees were categorised into three age groups as follows: 24–29, 30–44 and 45–65 years. Participants were included in the study if they were within the age categories and deemed healthy. Standing height was measured to the nearest 0.1 cm, using a Harpenden portable stadiometer (Holtain Ltd, Crymych, Dyfed, UK). Body mass was measured using a portable calibrated scale (SECA) and recorded to the nearest 0.5 kg. BMI was calculated as body mass (kg) divided by height (m) squared (kg/m²).

Waist circumference (WC) was measured using a steel tape measure and in accordance with the procedure recommended by the American College of Sports Medicine.[37] For men, low WC in this classification is defined as less than 94 cm, high is 94 to 102 cm, and very high is greater than 102 cm. For women, low WC is less than 80 cm, high is 80 to 88 cm, and very high is greater than 88 cm.[38,39] Waist-to-height ratio (WHtR) was determined from waist circumferences (cm) divided by height (cm). The norms for WHtR were as follows: normal is WHtR < 0.5, while WHtR > 0.5 indicates increased risk for both males and females.[40]

BP was measured by using an automated sphygmomanometer (Omron, Health Care, Inc, USA). The participants were seated, and systolic (SBP) and diastolic (DBP) blood pressure measurements were determined according to the protocols suggested by the American College of Sports Medicine (ACSM).[37]

The ACSM has identified thresholds above which individuals may be at an increased risk for cardiovascular disease.[37] The thresholds that were used to describe risk included the following:

- overweight = BMI between 25 and 29.9 kg/m²; obesity = BMI ≥ 30 kg/m²
- hypertension = SBP ≥ 140 mmHg and DBP ≥ 90 mmHg, as well as for participants on hypertension treatment.

The aim of the study was explained to the participants and their employers, who were also informed that the data would be treated confidentially and would only be used for the purposes of research. The participants were requested to complete and sign an informed consent form before participating in the study. The measurements took place during weekdays, as arranged with the participants. The researcher (a biokineticist registered with the Health Professions Council of South Africa: registration number BK 0016195-HPCSA) was assisted by well-trained research assistants conducting the measurements. The anthropometric measurements of height, weight, WC and BP were taken in allocated separate rooms for males and females. The study received ethical approval (Ref: NWU-00125-13-S1) from the ethics committee of North West University, Potchefstroom, South Africa.

Statistical analysis

Descriptive statistics were calculated for all variables according to gender. Numerical data are expressed as mean and standard deviation (mean ± SD) and categorical data are expressed as percentages. A *t*-test was used to determined differences in the means of variables (age, height, weight, BMI, WC, WHtR, and SBP and DBP between the study groups), and the chi-squared test was used to compare the prevalence of general obesity and central/abdominal obesity in men and women. The differences in BMI and WC across age groups were described by gender, and the chi-squared test was used to compare the prevalence of obesity between the various age groups. To determine the differences between the BMI categories/groups, an analysis of variance (ANOVA) was calculated for all variables. Descriptive characteristics of the hypertensive and normotensive groups were determined and compared. Pearson correlation coefficients were used to determine the relationship between obesity and BP among employees. All statistical analyses were performed with the SPSS, version 21. The statistical level of the p-values was set at $p \leq 0.05$.

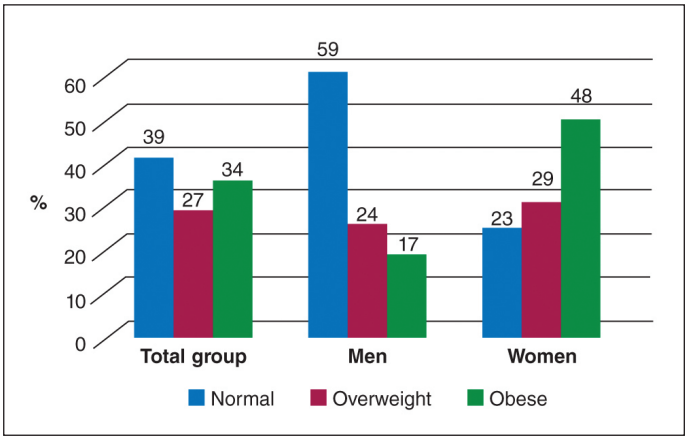

Fig. 1. BMI categories for the total group and by gender.

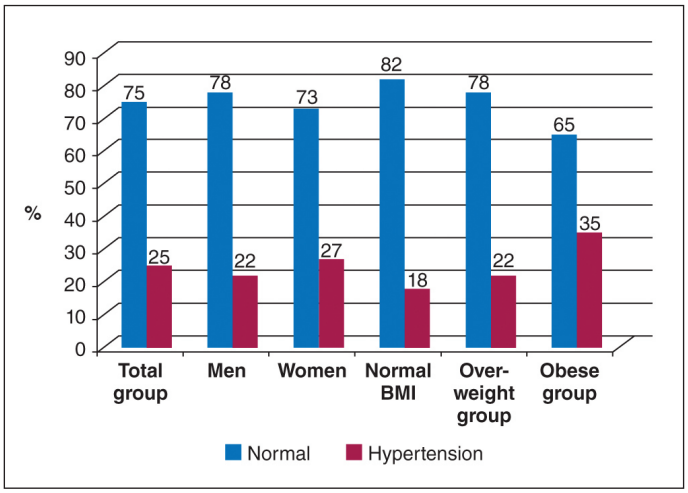

Fig. 2. Hypertension for the total group by gender and BMI categories

Results

Fig. 1 presents the percentage for BMI categories for the total group and by gender. The results show that of the total group, 39% had normal weight, 27% were overweight and 34% were obese. The findings also indicate that 29% of women were overweight compared to 24% of men. Similarly 48% of women were obese in comparison to 17% of men.

Fig. 2 presents the percentage of hypertension for the total group by gender and BMI categories. In the total group, the results show that 25% of the employees presented with hypertension in which the women (27%) were more affected than men (22%). When the data were analysed according to BMI categories, the results showed a significantly higher percentage of hypertension in both the overweight and obese groups.

Table 1 presents the percentages regarding the subjects' characteristics for the total, non-obese and obese groups. The women in the age group of 45 to 65 years had a higher prevalence of overweight (84.7%) and obesity (87.3%) compared to 76.6 and 82.9% of the men (Table 1). The results also show that participants with no education tended to be more overweight (71.1%) compared to those with qualifications, where women were 76.4% overweight and 66.1% obese, in contrast to men who were 63.3% overweight and 65.7% obese. The findings also indicate that 83.5% of grounds maintenance employees were overweight and 79.7% were obese in comparison to participants in other occupations, where women showed a higher preponderance of overweight (90.3%) and obesity (77.1%) compared to men who were 73.5% overweight. Accounting clerks showed a higher percentage of obesity (88.6%) within the obese category.

Presented in Table 2 are the means and standard deviations for overweight and obesity for the total group and by gender. As

Table 1. Subject characteristics of the men, women and total participants in the non-obese and obese groups

	Non-obese group, *n* (%)			Obese group, *n* (%)					
				Total participants		Men		Women	
Variables	Total participants	Men	Women	OV	OB	OV	OB	OV	OB
Age group (years)									
24–29	17 (9.6)	4 (3.3)	13 (23.6)	8 (7)	5 (3)	1 (2)	2 (5.7)	7 (9.7)	3 (2.5)
30–44	14 (7.9)	8 (6.5)	6 (10.9)	13 (11)	16 (11)	9 (18)	4 (11.4)	4 (5.6)	12 (10.2)
45–65	147 (82.6)	111 (90.2)	36 (65.5)	100 (83)	132 (86)	39 (76.6)	29 (82.9)	61 (84.7)	103 (87.3)
Qualification									
No formal education	124 (69.7)	92 (74.8)	32 (58.2)	86 (71.1)	101 (10)	31 (63.3)	23 (65.7)	55 (76.4)	78 (66.1)
Std 8	8 (4.5) 8 (6.5)	8 (14.5)	4 (8.3)	10 (6.5)	2 (4.1)	4 (11.4)	2 (2.8)	6 (5.1)	
Matric	20 (11.2)	12 (9.8)	10 (18.2)	7 (5.8)	18 (12)	3 (6.1)	2 (5.7)	4 (5.6)	16 (13.6)
Diploma	17 (9.6) 7 (5.7)	1 (1.8)	9 (7.4)	16 (10.5)	5 (10.2)	4 (11.4)	4 (5.6)	12 (10.2)	
Degree	1 2 (1.1)	1 (0.8)	1 (1.8)	2 (1.7)	3 (2)	2 (4.1)	1	–	2 (1.7)
Degree	3 1 (0.6)	1 (0.8)	2 (3.6)	5 (4.1)	4 (2.6)	3 (6.1)	1	2 (2.8)	3 (2.5)
Degree 4	3 (1.7)	1 (0.8)	1 (1.8)	7 (5.8)	–	3 (6.1)		4 (5.6)	
Certificate	2 (1.1)	1 (0.8)	–	1 (0.8)	1 (0.7)	–		1 (1.4)	1 (0.8)
Occupation									
General clerk	12 (6.7)	11 (8.9)	1 (1.8)	11 (9.1)	18 (11.8)	8 (16.3)	4 (11.4)	3 (4.2)	14 (11.9)
Accounting clerk	3 (1.7)	1 (0.8)	2 (3.6)	2 (1.7)	7 (4.6)	1 (2.0)	31 (88.6)	1 (1.4)	7 (5.9)
Grounds maintenance workers	160 (89.9)	111 (90.2)	49 (89.1)	101 (83.5)	122 (79.1)	36 (73.5)		65 (90.3)	91 (77.1)
Municipality manager (MM)	1 (0.6)	–	1 (1.8)	6 (6)	2 (1.3)	4 (8.2)		2 (2.8)	2 (1.7)
Councillors	2 (1.1)	–	2 (3.6)	1 (1)	4 (2.6)	–		1 (1.4)	4 (3.4)

OV = overweight; OB = obese, Std 8 = Standard eight (grade 10).

Table 2. Descriptive statistics (mean and standard deviations) of the men, women and total participants in the overweight and obese groups

	Non-obese group, mean ± SD				Overweight and obese group, mean ± SD (n = 274)							
	Total participants				Total participants		Overweight			Obese group		
	(*n* = 178)	Men (*n* = 123)	Women (*n* = 55)	*p*-values	OV (*n* = 121)	OV (*n* = 153)	Men (*n* = 49)	Women (*n* = 72)	*p*-values	Men (*n* = 35)	Women (*n* = 118)	*p*-values
Height	167.94 ± 8.80	170.71 ± 7.19	161.76 ± 9.27	< 0.001	164.15 ± 8.39	160.87 ± 10.73	170.22 ± 7.38	160.01 ± 6.26	< 0.001	165.60 ± 17.34	159.47 ± 7.31	0.003
Weight	64.90 ± 7.97	66.75 ± 7.93	60.75 ± 6.38	< 0.001	76.67 ± 7.77	92.85 ± 14.67	81.50 ± 7.68	73.38 ± 5.93	< 0.001	95.09 ± 14.77	92.19 ± 14.77	0.31
BMI	22.99 ± 2.05	22.89 ± 2.13	23.23 ± 1.83	0.30	28.42 ± 1.46	35.92 ± 4.92	28.09 ± 1.42	28.65 ± 1.46	0.04	34.97 ± 5.06	36.20 ± 4.87	0.19
WC	84.20 ± 11.02	85.24 ± 12.30	81.85 ± 6.92	0.05	93.92 ± 10.76	105.42 ± 14.42	96.53 ± 7.13	92.15 ± 12.39	0.03	105.81 ± 15.70	105.31 ± 14.08	0.86
SBP	138.53 ± 23.10	142.20 ± 23.05	130.31 ± 21.17	0.001	137.74 ± 21.71	145.76 ± 24.06	138.45 ± 18.07	137.25 ± 23.98	0.77	138.23 ± 21.06	147.99 ± 24.52	0.05
DBP	77.04 ± 13.62	78.05 ± 14.53	74.80 ± 11.11	0.14	79.26 ± 11.26	84.90 ± 12.49	80.67 ± 10.97	78.31 ± 11.43	0.26	79.57 ± 10.49	86.48 ± 12.63	0.004
WHtR	0.50 ± 0.07	0.50 ± 0.07	0.51 ± 0.05	0.58	0.57 ± 0.07	0.65 ± 0.08	0.57 ± 0.04	0.58 ± 0.08	0.43	0.62 ± 0.07	0.66 ± 0.08	0.04

OW = overweight; OB = obese.

shown in the results, the mean height for the non-obese group was 167.94 ± 8.80 cm (from the total group of 178 participants). Men were taller on average (170.71 ± 7.19 cm) than women (161.76 ± 9.27 cm). The mean weight was 64.90 ± 7.97 kg for the total group, in which men were heavier (66.75 ± 7.93 kg) than women (60.75 ± 6.38 kg). Regarding BMI, the mean value for the total group was 22.99 ± 2.05 kg/m²; however, specific values were 22.89 ± 2.13 kg/m² for men and 23.23 ± 1.83 kg/m² for women.

Mean BP data for the total group were as follows: SBP (138.53 ± 23.10 mmHg), DBP (77.04 ± 13.62 mmHg), whereas corresponding values for men and women, respectively, were SBP 142.20 ± 23.05 mmHg and DBP 78.05 ± 14.53 mmHg, and SBP 130.31 ± 21.17 mmHg and DBP 74.80 ± 11.11 mmHg. The mean height for participants who were overweight and obese was 164.15 ± 8.39 cm and 160.87 ± 10.73 cm, respectively, for the total participants. In total, participants who were overweight and obese had a mean weight of 76.67 ± 7.77 and 92.85 ± 14.67 kg, respectively. However, the mean BMI for overweight and obese groups was, respectively, 28.42 ± 1.46 and 35.92 ± 4.92 kg/m². For the total group, the average SBP for overweight and obese participants, respectively, was 137.74 ± 21.71 and 145.76 ± 24.06 mmHg, with a mean DBP of 79.26 ± 11.26 and 84.90 ± 12.49 mmHg.

Table 3 presents ANOVA results for the variables of interest according to the three BMI categories. The results show significant group differences ($p = 0.05$) for height, with normal and overweight men being taller than underweight and obese counterparts, while no significant group differences ($p = 0.18$) were found among the women's BMI categories. Significant group differences ($p \leq 0.05$) were observed for body weight, BMI, WC and WHtR, with the overweight and obese groups having high mean values. Additionally, the results showed significant differences in the SBP and DBP for both overweight and obese women. No significant group differences ($p \geq 0.05$) were found in the blood pressure variables for men.

Provided in Table 4 are the descriptive data (mean, minimum, maximum and SD) for the overweight and obese groups by gender. The mean age and height of the participants in the obese group were as follows: men (51.84 ± 8.60 years; 168.34 ± 11.90 cm) and women (52.95 ± 9.07 years; 159.46 ± 6.94 cm). Corresponding data for body weight included the following: men (83.97 ± 13.43 kg) and women (83.80 ± 15.67 kg). The mean BMI of the obese group was 29.76 ± 4.81 kg/m² in men, and 32.91 ± 5.52 kg/m² in women, with a mean WC of 98.06 ± 11.96 and 99.41 ± 15.04 cm obtained for men and women, respectively. In the obese group the mean SBP was 140.44 ± 20.21 mmHg for men, and 143.61 ± 24.61 mmHg for women. However, the mean DBP was 80.23 ± 12.93 and 82.79 ± 12.93 mmHg for the men and women, respectively. The results also show that there was a significant difference ($p \leq 0.05$) in height, BMI and WHtR among men and women.

Table 5 presents the correlation coefficients for the normal, overweight and obese groups. In all three BMI groups, BW, WC, BMI and WHtR were significantly and positively related to each other. In the normal group, SBP was positively ($p \leq 0.05$) correlated with BMI ($r = 0.150$), WC ($r = 0.26$) and WHtR ($r = 0.29$). In the overweight category, WC was significantly ($p \leq 0.05$) and positively correlated with SBP ($r = 0.23$), and WHtR was positively associated with both SBP ($r = 0.26$) and DBP ($r = 0.19$).

Discussion

The purpose of this study was to investigate the relationship between obesity and BP among employees in the Vhembe district municipality of the Limpopo Province, South Africa. The study showed that 27 and 35% of the total participants were overweight and obese, respectively. These findings were higher in comparison to a study by Lategan, *et al*.,[41] which found that half of the participants from the black urban population of the Free State community had a BMI above normal (23% overweight and 32% obese). The results of this study concur with the findings of WHO,[42] which estimated that 45.1% of the South African population were overweight and obese. Schutte, *et al*.[34] reported a prevalence of 48% overweight and obesity among South African employees from 18 companies participating in health-screening programmes.

The findings of this study, according to gender, showed that females were more overweight and obese (29, 48%) compared to males (24, 17%). This is higher when compared to findings by the South African Demographic and Health Survey,[43] reporting that 18.7% of urban black men were overweight and 8.1% were obese, with 27.1% of urban black women being overweight and 33.8% obese. Our findings confirmed the trend that black South African women have substantially higher BMIs than their male counterparts. Overweight or obese individuals are at greater risk of developing metabolic (type 2 diabetes and dyslipidaemia) and non-metabolic disorders.[44]

The study also found a 25% prevalence of hypertension in the total group; this is lower when compared with a study by Maepa *et al*,[45] which reported a 39.5% prevalence of hypertension among employees in the gold mines of Gauteng's Harmony Gold Mining Company in South Africa. This also corresponds

Table 3. Participants' anthropometric and physiological characteristics according to BMI categories by gender

	Men				Women			
Variables	***n***	**Mean**	**SD**	***p*-value of the differences**	***n***	**Mean**	**SD**	***p*-value of the differences**
Height (cm)								
Underweight	15	169.73	9.94	0.05	1	169.00	.	0.18
Normal	123	170.71	7.19		55	161.76	9.27	
Overweight	49	170.22	7.38		72	160.01	6.26	
Obese	35	165.60	17.34		118	159.46	7.31	
Total	222	169.73	9.81		246	160.18	7.55	
Body weight (kg)								
Underweight	15	49.51	5.77	< 0.001	1	51.00	.	< 0.001
Normal	123	66.75	7.93		55	60.75	6.38	
Overweight	49	81.50	7.68		72	73.38	5.93	
Obese	35	95.09	14.77		118	92.19	14.63	
Total	222	73.31	15.35		246	79.49	17.09	
BMI (kg/m^2)								
Underweight	15	17.17	1.23	< 0.001	1	17.85	.	< 0.001
Normal	123	22.89	2.13		55	23.23	1.84	
Overweight	49	28.09	1.42		72	28.65	1.46	
Obese	35	34.97	5.07		118	36.20	4.87	
Total	222	25.55	5.58		246	31.01	6.45	
WC (cm)								
Underweight	15	73.47	4.56	< 0.001	1	79.00	.	< 0.001
Normal	123	85.24	12.30		55	81.85	6.92	
Overweight	49	96.53	7.13		72	92.15	12.39	
Obese	35	105.81	15.70		118	105.31	14.08	
Total	222	90.18	14.63		246	96.11	15.56	
SBP (mmHg)								
Underweight	15	138.80	27.28	0.65	1	156.00	.	< 0.001
Normal	123	142.20	23.05		55	130.31	21.17	
Overweight	49	138.45	18.07		72	137.25	23.98	
Obese	35	138.23	21.06		118	147.99	24.52	
Total	222	140.52	21.98		246	140.93	24.63	
DBP (mmHg)								
Underweight	15	83.27	15.13	0.44	1	92.00	.	< 0.001
Normal	123	78.05	14.53		55	74.80	11.11	
Overweight	49	80.67	10.96		72	78.30	11.43	
Obese	35	79.57	10.49		118	86.48	12.63	
Total	222	79.22	13.29		246	81.50	12.91	
WHtR								
Underweight	15	0.43	0.02	< 0.001	1	0.46	.	< 0.001
Normal	123	0.50	0.08		55	0.50	0.05	
Overweight	49	0.56	0.04		72	0.57	0.07	
Obese	35	0.62	0.07		118	0.65	0.08	
Total	222	0.53	0.08		246	0.60	0.09	

BMI = body mass index, WC = waist circumference. SBP = systolic blood pressure, DBP = diastolic blood pressure, WHtR= waist-to-height ratio, n = number, SD = standard deviation.

with findings by Owalabi *et al*.,[46] which revealed that 49.2% of the Buffalo City metropolitan municipality adults had a high prevalence of hypertension. The findings of the study are also lower when compared to a study by Day *et al*.,[47] which reported a 40% prevalence of hypertension among adults in South African provinces during 2010. Peer *et al*.[48] also reported a lower prevalence of hypertension (38.9%) among black urban South African adults between the ages of 24 and 65 years in Cape Town.

The study showed that women (27%) had a higher prevalence of hypertension compared to males (22%). This is lower than the study by Ntuli *et al*.[49] in adults in a rural community of Dikgale in the Limpopo Province, which showed that 42% of males and 41% of females were hypertensive.

The findings of our study are also similar to those of the South Africa Demographic and Health Survey (SADHS),[50] which reported that using a cut-off of 140/90 mmHg and gender adjustment, 25% of men and 26% of women had hypertension. Based on BMI categories, our study showed that obese groups (35%) had a high prevalence of hypertension when compared to the normal (18%) and overweight groups (22%). These findings are similar to a study by Dua *et al*.,[51] which found that the prevalence of high BP was greater in those with high BMI. This has also been reported in other studies.[52,53] The WHO[4] reported that hypertension was globally responsible for 45% of deaths due to cardiovascular disease and 51% of deaths due to stroke. According to Ibrahim and Damasceno,[54] as well as the WHO,[4] an estimated one billion people worldwide are hypertensive, and this number is expected to rise to 1.56 billion by 2025.

Table 4. Descriptive statistics of age, height, BMI, WC, SBP, DBP and WHtR for the overweight and obese group by gender

Variables	*n*	Min	Max	Mean	SD	F	*p*-value
Age, years							
Men	108	25.0	65.0	51.84	8.60	1.096	0.30
Women	201	24.0	65.0	52.95	9.07		
Height, cm							
Men	108	107.0	189.0	168.34	11.90	68.607	< 0.001
Women	201	135.0	182.0	159.46	6.94		
Weight, kg							
Men	108	55	132	83.97	13.43	0.009	0.93
Women	201	51	172	83.80	15.67		
BMI, kg/m^2							
Men	108	25.10	55.11	29.76	4.81	24.941	< 0.001
Women	201	25.09	64.06	32.91	5.52		
WC, cm							
Men	108	70	170	98.06	11.96	0.645	0.42
Women	201	37	152	99.41	15.04		
SBP, mmHg							
Men	108	91.0	193.0	140.44	20.21	1.308	0.25
Women	201	86.0	229.0	143.61	24.61		
DBP, mmHg							
Men	108	54.0	115.0	80.23	11.12	3.041	0.08
Women	201	54.0	141.0	82.79	12.93		
WHtR							
Men	108	0.42	0.91	0.5786	0.06	18.969	< 0.001
Women	201	0.23	0.94	0.6215	0.09		

BMI = body mass index, WC = waist circumference. SBP = systolic blood pressure, DBP = diastolic blood pressure, WHtR= waist-to-height ratio, *n* = number, SD = standard deviation.

These studies also found that all measures of body composition (WC, BMI and WHtR) significantly correlated with WC and WHtR. BMI and WC positively correlated with SBP in the normal group. The same trend was observed in other studies, where a statistically significant association was found between hypertension and BMI among employees working at Port Said University.[55] The results of the study also found that, in the overweight group, WC correlated significantly with SBP, and WHtR correlated positively with both SBP and DBP. These findings correspond with those of Dua *et al*.,[51] who showed a statistically significant positive correlation between all the anthropometric measures and BP parameters (SBP and DBP). These findings are also in agreement with other studies, which found that anthropometric variables such as BMI, WC and WHtR were frequently positively associated with BP among employees in West Africa.[28] Obesity emerged as a strong predictor of hypertension among employees in Ghana.[31]

Table 5. Correlation coefficients (*r*) for normal, overweight and obese groups

Groups	BW, *r*	BMI, *r*	WC, *r*	SBP, *r*	DBP, *r*	WHtR, *r*
Normal						
BW (kg)	–	0.51**	0.50**	0.05	–0.02	0.09
BMI	0.51**	–	0.42**	0.15*	0.004	0.52**
WC	0.50**	0.42**	–	0.26**	0.11	0.82**
WHtR	0.09	0.52**	0.82**	0.29**	0.14	–
Overweight						
BW (kg)	–	0.22*	0.51**	0.01	0.08	–0.09
BMI	0.22*	–	0.23*	0.17	0.23*	0.44**
WC	0.51**	0.23*	–	0.23*	0.18	0.71**
WHtR	–0.09	0.44**	0.71**	0.26**	0.19*	–
Obese group						
BW (kg)	–	0.57**	0.59**	0.02	0.09	0.19*
BMI	0.57**	–	0.47**	0.04	0.11	0.57**
WC	0.59**	0.47**	–	0.15	0.07	0.78**
WHtR	0.19*	0.57**	0.78**	0.14	0.08	–

**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).
BW = body weight, BMI = body mass index, WC = waist circumference, SBP = systolic blood pressure, DBP = diastolic blood pressure, WHtR = waist-to-height ratio.

The high prevalence of overweight/obesity in this study linked to the prevalence of hypertension agrees with the International Study of Salt and Blood Pressure,[56] which reported a strong, significant, independent association between BMI and BP. From the literature, it was revealed that obesity is associated with more pronounced changes in BP during a 24-hour cycle and a higher SBP, DBP and pulse pressure, indicating autonomic dysfunction or hypertension.[57] All these risk factors may contribute to the increase in prevalence of chronic diseases and absenteeism among employees.[58,59]

The major constraint of the study was the difficulty in collecting data from all the municipalities that participated. Inclusion of all employees from the Vhembe district would have enriched the data collected. In addition, it was not feasible to collect 24-hour BP data from the participants due to logistical challenges. This would have shed more light on the observed relationships between WC and WHtR measures. It would be important in future studies to address these challenges.

Conclusion

Females showed a higher percentage of obesity and hypertension than their male counterparts. The obese group showed a high prevalence of hypertension compared with the other groups. Body composition measures were associated with BP parameters (more especially, BMI, WC and WHtR), which showed a positive significant relationship in both normal and overweight groups. Therefore, this study recommends that intervention regimes designed to address the risk of obesity and hypertension should focus on the awareness of cardiovascular diseases, impaired quality of life, and low productivity associated with obesity and hypertension among local government employees in the Vhembe district of Limpopo Province.

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How to drink responsibly if you are diabetic

According to the World Health Organisation (WHO), the average South African consumes 11 litres of alcohol in a year, which is almost twice as much as the global average. Out of 195 countries surveyed, South Africa closes in the top 30. In addition, the International Diabetes Federation (IDF) counts 3.5 million diabetics in South Africa and about two million further cases are undiagnosed.

With these statistics in mind and the country now being in Advanced Level 3 for Covid-19, which entails a further easing of restrictions on alcohol and ludic activities, the need is great for education on alcohol consumption for people living with diabetes or those who are at risk.

'When you eat a meal, your blood sugar level usually spikes within two hours and drops after four hours. At this point the liver releases stored glucose into the bloodstream to keep your sugar level up within the normal range. When you drink, ethanol, which is a substance found in alcohol, it is toxic to the body. It therefore takes priority to be metabolised by the liver. During this process, the liver is unable to release glucose into the bloodstream, which causes hypoglycaemia, or low blood sugar level,' says Omy Naidoo, Dietician at Newtricion Wellness Dieticians.

However, the real danger resides in the fact that the symptoms displayed by a hypoglycaemic are very similar to that of a person who is intoxicated. 'You may slur your speech, wobble around, feel dizzy or weak. So if you are having a night out with people, and have a low blood sugar level, your mates may think you have just had too much to drink rather than thinking you are having a medical emergency,' added Naidoo.

When this goes untreated, low blood sugar level can cause seizures, loss of consciousness, and, in worst cases, death. There is a popular maxim among diabetics: a high sugar level may be fatal over the year, but a low blood sugar level will kill you in a matter of hours.

As a diabetic, being mindful of the following may assist in minimising the risks associated with alcohol:

- Drink according to what diabetes experts recommend, which is two alcoholic drinks per day for men and one drink per day for women. A single drink is the same as a tot of spirits, or 330 ml of beer or a medium glass of wine.
- If taking medication in the evening, such as insulin or tablets, try to have a sober person around to assist you. A common scenario is that the intoxicated patient dials up more insulin than usually taken.
- Exercise lowers your blood sugar levels, and in the event of heavy drinking as well as late-night dancing, this could increase your risk of having hypoglycaemia.
- Work with a dietician to formulate a plan as to how you incorporate alcohol into your diet without compromising your health goals.
- Always wear a medic alert bracelet that states you are diabetic, so that people around you may pick up that you could be having a medical emergency rather than being intoxicated.

Prevalence of hypertension and selected cardiovascular risk factors among adolescents in selected rural and urban secondary schools in Botswana

MATSHIDISO MOKGWATHI, JULIUS CHACHA MWITA

Abstract

Background: **Adolescent hypertension and other cardiovascular risk factors tend to track into adulthood. Consequently, there is a need to determine the prevalence of hypertension and pre-hypertension, and its co-existence with glycaemia, obesity, tobacco and alcohol use among senior secondary school students in Botswana.**

Methods: **A cross-sectional study was undertaken between December 2015 and March 2016 among students in selected rural and urban senior secondary schools in Botswana. Data were collected through a self-administered questionnaire, measurements and fasting blood glucose testing. Participants were asked about cigarette smoking, alcohol use and levels of physical activity. Body weight, height, waist circumference, blood pressure and fasting blood glucose levels were measured. Hypertension, pre-hypertension, overweight and obesity were defined based on gender, age and height from normative tables.**

Results: **A total of 252 students with a mean age (standard deviation) of 17.1 (0.9) years participated in the study. Rural students were older than urban students (17.5 vs 16.7 years; $p < 0.001$). The prevalence of hypertension and prehypertension were 13.1 and 15.5%, respectively. Physical inactivity (37.7%), overweight/obesity (10.3%) and alcohol intake (9.1%) were also prevalent. Cigarette smoking was rare (2.0%). Impaired fasting glucose levels were found in 1.6% of participants, and none had diabetes mellitus. Hypertension ($p < 0.001$) and cigarette smoking ($p = 0.019$) were more prevalent among male than female participants. Female students were more likely to be overweight or obese than male students ($p < 0.001$). There were no urban–rural differences in hypertension, pre-hypertension and smoking. Urban students were more likely to drink alcohol than rural students ($p = 0.008$).**

Conclusion: **Hypertension, overweight/obesity and alcohol intake were common among these adolescents in Botswana. Strategies to reduce the risk factors of cardiovascular diseases should be urgently developed and implemented to prevent cardiovascular disease-related morbidity and mortality in the future.**

Keywords: hypertension, cardiovascular risk factors, adolescents, Botswana

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Demographic and epidemiological changes in sub-Saharan Africa (SSA) have resulted in an increase in non-communicable diseases, including hypertension, leading to concerns and activities to reduce rising rates.[1-4] In children and adolescents, hypertension is often underdiagnosed and may progress into adulthood.[5-8] The prevalence of hypertension among children in developed countries is 1–5%.[9] By contrast, the prevalence of hypertension in SSA paediatric populations is 0–12.5 and 0–21.5% for boys and girls, respectively.[10]

Hypertension is usually found in constellation with obesity, smoking, alcohol intake and physical inactivity.[10] All these may track from childhood to adulthood and are predictive of cardiovascular risk later in adult life.[10] The prevalence of all the above risk factors has been increasing among children, mainly as a consequence of urbanisation and changes in lifestyle.[11-13] Urbanisation has led to an increase in the use of tobacco and alcohol, poor diet and physical inactivity.[14-16]

For a country with a high burden of HIV/AIDS, the increase in non-communicable diseases, including cardiovascular disease (CVD) and diabetes, poses a challenge for health policymakers and providers to the already stretched health system and progress towards the development of millennium goals.[17-19] This is particularly important in Botswana with its high rate of HIV/AIDS, alongside the wish to maintain universal healthcare.

There is evidence that early identification and modification of risk factors during childhood decreases the occurrence and magnitude of associated complications due to CVD.[10,20] However, data on the burden of hypertension and other cardiovascular risk factors among adolescents in Botswana are currently scarce. Consequently, the objective of this study was to determine the prevalence of hypertension and co-existing selected cardiovascular risk factors among secondary school students in Botswana and to use the findings, if pertinent, to guide future strategies in Botswana.

Methods

This cross-sectional study was conducted from December 2015 to March 2016 among students in the rural Shakawe senior secondary school and the urban St Joseph's College in Botswana. Shakawe is

the only senior secondary school in the Okavango, a sub-district with a population of 2 529 inhabitants, mostly subsistent farmers and pastoralists.[21] St Joseph's College is located in Gaborone, the capital city, with a population of 231 592.[21]

The two schools were conveniently selected based on their ease of accessibility and to provide widely different populations. There were 36 and 42 classes at St Joseph's College and Shakawe senior secondary school, respectively. Four classes were selected from each school using a simple random-sampling technique.

All students in the selected classes were invited to participate in the study and were provided with a written description of the study, and informed consent forms to take to their parents/guardians (written in both English and Setswana). If willing to allow their child to participate, parents/guardians were then asked to sign the consent form. Students agreeing to participate signed assent forms.

Ethical approval for this study was obtained from the Ministry of Health institutional review board [HPDME: 13/18/1 Vol. X (152)]. Permits were obtained from the Ministry of Education and Skills Development, local authorities in Okavango and Gaborone and from each school administration.

Information on date of birth, gender, alcohol intake and tobacco use, and the level of physical activity was obtained using self-administered questionnaires. Personal and family history of heart disease, hypertension, kidney disease, diabetes mellitus, dyslipidaemia and stroke were also documented. Height was measured in all participants without footwear to the nearest 0.1 cm using a stadiometer. Weight was measured using a digital scale to the nearest 0.1 kg in light clothing and without footwear.

We used WHO AnthroPlus version 1.0.4 software to calculate body mass index (BMI) for all participants aged below 18 years.[22] BMI z-scores according to age, gender and height were recorded for each participant and designated as underweight [z-score < –2 standard deviations (SD)]; normal weight (z-score –2 SD – +1 SD); overweight (z-score +1 SD – +2 SD); and obese (z-score > +2 SD). For participants ≥ 18 years, adult BMI reference values were used for underweight (≤ 18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25–30 kg/m^2) and obesity (≥ 30 kg/m^2).[23]

Waist circumference (WC) was measured to the nearest centimetre in light clothing at the level of the umbilicus using a non-distensible measuring tape. Using the Canadian percentile charts for WC based on gender and age, WC > 90th percentile was categorised as overweight for students < 18 years.[24] For students ≥ 18 years, adult cut-offs of 94 cm and 80 cm were used for males for females, respectively.[23]

After five minutes of rest, two seated blood pressure (BP) measurements were taken from the participants' right arms using portable sphygmomanometers (BPCB0A–2H, China). The second measurement was taken after a five-minute interval and the average of the two BP readings was recorded. An average systolic blood pressure (SBP) or diastolic blood pressure (DBP) ≥ 95th percentile for age, gender and height was used to define hypertension. Pre-hypertension was defined as SBP and/or DBP ≥ 90th percentile but < 95th percentile.

A repeat blood pressure measurement was done after one week for participants whose readings were consistent with pre-hypertension and hypertension during the initial measurement. Participants whose average SBP and/or DBP remained high in the second visit were categorised as hypertensive and pre-hypertensive as appropriate.[25,26] We also defined hypertension among participants who self-reported current antihypertensive medication use.

Fasting blood glucose (FBG) level was measured in mmol/l on capillary blood from a finger-prick test using the Accucheck Performa system (Roche Diagnostics, Mannheim, Germany) following a minimum fasting period of eight hours in participants not known to have diabetes mellitus. Using the American Diabetes Association diagnostic criteria, participants were classified as having normal fasting glucose levels (< 5.6 mmol/l), impaired fasting glucose (5.6–6.9 mmol/l) or diabetes mellitus (≥ 7.0 mmol/l).[27]

Alcohol use was defined as any reported alcohol consumption in the previous year, while cigarette smokers were current smokers. We assessed self-reported physical exercise duration and intensity in the previous week (both at school and during leisure time) to three levels of physical activity: inactive, minimally active and health-enhancing physical activity.[28]

Statistical analysis

The prevalence of hypertension and selected risk factors among adolescents is unknown in Botswana. Consequently, the sample size was calculated from the assumption that the prevalence of hypertension in Botswana was 20%, similar to that found in South Africa.[29] We needed 250 participants to determine the true prevalence of hypertension with a margin of error of ± 5%.

Data were entered and analysed using SPSS for Windows, version 23.0 (IBM Corporation). Continuous variables (fasting blood glucose, height, weight, WC, SBP, DBP and age) were summarised by means (± SD). Counts and percentages summarised categorical variables. A Pearson's chi-squared test was used to compare the prevalence of selected cardiovascular risk factors (hypertension, diabetes mellitus, smoking, obesity/overweight, level of physical activity and alcohol use) between urban and rural students.

For univariate analysis of continuous variables (fasting blood glucose, height, weight, WC, age), the Student's *t*-test was used. A *p*-value less than 0.05 was considered statistically significant. Variables that were variables with $p < 0.25$ in the univariate analysis were included as independent variables for the multivariable logistic regression.

Results

A total of 252 students (132 from Shakawe senior secondary school and 120 from St Joseph's College) participated in the study (Table 1). Of these, 172 (68.3%) were females, and the mean (SD) age was 17.1 (0.9) years. Students from the rural school were older than those from the urban school (17.5 vs 16.7 years; $p < 0.001$). None of the participants had a history of diabetes mellitus, stroke or dyslipidaemia.

Overall, obesity or overweight was observed in 10.3% of students (12.5% in the urban school and 8.3% in the rural school). Female students were more likely to be overweight or obese than male students (Table 2). Underweight was found in 25 (9.9%) students, and was more prevalent in male than in female students. There were no urban–rural differences in the prevalence of underweight. None of the study participants had diabetes mellitus. Impaired fasting glucose was found in 1.6% of participants (all females), 1.7 and 1.5% among urban and rural school participants, respectively.

Twenty-three (9.1%) participants reported drinking alcohol. Urban students were more likely to drink alcohol than rural students (14.2 vs 4.5%; $p = 0.008$). Smoking was rare in both schools. However, male students were more likely to report cigarette smoking than female students (0.6 vs 5%; $p = 0.019$).

Table 1. Characteristics of student participants at St Joseph's and Shakawe senior secondary schools (*n* = 252)

Characteristics	All (*n* = 252)	St Joseph's (*n* = 120)	Shakawe (*n* = 132)	*p*-value
Mean age (SD), years	17.4 ± 0.9	16.74 ± 0.74	17.49 ± 0.9	< 0.001
Age groups, years				
< 18 years, *n* (%)	182 (72.2)	104 (86.7)	78 (59.1)	< 0.001
≥ 18 years, *n* (%)	70 (27.8)	16 (13.3)	54 (40.9)	
Gender				
Girls, *n* (%)	172 (68.3)	83 (69.2)	89 (67.4)	0.767
Boys, *n* (%)	80 (31.7)	37 (30.8)	43 (32.6)	
Height, mean (SD), cm	164.9 ± 8	163.42 ± 7.8	166.19 ± 8	0.006
Mean WC (SD), cm	69.3 ± 7.1	68.00 ± 7.8	70.49 ± 6.3	0.006
Mean weight (SD) kg	55.6 ± 9.9	55.3 ± 11.4	55.88 ± 8.7	0.670
Mean HC (SD), cm	91.3 ± 9.5	90.45 ± 11.2	92.0 ±7.5	0.208
Mean FBG (SD), mmol/l	4.70 ± 0.5	4.70 ± 0.44	4.71 ± 0.47	0.788
Mean SBP (SD), mmHg	118 ± 13.2	112.39 ± 12.6	122.62 ± 12.7	< 0.001
Mean DBP (SD), mmHg	71.8 ± 9.5	68.5 ± 9.5	74.8 ± 8.4	< 0.001
Mean pulse (SD), bpm	80.3 ± 13.3	79.1 ± 11.7	81.4 ± 14.6	0.164
Family history of HPT, *n* (%)	75 (29.8)	42 (35)	33 (25)	0.083
Family history of DM, *n* (%)	15 (6)	10 (8.3)	5 (3.8)	0.128
Family history of stroke, *n* (%)	16 (6.3)	2 (1.7)	16 (10.6)	0.004

HPT: hypertension; DM: diabetes mellitus; FBG: fasting blood glucose; WC: waist circumference; HC: hip circumference; BMI: body mass index; SBP; systolic blood pressure; DBP: diastolic blood pressure; bpm: beats per minute, SD: standard deviation.

There were 37.7% inactive students, and inactivity was more common in Shakawe senior secondary school students than those at St Joseph's College. Physical activity did not vary with gender in the two schools.

The mean (SD) SBP and DBP was 118 (13.2) and 71.8 (9.5) mmHg, respectively, and BP was significantly higher among students in the rural school than those in the urban school (Table 1). Overall, the prevalence of hypertension and pre-hypertension was 13.1 and 15.5%, respectively (Table 2). There were no urban–rural differences in hypertension and pre-hypertension. Hypertension was more prevalent among male (OR = 4.3) than female participants (Table 3).

Discussion

In this study, conducted among adolescents in a rural and urban setting in Botswana, a high burden of hypertension was found in constellation with obesity, tobacco use, alcohol use, obesity and physical inactivity. All these may track from childhood to adulthood and are predictive of increased cardiovascular morbidity and mortality later in adult life.[10] For a country with a high burden of HIV/AIDS, the increase in non-communicable diseases is a challenge to the already stretched health system.[17,18]

The prevalence of all the above risk factors has been increasing among children, mainly as a consequence of urbanisation and change in lifestyle,[11-13] with urbanisation leading to an increase in the use of tobacco and alcohol, poor diet and physical inactivity.[14-16] The prevalence of hypertension found in this study was within the prevalence of 0.2 to 24.8% reported in the recent meta-analysis of hypertension studies among African children and adolescents.[30]

Although our findings are consistent with previous studies, we recognise that comparing the prevalence of paediatric hypertension is a challenge due to differences in the definition of hypertension, the age groups of the studied populations and the blood measurement methodology. Nonetheless, the burden of hypertension among our participants was appreciably higher than the prevalence of 3 to 5% among adolescents in the developed world.[31] We also observed a high prevalence of pre-hypertension in our adolescents.

Table 2. Table showing the distribution of cardiovascular risk factors among students at St Joseph's and Shakawe senior secondary schools (*n* = 252)

	School				Gender		
Parameters	All (*n* = 252)	St Joseph's (*n* = 120)	Shakawe (*n* = 132)	*p*-value	Female (*n* = 172)	Male (*n* = 80)	*p*-value
Hypertension, *n* (%)							
Normal	180 (71.4)	89 (74.2)	91 (68.9)	0.380	138 (80.2)	42 (52.5)	< 0.001
PreHPT	39 (15.5)	19 (15.8)	20 (15.2)		20 (11.6)	19 (23.8)	
Hypertension	33 (13.1)	12 (10)	21 (15.9)		14 (8.1)	19 (23.8)	
Overweight or obesity, *n* (%)							
Underweight	25 (9.9)	11 (9.2)	14 (10.6)	0.536	9 (5.2)	16 (20)	< 0.001
Normal weight	201 (79.8)	94 (78.3)	107 (81.1)		141 (82)	60 (75)	
Overweight/obese	26 (10.3)	15 (12.5)	11 (8.3)		22 (12.8)	4 (5.0)	
WC, cm							
Normal	229 (90.9)	108 (90)	121 (91.7)	0.109	162 (94.2)	77 (96.3)	
0.491							
Increased	23 (9.1)	12 (10)	11 (8.3)		10 (5.8)	3 (3.8)	
Fasting blood glucose, mmol/l							
Normal	248 (98.4)	118 (98.3)	130 (98.5)	0.923	168 (97.7)	80 (100)	0.169
IFG	4 (1.6)	2 (1.7)	2 (1.5)		4 (2.3)	0 (0.00)	
Level of physical activity, *n* (%)							
Inactive	95 (37.7)	32 (26.7)	63 (47.7)	0.002	70 (40.7)	25 (31.3)	0.164
Minimal	76 (30.2)	45 (37.5)	31 (23.5)		53 (30.8)	23 (28.8)	
Highly active	81 (32.1)	43 (35.8)	38 (28.8)		49 (28.5)	32 (40)	
Smoking, *n* (%)	5 (2)	3 (2.5)	2 (1.5)	0.567	1 (0.6)	4 (5.0)	0.019
Alcohol intake, *n* (%)	23 (9.1)	17 (14.2)	6 (4.5)	0.008	14 (8.1)	9 (11.3)	0.425

PreHPT: pre-hypertension; HPT: hypertension; BMI: body mass index; WC: waist circumference; IFG: impaired fasting glucose.

Table 3. Factors associated with hypertension among students at Shakawe and St Joseph's senior secondary schools (*n* = 252)

	Bivariate analysis			Multivariate analysis		
Variable	**Crude OR**	**95% CI**	***p*-value**	**Adjusted**	**95% CI**	***p*-value**
Gender						
Female	1 (ref)	1 (ref)		1 (ref)	1 (ref)	1 (ref)
Male	3.5	1.66–7.44	0.001	* 4.31	1.83–10.13	< 0.001
School						
Shakawe (rural)	1					
St Joseph's (urban)	0.59	0.28–1.25	0.168*	0.62	0.26–1.44	0.263
Age	0.98	0.66–1.46	0.923			
Alcohol intake						
No	1 (ref)	1 (ref)				
Yes	3.57	0.47–27.44	0.221	4.86	0.44–54.0	0.198
Smoking						
No	1 (ref)	1 (ref)				
Yes	4.65	0.75–28.91	0.1	7.47	0.544–102.59	0.132
BMI category						
Normal weight	1 (ref)	1 (ref)				
Underweight	0.64	1.03–7.13	0.563	0.457	0.089–2.345	0.348
Overweight/obese	2.72	1.03–7.13	0.043*	2.998	0.716–12.56	0.133
WC	1.07	1.02–1.13	0.005			
Fasting blood glucose	1.32	0.59–2.93	0.496			
Physical activity						
Inactive	1.19	0.51–2.77	0.681	–	–	–
Minimally active	0.65	0.24–1.76	0.393	–	–	–
Highly active	1 (ref)	1 (ref)		–	–	–
Family history of hypertension	0.73	0.31–1.69	0.458	–	–	–
Family history of diabetes	1.022	0.22–4.75	0.980	–	–	–
Family history of stroke	0.425	005–3.33	0.415	–	–	–

PreHPT: pre-hypertension; HPT: hypertension; BMI: body mass index; WC: waist circumference; IFG: impaired fasting glucose.

This is a cause for concern in Botswana where about a third of adults are hypertensive.[32,33] As childhood hypertension progresses to adulthood, the findings suggest that a significant proportion of our participants are at high risk of becoming hypertensive in adulthood.[34] We did not observe an urban–rural difference in the prevalence of hypertension. However, our participants from the rural school were significantly older than their urban counterparts, making it difficult to compare the two populations.

Both hypertension and pre-hypertension were more common in the male students than the females in our study. Our finding may be explained by the fact that male students were significantly older than their female colleagues. Results from the most recent meta-analysis on hypertension in adolescents in Africa however showed no difference between boys and girls in the prevalence of hypertension.[30,35-37]

Similar to other studies, overweight/obesity was associated with up to a four-fold increased risk of hypertension among our participants.[5, 29,35,36,38-41] A similar link between obesity and CVD has been established among adults.[42] Overweight/obesity and hypertension are some of the components of the metabolic syndrome, an indicator of high risk for CVD as well as type 2 diabetes.[43]

The burden of overweight and obesity among our participants is consistent with reports from other SSA countries where between 2.5 and 10.6% of adolescents are overweight or obese.[2,39,41,44] There is evidence that the increase in overweight/obesity is associated with urbanisation.[2] Although we did not see a rural–urban difference in the prevalence of overweight/obesity, earlier data from urban students in Botswana reported a higher proportion of overweight and obesity.[45] Consistent with other studies, overweight/obesity affected more girls than boys.[29]

Although none of the students was found to have diabetes mellitus, 1.6% of participants had IFG. As for the other components of the metabolic syndrome, IFG is a cardiovascular risk factor.[43] This is in contrast to findings from Cote d'Ivoire where 0.4 and 14.5% of adolescents had diabetes mellitus and IFG, respectively.[46] The reasons for this discrepancy are not clear.

A small proportion of both rural and urban students reported using tobacco. This is lower than earlier data from Botswana, in which 10% of the students were current tobacco smokers, and up to 29% reported having tried smoking.[47] Our findings are also inconsistent with the Global Youth Tobacco Survey (GYTS), which reported a prevalence of 10–33% among 13–15-year-olds.[48] Tobacco use was more common among males than females, consistent with a previous study in Botswana.[32] The lower prevalence of tobacco use among our participants was possibly due to under-reporting of tobacco use because of its prohibited use within schools in Botswana.

Only about 9% of our students reported using alcohol. The figure is lower than what would be expected in a country where nearly half (48.4%) of adults are said to consume alcohol regularly,[32] and again may be due to under-reporting. Similar to a study in Australia, our urban students were more likely to use alcohol than their rural counterparts.[49] It is possible that urban students have more access to alcohol than those in the rural setting, contributing to these findings.

We observed a lower level of physical activity among rural than urban students. This finding was unexpected, most likely explained by the fact that rural students were in a boarding school therefore had minimal travelling distance to their classes.[45]

There are some limitations. The study had a small sample size and relied on some self-reported variables that were prone to recall bias. We measured blood pressure on only two visits. More than two readings would have been needed to provide the best estimate of blood pressure.

Conclusion

This study has shown that hypertension, overweight/obesity and alcohol intake were common among these senior secondary school students in Botswana. Strategies to prevent the risk factors of CVD should be developed and implemented to avoid CVD-related morbidity and mortality in the future. These strategies are being advanced and will be the subject of future research.

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Yale study adds to evidence of diabetes drug's link to heart risk

Rosiglitazone was associated with a 33% increased risk of a composite cardiovascular event (heart attack, heart failure, cardiovascular and non-cardiovascular related death) compared with controls, found a Yale analysis of 130 trials involving 48 000 patients.

This study is the most comprehensive evaluation of the cardiovascular risk of rosiglitazone ever done. Rosiglitazone belongs to a class of drugs called thiazolidinediones. It helps control blood sugar levels in patients with type 2 diabetes, but it can also increase the risk of serious heart problems. This has led to suspension of the drug in Europe and previous restrictions on its use in the US.

However, since 2007, studies have reported conflicting findings about whether rosiglitazone increases the risk of heart attacks. But these studies didn't have access to the raw data, also known as individual patient-level data (IPD), from clinical trials and mostly relied on summary-level data (results reported in publications and clinical trial registries), which are not as reliable when estimating the true safety profile of drugs.

Recent efforts by GlaxoSmithKline (GSK), the maker of rosiglitazone, to make IPD available to external investigators prompted a team of US researchers at Yale School of Public Health and the Yale-New Haven Health System to re-analyse the data and clarify some of the uncertainties about rosiglitazone's cardiovascular risk. They analysed the results of more than 130 trials involving over 48 000 adult patients that compared rosiglitazone with any control for at least 24 weeks. IPD were available for 33 trials, which included 21 156 patients; the remaining trials had only summary-level data available.

When the researchers analysed the IPD from trials made available by GSK, they found rosiglitazone was associated with a 33% increased risk of a composite cardiovascular event (heart attack, heart failure, cardiovascular and non-cardiovascular related death) compared with controls. This was estimated from the 274 events among 11 837 rosiglitazone patients and 219 events among 9 319 control patients.

When examining cardiovascular events independently, the analyses of the 33 GSK trials with IPD resulted in higher estimates of the risk of heart attacks than the analyses of trials with IPD and summary-level data.

'These findings highlight the potential for different results derived from different data sources, and demonstrate the need for greater clinical trial transparency and data sharing to accurately assess the safety of drugs,' say the researchers.

'Our study suggests that when evaluating drug safety and performing meta-analyses focused on safety, IPD might be necessary to accurately classify all adverse events,' they write. 'By including these data in research, patients, clinicians and researchers would be able to make more informed decisions about the safety of interventions.'

They add: 'Our study highlights the need for independent evidence assessment to promote transparency and ensure confidence in approved therapeutics, and post-market surveillance that tracks known and unknown risks and benefits.'

Source: Medical Brief 2020

Persistent cardiac arrest caused by profound hypokalaemia after large-dose insulin injection in a young man with type 1 diabetes mellitus: successful rescue with extracorporeal membrane oxygenation and subsequent ventricular assist device

YING-HSIANG WANG, CHIEN-SUNG TSAI, YI-TING TSAI, CHIH-YUAN LIN, HSIANG-YU YANG, JIA-LIN CHEN, PO-SHUN HSU

Abstract

A 28-year-old man who had a history of type 1 diabetes mellitus with poor medication compliance was referred to the emergency department of our institute with suspected diabetic ketoacidosis. The patient developed sudden cardiac arrest following continuous insulin administration. Laboratory data revealed severe hypokalaemia. Cardiopulmonary resuscitation was performed immediately for 63 minutes. Although his spontaneous circulation resumed, the haemodynamics remained unstable. Peripheral extracorporeal membrane oxygenation was therefore employed for mechanical circulatory support. Echocardiography under these conditions revealed generalised hypokinesia of the bilateral ventricles. The left ventricular ejection fraction was only 10–15%. The chest film revealed bilateral pulmonary congestion. The patient developed multiple organ dysfunction, including acute kidney injury, liver congestion and persistent pulmonary oedema, although the hypokalaemia resolved. A temporary bilateral ventricular assist device (Bi-VAD) was used for superior systemic perfusion and unloading of the bilateral ventricles after 16 hours of extracorporeal membrane oxygenation support. After the start of maintenance using the Bi-VAD, extracorporeal membrane oxygenation was discontinued and the inotropic agents were tapered down immediately. Subsequently, the haemodynamics stabilised. All the visceral organs were well perfused with Bi-VAD support. Subsequent echocardiography demonstrated recovery from the myocardial stunning, with the left ventricular ejection fraction returning to 50–60%. The Bi-VAD was gradually weaned and successfully removed 12 days after implantation. The patient had an uneventful recovery and was discharged without organ injury. Over one year of follow up in our out-patient clinic, adequate cardiac function and improved diabetes control were found.

Keywords: hypokalaemia, cardiac arrest, cardiogenic shock, ventricular assist device

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Profound hypokalaemia (< 2.5 mmol/l), a severe complication following subcutaneous administration of insulin, is reported in 5–10% of patients with type 1 diabetes mellitus,[1] and can easily be resolved through potassium infusion. Clinical manifestations of hypokalaemia vary in severity, depending on the acuteness and degree of the hypokalaemia. Although mild degrees of hypokalaemia are usually asymptomatic, severe degrees can lead to marked muscle weakness, ileus, and lethal arrhythmia, including cardiac arrest, ventricular tachycardia (VT) and ventricular fibrillation (Vf). The incidence of Vf has been found to be three- to five-fold higher in patients with low serum potassium compared with patients with high serum potassium concentrations.[2,3]

Although the mortality rate for hypokalaemia-related VT/ Vf has not been reported, the mortality rate for cardiogenic shock following cardiopulmonary resuscitation (CPR) is 50–80%.[4] Herein, we report on a young man who developed refractory hypokalaemia-induced VT/Vf and cardiogenic shock following CPR. We performed emergent veno-arterial (VA)-mode extracorporeal membrane oxygenation (ECMO) in the emergency room; thereafter, a bilateral ventricular assist device (Bi-VAD) was implanted to provide cardiogenic shock after CPR.

Case report

A 28-year-old man with a history of type 1 diabetes mellitus and inadequate compliance with insulin administration was referred to our emergency department due to general weakness with impaired consciousness lasting one day. Laboratory data revealed hyperketonaemia (blood ketone level 7.6 mmol/l), hyperglycaemia

[glucose level 1 091 mg/dl (60.55 mmol/l)] and diabetic ketoacidosis (serum bicarbonate level 6.8 mmol/l). Additionally, leukocytosis (white blood cell count 20.90 × 103 cells/µl) and hyperkalaemia (K^+ 5.3 mmol/l) were noted.

Under suspicion of diabetic ketoacidosis, an insulin pump (insulin actrapid 50 units usage in 500 ml normal saline) was immediately administered at a rate of 60 ml/h. However, cardiac arrest occurred abruptly. An electrocardiogram revealed pulseless VT (Fig. 1) and CPR was immediately performed with sequential defibrillation, which was repeated five times. Laboratory data revealed severe hypokalaemia (K^+ 1.6 mmol/l). Large-dose inotropes including dopamine (17.3 mcg/kg/min) and norepinephrine (26.5 mcg/kg/min) were administered. Simultaneously, continuous KCl infusion was performed. However, the haemodynamic status remained inadequate with refractory VT and low cardiac output.

Peripheral VA-ECMO implantation was therefore performed through the right femoral vein and artery at a pump speed of 3 000 rpm and flow rate of 3.3 l/min. A Glasgow coma scale result of E2M2Vt was observed. Blood pressure was approximately 70/60 mmHg irrespective of the high doses of inotropes, and occasional VT was noted despite anti-arrhythmia medication. Moreover, echocardiography revealed generalised hypokinesia of the bilateral ventricles with left ventricular ejection fraction of 10–15%. However, despite the VA-ECMO support, the patient developed multiple organ dysfunction, including acute kidney injury, congestive liver and severe pulmonary oedema.

We therefore changed the VA-ECMO to a temporary continuous-flow Bi-VAD (Levitronix® CentriMag) for better systemic perfusion (Fig. 2). Using a sternotomy and under the guidance of transoesophageal echocardiography, the left ventricular assist device (L-VAD) inflow tube was inserted from the right superior pulmonary vein into the left ventricular apex, whereas the outflow tube was cannulated on the ascending aorta.

The right VAD (R-VAD) inflow tube was inserted into the right atrium, and the outflow tube was inserted into the pulmonary artery. The operation time was approximately two hours. The initial L-VAD pump speed was 3 700 rpm and flow rate was 4.74 l/min. The R-VAD pump speed was 3 000 rpm and flow rate was 4.87 l/min (Table 1).

For severe hypoxaemia resulting from pulmonary oedema, an oxygenator was inserted into the L-VAD outflow to optimise systemic oxygenation. Mean arterial pressure (MAP) was maintained at 75–80 mmHg with low-dose norepinephrine (4.3 mcg/kg/min). Potassium level was maintained within the range 4.2–4.7 mmol/l and serum glucose level within 180–220 mg/dl (9.99–12.21 mmol/l).

At the time of maintaining support with Bi-VAD, the ventilator was set at 40% FiO_2 with positive end-expiratory pressure at 8 cmH_2O to prevent alveolar collapse. The support pressure was set at 12–15 cmH_2O to achieve an optimal tidal volume status (6–8 ml/kg), and the plateau pressure was controlled under 24 cmH_2O. During the time of support with VAD, the patient's MAP was closely monitored and both VAD and inotropic agents were gradually tapered down to prevent vasoconstriction in the vital visceral organs.

Systemic heparinisation was performed to maintain an active clotting time of 140–160 seconds to prevent thromboembolism. Additionally, a broad-spectrum antibiotic was prophylactically prescribed following the Bi-VAD implantation. On day three of Bi-VAD implantation, the pulmonary oedema was completely resolved; subsequently, the oxygenator was taken down from the L-VAD outflow. Although renal function did not recover immediately, it recovered completely after hospitalisation with temporary haemodialysis (post-VAD implantation days one to nine). Following 12-day support with the Bi-VAD, the myocardial stunning was adequately improved; eventually, the Bi-VAD was removed successfully.

Table 1 presents the biochemistry data, inotrope dosages and echocardiography presentation during the VAD course. The patient was weaned off the ventilator, and extubation was performed three days after VAD removal. The day after extubation, the patient was transferred to an ordinary ward and discharged one week later. Out-patient follow up revealed normal cardiac and renal function and cognition, and adequate control of diabetes.

Discussion

Hypokalaemia is a common electrolyte imbalance present in 20% of hospitalised patients,[5] and some of these patients require immediate

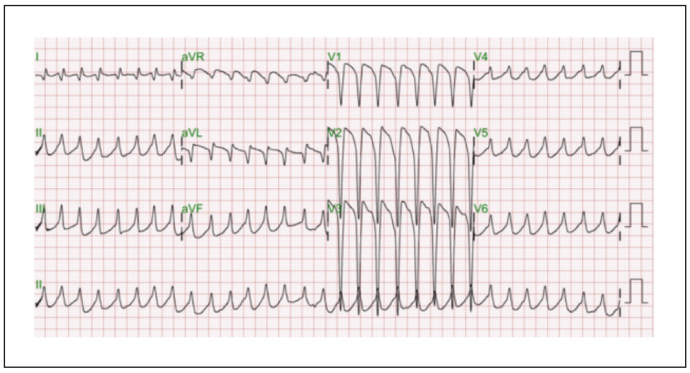

Fig. 1. Electrocardiogram demonstrating refractory ventricular tachycardia despite correction for profound hypokalaemia.

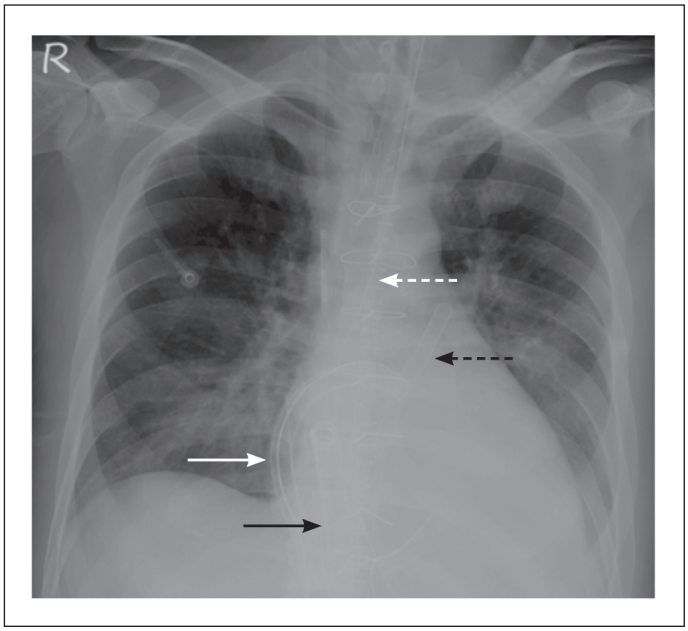

Fig. 2. The chest plain film demonstrates the L-VAD inflow tube from the right superior pulmonary vein (solid white arrow), outflow tube into the ascending aorta (dotted white arrow), R-VAD inflow tube from the right atrium (solid black arrow), and outflow tube into the pulmonary artery (dotted black arrow).

Table 1. Biochemistry data, inotrope dosage and echocardiography presentation during the VAD course

	Before VAD	POD1	POD2	POD3	POD4	POD5	POD7	POD11	Day 3 after removal
K^+ (mmol/l)	1.6	4.2	4.7	3.7	3.5	3.5	3.3	3.5	3.1
BNP (pg/ml)	176								
CK (U/l)	4862	> 10000	> 10000	> 10000			3292		
Tro-I (ng/ml)	8.28	7.11	5.765	3.813			1.516		
BUN (mg/dl)	60		26		28		31	61	78
Cr (mg/dl)	4.2		2.5		2.6		2.1	3.7	3.0
Urine output (ml/day)	170	995 (haemodyalysis)	1720 (haemodyalysis)	1620 (haemodyalysis)	3060 (haemodyalysis)	3420 (haemodyalysis)	4160 (haemodyalysis)	1480	2295
Norepinephrine (mcg/kg/min)	26.5	14.4	12.8	2.65	–	–	–	–	–
Dopamine (mcg/kg/min)	17.3	9.4	9.35	8.7	8.65	8.65	8.65	8.65	–
Epinephrine (mcg/kg/min)	16.7	13.3	13	2.7	–	–	–	–	–
L-VAD (rpm/flow)	3700/4.74	3700/5.07	3700/4.86	3600/4.5	3500/4.14	3400/3.81	2100/1.30	–	
R-VAD (rpm/flow)	3000/4.87	3000/5.02	2700/4.4	2600/4.2	2400/3.75	2200/3.31	1200/0.91	–	
MAP (mmHg)	65	65–75	65–75	80–90	78–86	88–100	97–105	72–82	95–100
Echocardiography LVEF (%)	10–15			30–35			51		

POD = post-operative day; L-VAD = left ventricular assist device; R-VAD = right ventricular assist device, BUN = blood urea nitrogen; CK = creatinine kinase.

pharmacological treatment. Insulin-induced hypokalaemia results in a decrease in serum potassium level due to intracellular potassium shifts and, potentially, the aldosteronelike effect of insulin on the renal tubule further increases urinary potassium losses.

The goal of the treatment for insulin-induced hypokalaemia (K^+ < 2.5 mmol/l) is to replenish potassium stores through slow intravenous infusion of KCl,[6] with insulin therapy delayed until serum potassium levels are corrected back to > 2.5 mmol/l.[7] The most severe complication of hypokalaemia is lethal arrhythmia, such as VT/Vf. Potassium replenishment and cardioversion defibrillation should be performed immediately.

In our case, the patient experienced in-hospital cardiac arrest (IHCA) resulting from hypokalaemia-induced VT/Vf. Extracorporeal CPR (ECPR) restored tissue and end-organ perfusion to allow stabilisation and recovery of function. ECPR can be defined as the implantation of VA-ECMO in a patient who has experienced a sudden and unexpected pulseless condition attributable to cessation of cardiac mechanical activity.[8] Many prospective and retrospective studies have demonstrated the superiority of ECPR over conventional CPR regarding the odds of survival and neurological outcome.[9–11] ECPR can be viewed as a late intervention in a moribund patient, possibly a candidate for an earlier circulatory support system in case of IHCA.

Compared with ECMO, which provides both cardiac and pulmonary support, a Bi-VAD usually provides cardiac support only. However, a Bi-VAD can be implemented long term with more cardiac support than ECMO, especially when the ECMO is set up peripherally. Moreover, patients on ECMO support usually require large doses of inotropes, which cause extreme vasoconstriction and lead to malperfusion of the visceral organs. In patients with refractory cardiogenic shock, a VAD has been reported to provide a better survival rate than VA-ECMO.[12]

In the current case, although VA-ECMO was instituted for mechanical circulatory support and the potassium level was corrected back to the normal range, the patient experienced cardiogenic shock with multiple organ dysfunction and exacerbations. Therefore, ECMO was substituted with Bi-VAD implantation for optimal systemic perfusion. More importantly, the Bi-VAD completely unloaded the bilateral ventricle, maximising the likelihood of recovery from myocardial stunning.[13] Based on our experience, the indications for VAD intervention can be defined for these critical patients with ECMO support (Table 2).

In our case, following Bi-VAD implantation, we were able to immediately withdraw the inotropes and all the visceral organs were preserved. Bedside echocardiography showed no distention of the bilateral ventricle. Initially, the pulse pressure was narrowed but returned three days later, which implied that the myocardial stunning was completely resolved.

The CentriMag VAD (Levitronix LLC) was chosen for several reasons. First, it has continuous flow, which is reported to have better outcomes than pulsatile flow, especially for lower incidence of bleeding and thromboembolism.[14,15] Second, Levitronix CentriMag VAD was used as a temporary short-term VAD as a bridge towards recovery and transplantation, if not the destination. Unlike with a long-term VAD, it is easy to implant the device without extensively damaging the myocardium. More crucially, repairing the cannulation sites during explanation of the VAD is simple. Third, from the economic perspective, it is much cheaper than a permanent long-term VAD such as the HeartMate and HeartWare devices. Fourth, after CPR, most patients develop pulmonary oedema and poor oxygenation, and an oxygenator is always required for optimal oxygenation. The Levitronix CentriMag VAD, categorised as an extracorporeal VAD, can be easily integrated with an oxygenator, which is not possible with an intracorporeal VAD.

Table 2. Indications of VAD intervention after ECMO support

1. ECMO flow insufficiency; ECMO complications
2. Any organ dysfunction with ECMO maximal flow
3. Three or more inotropes or large dose
4. Narrow pulse pressure, ≥ 10 mmHg
5. Sustained VT resulted from LV distension
6. Echocardiography:
   - No opening of aortic valve
   - LV thrombus formation
   - Blood stasis in LV, presented as smoke swirl sign

Conclusion

The Levitronix® CentriMag VAD was able to temporarily provide satisfactory mechanical circulatory support in acute decompensated heart failure. It can provide better circulatory support than ECMO. Additionally, it is easy to set up and repair without causing considerable damage to the myocardium if a bridge to recovery is expected. In this case, the Levitronix® CentriMag VAD was successfully implemented to save the life of a young patient who had experienced hypokalaemia-related cardiac arrest resulting from iatrogenic insulin infusion.

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'Robust study' endorses link between red/processed meats and cardiovascular disease

Eating two servings of red meat, processed meat or poultry, but not fish, per week was linked to a 3–7% higher risk of cardiovascular disease and a 3% higher risk of all causes of death, the study found.

'It's a small difference, but it's worth trying to reduce red meat and processed meat like pepperoni, bologna and deli meats,' said senior study author Norrina Allen, associate professor of preventive medicine at Northwestern University Feinberg School of Medicine. 'Red meat consumption also is consistently linked to other health problems like cancer.'

'Modifying intake of these animal protein foods may be an important strategy to help reduce the risk of cardiovascular disease and premature death at a population level,' said lead study author Victor Zhong, assistant professor of nutritional sciences at Cornell University, who did the research when he was a postdoctoral fellow in Allen's laboratory.

The findings come on the heels of a controversial meta-analysis published last November that recommended people not reduce the amount of red meat and processed meat they eat. 'Everyone interpreted that it was OK to eat red meat, but I don't think that is what the science supports,' Allen said. 'Our study shows the link to cardiovascular disease and mortality was robust,' Zhong said.

'Fish, seafood and plant-based sources of protein such as nuts and legumes, including beans and peas, are excellent alternatives to meat and are under-consumed in the US,' said study co-author Linda van Horn, professor of preventive medicine at Feinberg who also is a member of the 2020 US Dietary Guidelines Advisory committee.

The study found a positive association between poultry intake and cardiovascular disease, but the evidence so far isn't sufficient to make a clear recommendation about poultry intake, Zhong said. Still, fried chicken is not recommended.

The study pooled together a large diverse sample from six cohorts, included long follow-up data of up to three decades, harmonised diet data to reduce heterogeneity, adjusted a comprehensive set of confounders and conducted multiple sensitivity analyses. The study included 29 682 participants (mean age of 53.7 years at baseline, 44.4% men and 30.7% non-white). Diet data were self-reported by participants, who were asked a long list of what they ate for the previous year or month.

Key findings: a 3–7% higher risk of cardiovascular disease and premature death for people who ate two servings a week of red meat and processed meat; a 4% higher risk of cardiovascular disease for people who ate two servings per week of poultry, but the evidence so far is not sufficient to make a clear recommendation about poultry intake and the relationship may be related to the method of cooking the chicken and consumption of the skin rather than the chicken meat itself; and no association between eating fish and cardiovascular disease or mortality.

'Limitations of the study are participants' dietary intake was assessed once, and dietary behaviours may have changed over time. In addition, cooking methods were not considered. Fried chicken, especially deep fat-fried sources that contribute trans fatty acids, and fried fish intake have been positively linked to chronic diseases,' Zhong said.

The study was funded by National Institutes of Health/National Heart, Lung, and Blood Institute (R21 HL085375), American Heart Association Strategically Focused Research Networks and the Feinberg School of Medicine.

Source: Medical Brief 2020

Report and case study

Diabetes and thromboembolic risk

PETER ROSSING, MANESH PATEL

Introduction

Today most practising clinicians are aware of the rampant spread of diabetes throughout the world. Most estimates suggest that diabetes affects between 30% and 35% of the population. This report considers the interface between diabetes and cardiovascular disease, which manifests as coronary artery disease, stroke and/or peripheral arterial disease, chronic kidney disease (CKD), atrial fibrillation (AF) and their individual and combined impacts on prognosis. Professor Peter Rossing discusses the links between diabetes and kidney disease and Professor Manesh Patel considers the interrelationships between diabetes, AF, chronic kidney injury and peripheral arterial disease, pointing out recent observations on the effect of NOACs in these settings. A significant percentage of patients with diabetes also have CKD; 28% will have albuminuria, 20% will have impaired renal function and 10% will have the combination of both of these. Approximately 60% of diabetics have normal kidney function (Fig. 1). Glycaemic control is important, as glycaemia is related not only to the occurrence of micro- and macrovascular complications in the kidneys, but also in the eyes, vascular system and heart. Type 2 diabetes mellitus (T2DM), often associated with obesity, can lead to kidney disease either via the metabolic pathway of hyperglycaemia or through a dynamic pathway caused by hypertension that leads to intense pressure in the kidney, glomerulosclerosis, fibrosis and the further increase of blood pressure. Resultant progressive kidney disease can lead to end-stage kidney disease (Fig. 2).[1-3]

Learning objectives

You will learn:

- The patient with diabetes is at increased risk of progressive kidney disease
- Diabetes increases the risk of developing atrial fibrillation; comorbidity is associated with increased risk of death and cerebrovascular events
- Diabetic patients with atrial fibrillation show a trend toward slower progression of acute kidney injury and reduced risk for end-stage renal disease when using non-vitamin K antagonist oral anticoagulant therapy in randomised controlled trials and real-world practice
- Diabetes patients with renal impairment have increased cardiovascular risk; randomised controlled trial and real-world data show benefit of rivaroxaban

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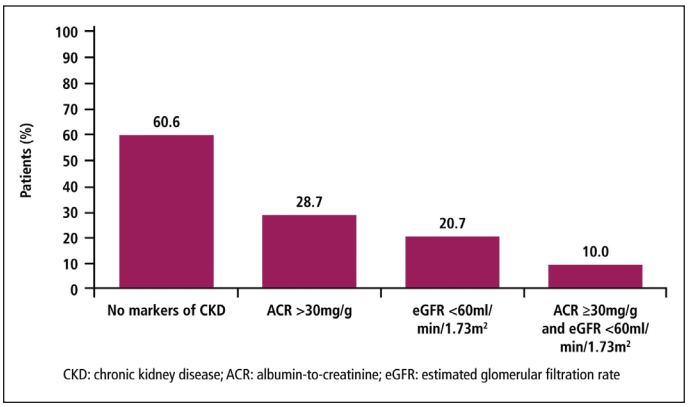

Fig. 1. Kidney disease in diabetes patients – distribution of markers for CKD in NHANES participants with diabetes, 2011–2014.

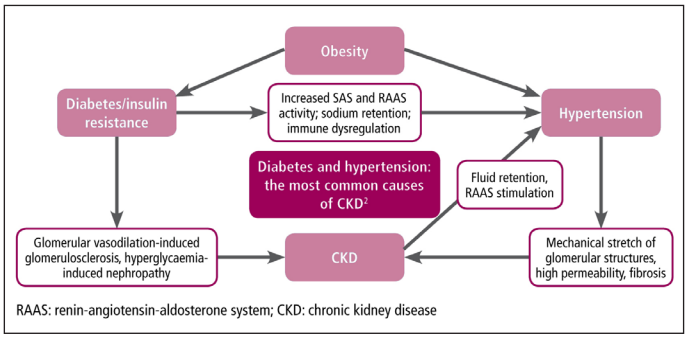

Fig. 2. Diabetes increases the risk of kidney disease.[1-3]

The impact of kidney disease affects the prognosis of the diabetic patient. The risk of mortality is relatively low when there is no kidney disease, but the presence of either albuminuria or impaired renal function significantly increases that risk. A combination of both proteinuria and impaired renal function significantly increases 10-year mortality in diabetes patients (Fig. 3).[4]

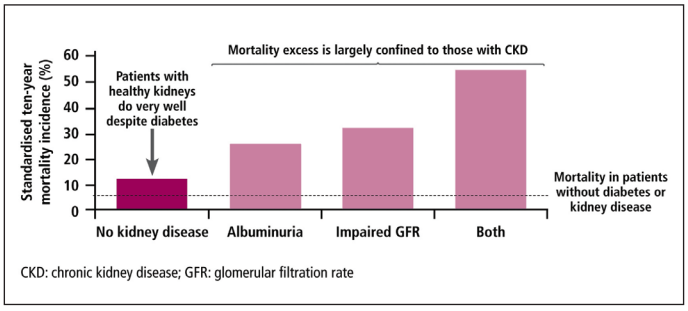

Fig. 3. Mortality risk – impact of kidney disease in T2DM.[4]

Diabetes predisposes patients to atrial fibrillation

Diabetes also increases the risk for the development of AF. Two cohort studies, the first based on Framingham data and the second on a large American register from the Veterans' Health Administration Hospitals, have associated diabetes with increased AF risk. The Framingham data reflected a 40% increased risk of AF and there was a doubling of risk in the American study (Fig. 4).[5,6]

In T2DM patients with AF, there is a substantially increased risk of death and cardiovascular events. This was shown in the ADVANCE trial of 11 140 T2DM patients, including 7% with AF. In this study, AF impacted on the outcome of both all-cause mortality and major cerebrovascular events over five years (Fig. 5).[7]

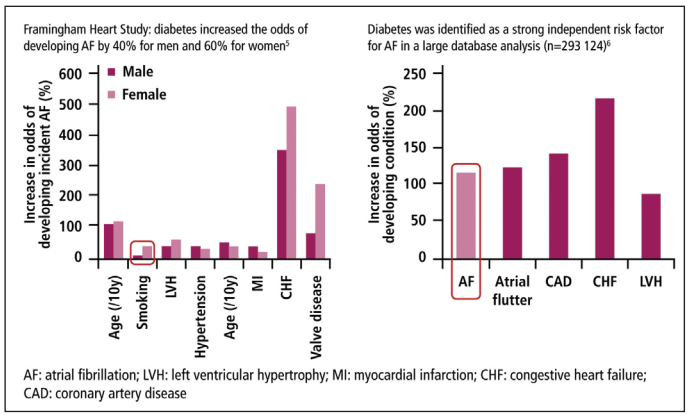

Fig. 4. Diabetes predisposes patients to AF.[5,6]

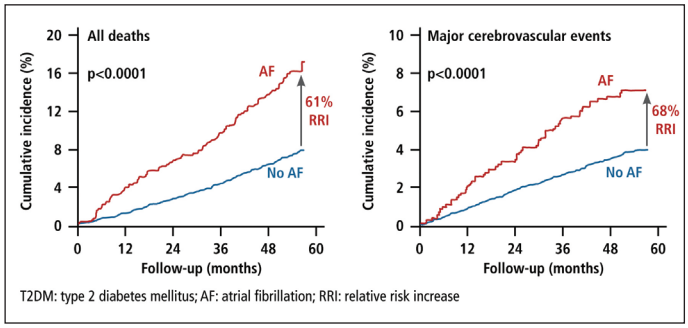

Fig. 5. AF and T2DM frequently co-exist and are associated with subsequent increased risk of death and cerebrovascular events.[7]

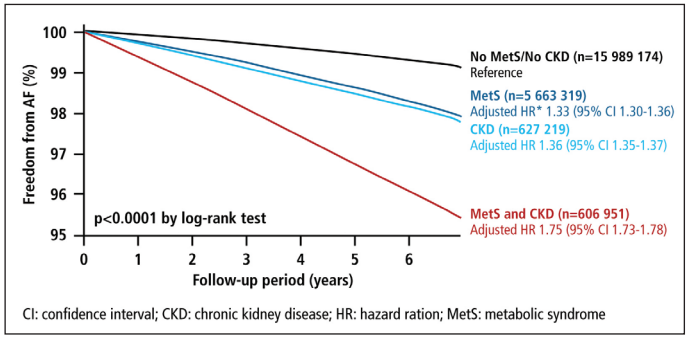

Fig. 6. The metabolic syndrome and CKD increase risk of AF.[8]
Kaplan-Meier curves showing the cumulative event-free survival for AF in patients classified into four groups based on the presence/absence of metabolic syndrome and CKD. *The associations were tested using a Cox proportional hazards model adjusted for age, sex, alcohol consumption, smoking status and physical activity.

The risk for development of AF is further increased in the patient with CKD and the metabolic syndrome, which is characterised by dysglycaemic traits other than diabetes (Fig. 6).[8] This stresses the need for clinicians to screen not only their T2DM patients' glucose levels, but for all relevant risk factors, and to consider appropriate interventions, including nonvitamin K antagonist oral anticoagulants (NOACs) for the management of AF.

Risk reduction in T2DM patients with AF using NOACs

The RELOADED study of diabetic patients with non-valvular AF (NVAF) using rivaroxaban showed a trend towards risk reduction for end-stage renal disease and a slower progression to acute kidney injury (AKI). There was no increase in ischaemic/systemic embolism, intracranial haemorrhage and fatal bleeding with the use of rivaroxaban (Fig. 7).[9]

Follow-up of patients, using ICD10 diagnostic codes for diabetes and AF and prescription information from MarketScan and other real-world data sets, evaluated progression to renal dysfunction (AKI, stage 5 CKD or haemodialysis) of those patients newly initiated

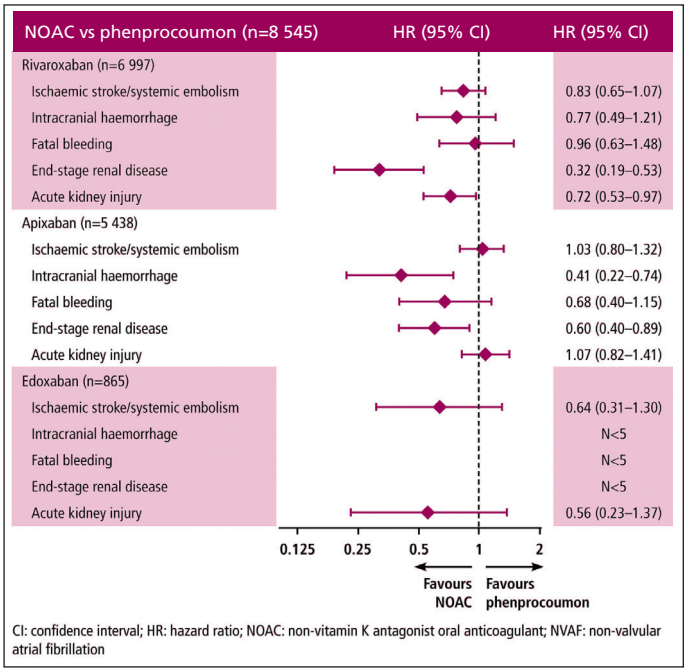

Fig. 7. RELOADED: Trend towards risk reductions observed in T2DM patients with NVAF using NOACs.[9]

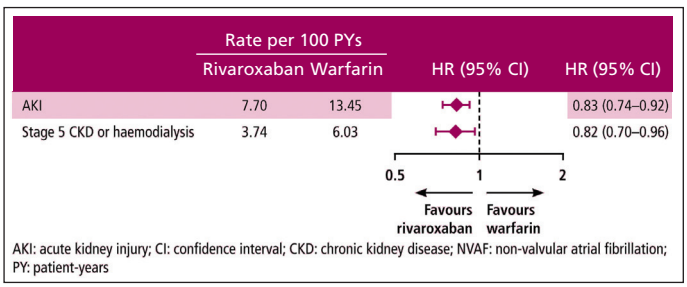

Fig. 8. Risk of major adverse renal outcomes in diabetic patients with AF receiving rivaroxaban vs warfarin.[10] Retrospective analysis of US MarketScan claims data for patients with NVAF and diabetes, newly initiating therapy with rivaroxaban (n = 10 017) or warfarin (n = 11 665). Patients with CKD stage 5 or on haemodialysis were excluded.

on either rivaroxaban or warfarin. Diabetic patients likely to be at higher risk showed renal protection using rivaroxaban treatment compared to warfarin (Fig. 8).[10]

It is important to recognise that the microvascular complications (nephropathy, neuropathy, retinopathy) and the macrovascular complications (coronary disease, peripheral disease, stroke) are all manifestations of the same pathobiology of vascular dysfunction, atherothrombosis and atherosclerosis in the patient with diabetes.

Patients with diabetes and renal impairment have increased cardiovascular risk

Meta-analysis of 1.2 million people from the Alberta Kidney Disease Network (AKDN) database and the National Health and Nutrition Examination Survey (NHANES) 2003–2006 showed, over a 48-month follow-up, a stepwise increase of cardiovascular risk in patients with diabetes and CKD as opposed to the presence of kidney dysfunction only or diabetes only (Fig. 9).[11]

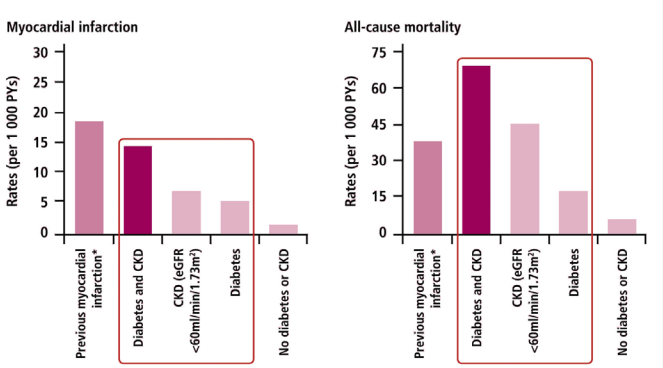

Fig. 9. Patients with diabetes and renal impairment have increased cardiovascular risk.[11]

What is the prevalence of diabetes in randomised controlled trials of NOAC use in patients with NVAF?

When interpreting the cardiovascular outcomes of randomised controlled trials (RCTs), it is important to consider the numbers of diabetic patients participating in these studies. ROCKET AF, in which almost 40% of patients had T2DM, is very representative of today's medical practice (Table 1).[12]

Table 1. Clinical features and prevalence of diabetes in NOAC RCTs of patients with NVAF[12]

Study	RE-LY	ROCKET AF	ARISTOTLE	ENGAGE-AF
Drug	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Age >75 years	40.1%	43.7%	31.2%	40.5%
$CHADS_2$ mean	2.2	3.48	2.1	2.8
Previous TIA/ stroke	20.3%	54.9%	19.2%	28.1%
Hypertension	78.9%	90.3%	87.3%	93.7%
Diabetes	23.3%	39.9%	25.0%	93.7%
Heart failure	31.8%	62.6%	35.5%	58.2%

AF: atrial fibrillation; NOAC: non-vitamin K antagonist oral anticoagulant; RCT: randomised controlled trial; TIA: transient ischaemic attack.

Effectiveness of rivaroxaban in patients with NVAF and diabetes has been evaluated in RCT and real-world settings

It is important to be aware that real-world data are consistent with the results of ROCKET AF. Rivaroxaban, as compared to warfarin, shows benefit for stroke/ systemic embolism, major bleeding and intracranial haemorrhage in the diabetic patient with NVAF (Fig. 10).

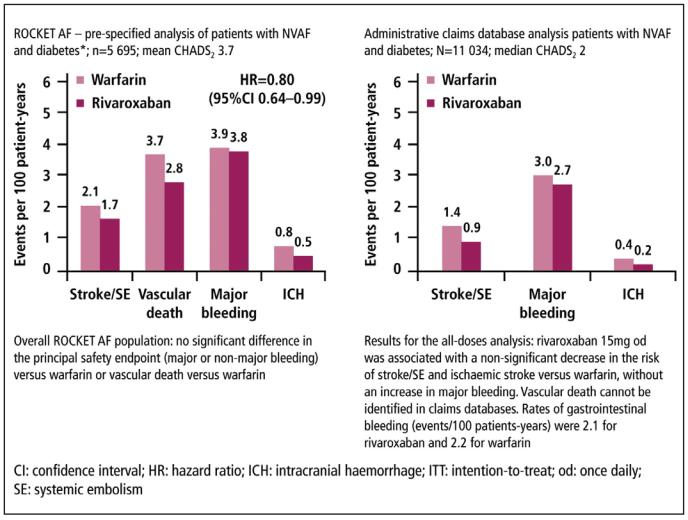

Fig. 10. Rivaroxaban vs warfarin in the diabetic patient with NVAF – RCT and real-world data.

Furthermore, rivaroxaban has been associated with lower risks of major adverse cardiovascular events (MACE) and major adverse limb events (MALE) compared to warfarin in patients with NVAF and T2DM (Fig. 11).[13] MarketScan data also show that in the real-

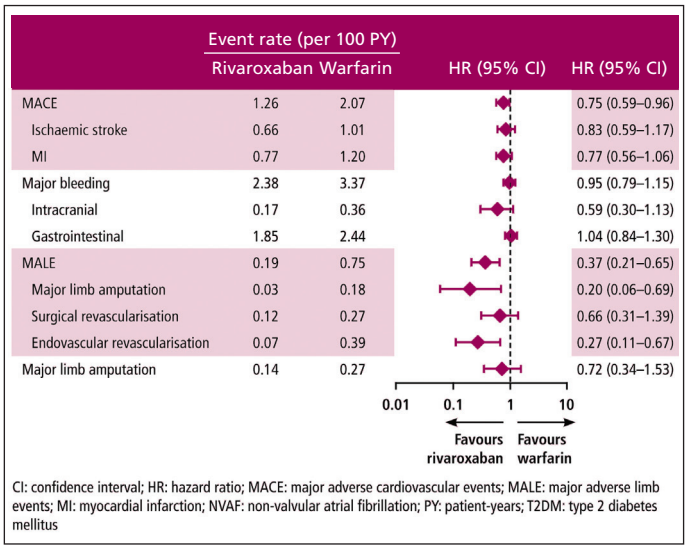

Fig. 11. Rivaroxaban was associated with a lower risk of MACE and MALE than warfarin in patients with NVAF and T2DM.[13]

Analysis of US MarketScan claims data for patients with NVAF and co-morbid T2DM initiating therapy with warfarin (n = 13 946) or rivaroxaban (n = 10 700; 24.1% of these received a reduced dose).

world setting, NVAF patients with T2DM were treated with warfarin or rivaroxaban at reduced doses, as suggested for the level of renal dysfunction in the patient with comorbid kidney disease – 24% of patients received a rivaroxaban dose of 15mg. Consistent with RCT data, there were no changes in bleeding rates. Observational reports suggest a reduction in MALE, another signal implying benefit of rivaroxaban beyond simply the heart, but also for the kidneys and limbs in T2DM patients with AF.

Key learnings

- Kidney disease in the T2DM patient may arise from both hyperglycaemia and hypertension, and significantly increases mortality and cardiovascular risk
- Diabetes predisposes toward the development of AF, with comorbidity substantially increasing all-cause mortality and major cardiovascular events
- Risk for development of AF is further increased in the diabetic patient with CKD
- Use of NOACs in diabetic patients with AF is associated with risk reduction for end-stage renal disease and slower progression to AKI.

Anticoagulation case study: special considerations in diabetes and CKD

ANTHONY DALBY

Patient and complaint: 68-year-old female, complains of leg pain and unsteadiness when walking.
Current treatment: Metformin, amlodipine, atorvastatin.
Medical history: NVAF, diabetes, hypertension, kidney injury: eGFR = 43.
Considerations: It is unclear whether she has peripheral neuropathy or peripheral arterial disease. Clinical examination confirms the presence of AF with a heart rate around 70 beats per minute. She and her family are concerned about her unsteadiness and have heard that she may need oral anticoagulation.

Should she be anticoagulated?

A. Yes
B. No

Expert comment

She has confirmed NVAF so we should be guided by the CHA_2DS_2-VASc score. When her age, sex, hypertension and diabetes are taken into account, there appears to be a strong indication for anticoagulation to prevent her having a stroke. However, her impaired kidney function needs to be carefully weighed up against the need for anticoagulants. Many clinicians are guilty of preferring an act of omission rather than an act of commission, meaning they would rather avoid anticoagulation and its attendant bleeding risk than reduce the patient's risk of stroke.

CHA_2DS_2-VASc score

Only males < 65 years can achieve a CHA_2DS_2-VASc score < 1

Risk factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age > 75 years	2
Diabetes mellitus	1
Stroke/TIA/thromboembolism	2
Vascular disease	1
Age 65–74 years	1
Sex category (i.e. female sex)	1
Maximum score	9

HAS-BLED score

The HAS-BLED score estimates bleeding risk, but except in patients who have a marginal indication for anticoagulation, the bleeding risk never outweighs the need to anticoagulate.

Letter	Clinical characteristic	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age > 65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

Having decided to anticoagulate, what should be the choice of anticoagulant?

A. Vitamin K antagonist – warfarin
B. Aspirin
C. NOAC

Expert comment

In this setting it is inappropriate to consider aspirin at all. Aspirin has little or no effect on stroke risk and carries as great a risk of bleeding as warfarin. So, our first decision is whether to use the vitamin K antagonist (warfarin) or a NOAC. Leaving aside the issues of inconvenience, drug interactions, monitoring and dose variations with warfarin, we must be aware that NOACs are equal if not better at preventing strokes in patients with NVAF and also carry a lower risk of brain bleeds. Though cost is frequently an issue that favours warfarin, we need to be aware that the best clinical advice is to use a NOAC.

Which NOAC?

Rivaroxaban Apixaban }	Anti-factor Xa
Dabigatran	Antithrombin

Among the NOACs we have the choice between one of two anti-factor Xa inhibitors (rivaroxaban and apixaban) and a thrombin antagonist (dabigatran). Although there were slight variations in the

inclusion criteria and the results of the trials of these agents, we can conclude that as a group they are as effective as or more effective than warfarin at preventing stroke, and all have a lower risk of brain bleeding. Because there is little difference in their respective costs, personal preference, tolerability and ease of dosing play a role when deciding which NOAC to prescribe.

Is there a treatment that could offer benefits beyond stroke prevention in this case?

A. Yes
B. No

Expert comment

In his presentation, Professor Patel included observational data on the effects of NOACs in preventing acute kidney injury and progression to end-stage kidney failure, as well as the reduction of revascularisation and amputations in peripheral arterial disease. Observational data do not carry the same weight as the results of a randomised clinical trial; these results strongly suggest that when dealing with patients who have diabetes and NVAF, specific NOACs should be the drug of choice for those with cardiovascular disease, impaired kidney function and/or evidence of peripheral arterialdisease.

In diabetes and NVAF, a NOAC should be preferred in the following settings:

- Established cardiovascular disease
- Chronic kidney injury
- Peripheral arterial disease

Acknowledgement

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MA-M_ZA-0044-1

Drug Trends in Diabetes
Statins linked to doubled risk of type 2 diabetes

A study of thousands of patients' health records found that those who were prescribed cholesterol-lowering statins had at least double the risk of developing type 2 diabetes. The detailed analysis of health records and other data from patients in a private insurance plan in the Midwest provides a real-world picture of how efforts to reduce heart disease may be contributing to another major medical concern, said Victoria Zigmont, who led the study as a graduate student in public health at The Ohio State University.

Statins are a class of drugs that can lower cholesterol and blood pressure, reducing the risk of heart attack and stroke. More than a quarter of middle-aged adults use a cholesterol-lowering drug, according to recent federal estimates.

Researchers found that statin users had more than double the risk of a diabetes diagnosis compared to those who didn't take the drugs. Those who took the cholesterol-lowering drugs for more than two years had more than three times the risk of diabetes. 'The fact that increased duration of statin use was associated with an increased risk of diabetes – something we call a dose-dependent relationship – makes us think that this is likely a causal relationship,' Zigmont said.

'That said, statins are very effective in preventing heart attacks and strokes. I would never recommend that people stop taking the statin they've been prescribed based on this study, but it should open up further discussions about diabetes prevention and patient and provider awareness of the issue.'

Researchers also found that statin users were 6.5% more likely to have a troublingly high HbA_{1c} value – a routine blood test for diabetes that estimates average blood sugar level over several months.

The study included 4 683 men and women who did not have diabetes, were candidates for statins based on heart disease risk and had not yet taken the drugs at the start of the study. About 16% of the group (755 patients) were eventually prescribed statins during the study period, which ran from 2011 until 2014. Participants' average age was 46 years.

Randall Harris, a study co-author and professor of medicine and public health at Ohio State, said that the results suggest that individuals taking statins should be followed closely to detect changes in glucose metabolism and should receive special guidance on diet and exercise for prevention.

Although statins have clear benefits in appropriate patients, scientists and clinicians should further explore the impact of statins on human metabolism, in particular the interaction between lipid and carbohydrate metabolism, said co-author Steven Clinton, a professor of medicine and member of Ohio State's Comprehensive Cancer Centre.

'In addition, researchers conducting large prospective cohort studies should be considering how statins impact on human health overall. They should consider both risks and benefits, not just the disease that is being treated by the specific drug,' Clinton said.

The study was done retrospectively, meaning that the researchers looked back at existing records from a group of patients to determine if there were any possible connections between statin prescriptions and diabetes. Previous research has suggested a connection, but this study design allowed for a glimpse at what is happening naturally in the clinical setting, rather than what happens in a prospective trial that randomly assigns some people to statins and some people to placebo, said Zigmont, who is now an assistant professor at Southern Connecticut State University.

The study was enriched by the availability of a variety of details on the study population, including data from biometric screenings and a health survey that asked about education, health behaviours and ethnicity, Zigmont said. She also had access to medical and pharmacy claims data.

'Zigmont was careful to take a wide variety of confounding factors into account in an effort to better determine if the statins were likely to have caused the diabetes,' she said. 'Those included gender, age, ethnicity, education level, cholesterol and triglyceride readings, body mass index, waist circumference and the number of visits to the doctor. Programmes that help patients improve their fitness and diets could be considered and discussed when doctors are prescribing statins, so that patients can be proactive about diabetes prevention,' she said.

'It would also be helpful for future research to better determine which statins and which doses might lead to the greatest risk,' Zigmont said. Her study didn't allow for an analysis based on different types of statins.

'Limitations of the research include the fact that the majority of statin users were white, and that the research team had no way of knowing how closely patients adhered to their doctors' prescriptions. There also was no way of determining who was at elevated risk of diabetes at the study's onset,' Zigmont says.

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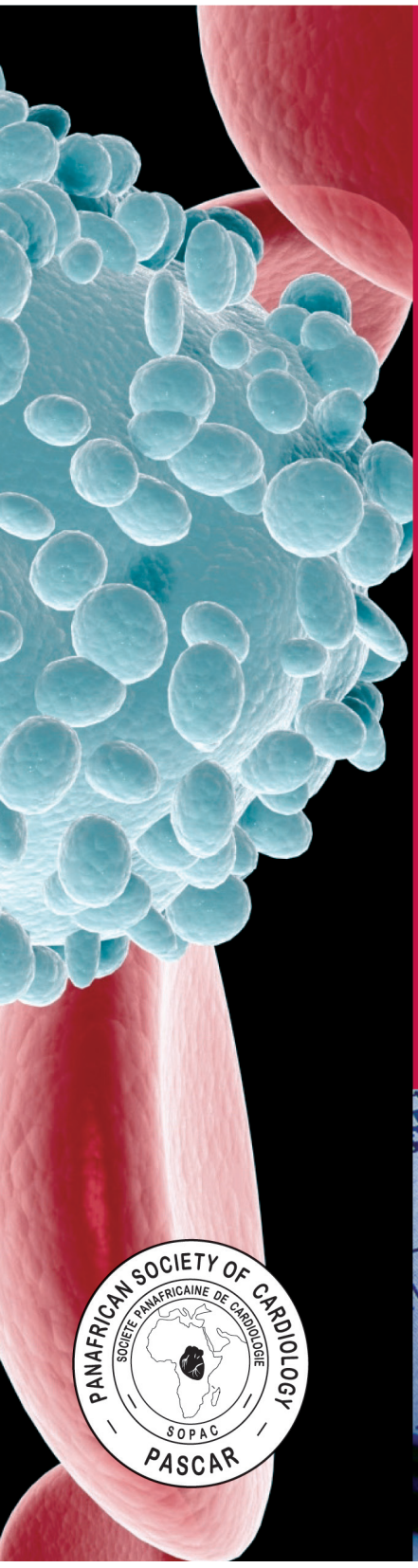

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