

Prevalence and determinants of metabolic syndrome: a cross-sectional survey of general medical outpatient clinics using National Cholesterol Education Program-Adult Treatment Panel III criteria in Botswana

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Background: Low- and middle-income countries, including Botswana, are facing rising prevalence of obesity and obesity-related cardiometabolic complications. Very little information is known about clustering of cardiovascular risk factors in the outpatient setting during routine visits. We aimed to assess the prevalence and identify the determinants of metabolic syndrome among the general outpatients' attendances in Botswana.

Methods: A cross-sectional study was conducted from August to October 2014 involving outpatients aged ≥ 20 years without diagnosis of diabetes mellitus. A precoded questionnaire was used to collect data on participants' sociodemographics, risk factors, and anthropometric indices. Fasting blood samples were drawn and analyzed for glucose and lipid profile. Metabolic syndrome was assessed using National Cholesterol Education Program-Adult Treatment Panel III criteria.

Results: In total, 291 participants were analyzed, of whom 216 (74.2%) were females. The mean age of the total population was 50.1 (± 11) years. The overall prevalence of metabolic syndrome was 27.1% ($n=79$), with no significant difference between the sexes (female =29.6%, males =20%, $P=0.11$). A triad of central obesity, low high-density lipoprotein-cholesterol, and elevated blood pressure constituted the largest proportion (38 [13.1%]) of cases of metabolic syndrome, followed by a combination of low high-density lipoprotein, elevated triglycerides, central obesity, and elevated blood pressure, with 17 (5.8%) cases. Independent determinants of metabolic syndrome were antihypertensive use and increased waist circumference.

Conclusion: Metabolic syndrome is highly prevalent in the general medical outpatients clinics. Proactive approaches are needed to screen and manage cases targeting its most important predictors.

Keywords: metabolic syndrome, determinants, general medical outpatient clinics, Botswana

Introduction

Metabolic syndrome is commonly encountered in clinical practice worldwide and is defined by co-occurrence of known risk factors for cardiovascular diseases (CVDs), including insulin resistance, atherogenic lipid profile, obesity, and hypertension.¹ Metabolic syndrome is associated with an excess risk of atherosclerotic CVDs and type 2 diabetes mellitus² and variable complications of nonalcoholic fatty liver diseases and obstructive sleep apnea.^{3,4} Although its pathogenesis is incompletely understood,

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behavioral and environmental factors such as diet, sedentary lifestyles, urbanization, industrialization, and underlying genetic predisposition are known to play a significant role in its development.⁵ The current decline in HIV/AIDS mortality has tremendously improved life expectancy of populations in developing countries, including Botswana. Ironically, this improvement has been countered by an alarming rise of noncommunicable diseases, including CVDs and type 2 diabetes mellitus within the same populations.⁶ A recent survey of noncommunicable disease risk factors in Botswana by the Ministry of Health has provided evidence of a high burden of obesity and hypertension in the community among adults aged 25–64 years, but its impact and related manifestations such as metabolic syndrome in clinical settings are not known.⁷

Currently, several expert groups and institutions have proposed different criteria for the diagnosis of metabolic syndrome in clinical practice,^{8–10} which include three or more of the five CVD risk factors. Although there are still no universally accepted diagnostic criteria,¹¹ the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATPIII) criteria are considered simple and most practical in clinical practice and have been widely used in most parts of the world.¹ It is particularly useful for the health care providers to screen for metabolic syndrome and aggressively intervene to reduce patients' cardiovascular risk.¹² In addition, individuals with metabolic syndrome should be aware of their risk status and the need to adhere to healthier lifestyle behaviors and medications. We aimed to determine the prevalence of metabolic syndrome among adults attending the general medical outpatient clinics and identify its major determinants among this population.

Methods

Research design and settings

This is a cross-sectional study that used the quantitative analytical approach to address the research questions. The study was conducted between August and October 2014 in two general medical outpatient clinics of Princess Marina Hospital (PMH) and Letsholathebe II Memorial (LM) Hospital. PMH is the main referral hospital in Gaborone (south of Botswana), and LM is a district hospital in Maun (north of the country). The general medical outpatient clinics at PMH and LM receive on average 40 and 30 patients daily, respectively.

Participants

All adults aged ≥ 20 years within the catchment area of the two hospitals who were attending the general medical outpatient clinics were eligible. Participants were excluded if they had

any of the following: any type of diabetes mellitus, acutely ill, or unable to undergo anthropometric evaluation.

Procedures and outcome measures

All recruitments and evaluations were done by research nurses who had prior training on the study protocol, including anthropometric measurements and good clinical practice certification. We used a systematic random sampling to recruit five patients per day from an average of 30 patients from each clinic. On each study day, a sampling frame was made from a list of patients on scheduled visit. The first patient was picked randomly and evaluated for study eligibility. If eligible, then every sixth patient on the list was subsequently evaluated for study eligibility and enrollment after obtaining informed consent, until the sample size for the day was attained.

After obtaining written informed consent, data were obtained from the respondents through oral interview using a precoded questionnaire and included the following: age, sex, level of education, marital status, occupation, daily consumption of fruit, berries, or vegetables, daily physical activity (defined as having at least 30 minutes of daily physical activity during work or leisure), history of antihypertensive drug treatment, family history of diabetes mellitus in the first-degree or second-degree relatives, and HIV infection status.

Blood pressure (BP), height, weight, and waist circumference (WC) were measured during the physical examination. BP was measured by the research nurse after the subject had rested for at least 5 minutes by using the standard mercury sphygmomanometer, with the participant sitting in an upright position. BP was recorded to the nearest 2 mmHg. For each patient, two readings were recorded within a 2-minute interval and averaged. Weight was measured to the nearest 0.1 kg, and standing height was measured to the nearest 0.1 cm using a stadiometer attached to the same medical balance weighing scale (HiCare International, Kerala, India). Body mass index was calculated as weight per square meters (kg/m^2). WC, to the nearest 0.1 cm, was taken using a nonstretchable tape measure at a level midway between the lowest rib and iliac crest. Waist-hip ratio was also calculated by dividing WC (cm) by hip circumference (cm) and categorized using WHO criteria.¹³

After the interview and physical examination, overnight fasting blood samples (5 mL) were collected by the research nurse from each participant. After the blood was drawn into ethylenediaminetetraacetic acid-containing vacutainer tube, it was gently shaken; plasma and red blood cells were then separated and frozen at -20°C . All samples from the two hospitals were transported on dry ice to a central laboratory and stored at -70°C before analysis. Plasma serum lipid levels

were analyzed by enzyme colorimetric methods using automatic chemistry analyzer machine (Abbott Architect; Abbott GmbH Diagnostika, Wiesbaden, Germany). Plasma glucose was analyzed by the research nurse at point of care using oxidase method (Betachek glucometer; National Diagnostic Products Pty Ltd, Sydney, NSW, Australia).

Operational definitions

Metabolic syndrome was diagnosed using NCEP-ATP III criteria, specifically when a subject had three or more of the following components: WC >102 cm (males) or >88 cm (females), triglycerides ≥ 1.7 mmol/L, high-density lipoprotein-cholesterol (HDL-C) <1.04 mmol/L (males) or <1.30 mmol/L (females), BP $\geq 130/\geq 85$ mmHg, and fasting glucose ≥ 6.1 mmol/L.⁸

Statistical analysis

Data were analyzed using IBM SPSS for Windows (Version 23.0; IBM Corporation, Armonk, NY, USA). Descriptive statistic was used to compute the demographic, clinical, and laboratory characteristics of participants. Continuous variables were expressed as mean value \pm SD, and categorical variables as frequencies and proportions (%). For skewed variables, median \pm interquartile ranges were computed and tabulated. Comparisons between groups or subgroups were carried out using Student's *t*-test for continuous variables and the Pearson's chi-squared test or Fisher's exact test for categorical variables. The prevalence estimates of metabolic syndrome were categorized based on the NCEP-ATP III criteria for all possible combinations, and cumulative total was determined.

Demographic and clinical CVD risk factors were investigated as potential predictors for the cumulative metabolic syndrome to compute unadjusted odd ratio (OR) and their 95% confidence interval (CI). All significant predictors were included in the multiple logistic regression analyses controlling for age and sex as possible confounders to compute for adjusted OR and their 95% CI as an approximation of the adjusted relative risk. How well the model fit the data was estimated using the Hosmer–Lemeshow test of goodness of fit. All reported *P*-values were two tailed, and the level of statistical significance was set at 0.05. The study was approved by the ethical committees of the PMH and LM Hospital, University of Botswana and Ministry of Health, and carried out in compliance with the Declaration of Helsinki.

Results

Participants' characteristics

A total of 704 outpatient attendees aged ≥ 20 years were sampled and screened for study eligibility. Two hundred

forty-four (35%) patients were excluded because of documented history of diabetes or being acutely ill (<2 weeks) or were unable to undergo anthropometric evaluation. Fifty-two (7%) patients had not fasted and failed to return for phlebotomy. Sixty-seven (9.5%) declined consent. Only 291 participants (41%) who had complete interview and blood data were included in the final analyses.

The general characteristics of the participants are presented in Table 1. The mean age of the participants was 50.1 (± 11) years, with no significant age differences between the sexes. Of the 291 participants analyzed, 216 (74.2%) were female. All participants were from the urban locations of Gaborone and Maun and were indigenous Batswana. A majority (71%) of the participants had either completed secondary education level or primary education levels, with only <7% having no formal schooling. Regarding employment status, 52% were formally employed and 23% were retired, while only 7% considered themselves unemployed. The most common reason for the visit was regular appointment for either one or more chronic disorders (197 [67.7%]), followed by new referrals (26.5%).

A majority of the participants (215 [73.9%]) had no symptom at presentation, and the common symptoms were headache, body pains, and shortness of breath. The most common chronic conditions were systemic hypertension (135 [46.4%]) and heart diseases (37 [12.7%]). However, 88 participants (26.9%) had no chronic disease. A total of 114 (39.2%) participants were HIV seropositive, 156 (53.6%) were seronegative negative, and 21 (7.2%) were unknown. Of those who were seropositive, 87 (76.3%) were on first-line antiretroviral therapy (ART; nucleoside/nucleotide analogues and nonnucleoside combinations). Only nine (7.9%) were on second-line ART (protease-based ART) and 18 (15.7%) were not on ART. Notably, there was very low prevalence of physical activity and consumption of vegetables, fruit, and berries in this population (Table 1). The prevalence of overweight and obesity was 93 (33%) and 98 (33.7%), respectively. Females had significantly higher prevalence of overweight and obesity.

Components and prevalence of metabolic syndrome

The most prevalent component of metabolic syndrome in this population was central obesity (162 [55.7%]), followed by hypertension (142 [48.8%]) and low HDL-C (65 [22.3%]). Hypertriglyceridemia was present in 58 (19.9%) participants. Only six (2.1%) had elevated fasting glucose. Females had significantly higher prevalence of central obesity ($P < 0.001$). The overall metabolic syndrome was present in 79 (27.1%) individuals among the total participants, there was

Table 1 Demographic and clinical characteristics of the study participants stratified by sex (N=291)

General characteristics	Total	Females	Males
Participants, n (%)	291 (100)	216 (74.2)	75 (25.8)
Mean age, years (\pm SD)	50.06 (11)	50.52 (12)	49.90 (10)
Mean heart rate, beats per min (\pm SD)	76.31 (13.8)	77.67 (13.33)	72.38 (14.68)
Mean pulse pressure (\pm SD)	50.13 (15.85)	49.75 (15.61)	51 (16.56)
Daily physical activity, n (%)	111 (38.1)	85 (76.6)	26 (23.4)
Daily consumption of vegetables, fruit, or berries, n (%)	38 (13.1)	29 (76.3)	9 (23.7)
Regularly used antihypertensive, n (%)	135 (46.4)	105 (77.8)	30 (22.2)
Family history of diabetes mellitus, n (%)			
First-degree relatives	51 (17.5)	38 (74.5)	13 (25.5)
Second-degree relatives	42 (14.4)	33 (78.6)	9 (21.4)
HIV positive	114 (39.2)	91 (79.8)	23 (20.2)
First-line ART	87 (29.9)	66 (75.9)	21 (24.1)
Second-line ART	9 (3.1)	9 (100)	0
Overweight (BMI: 25–30 Kg/m ²)	93 (32)	76 (81.7)	17 (18.3) ^a
Obesity (BMI: >30 kg/m ²)	98 (33.7)	84 (85.7)	14 (14.3) ^a
Waist–hip ratio (females >0.85 and males >0.90)	135 (48.8)	112 (81.2)	26 (18.8) ^a
Components of metabolic syndrome, n (%)			
Central obesity	162 (55.7)	146 (90.1)	16 (9.9) ^a
Elevated blood pressure (systolic BP: \geq 130 mmHg; diastolic Bp: \geq 85 mmHg)	142 (48.8)	107 (75.4)	35 (24.6)
Fasting glucose \geq 6.1 mmHg	6 (2.1)	5 (83.3)	1 (16.7)
Triglycerides \geq 1.7 mmHg	58 (19.9)	36 (62.1)	22 (37.9)
HDL-cholesterol, mmol/L (females <1.3 and males <1.0)	65 (22.3)	45 (69.2)	20 (30.8)

Note: ^aP-value statistically significant.

Abbreviations: ART, antiretroviral therapy; HDL, high-density lipoprotein; HIV, human immunodeficiency virus; SD, standard deviation.

no significance difference ($P=0.11$) between female (81%) and males (19%). A triad of central obesity, low HDL-C, and elevated BP was the most prevalent constituting 13.1% of the total cases, followed by a tetrad of central obesity, low HDL-C, hypertriglyceridemia, and elevated BP at 5.8% of cases. Only one participant had all the five components of the syndrome (Table 2).

Determinants

The results of both univariate and multivariate logistic regression analyses of risk factors for the overall metabolic syndrome are presented in Table 3. There were no significant associations between socioeconomic status (level of education and employment status), vital characteristics (pulse rate and pulse pressure) and metabolic syndrome. Although physical activity and consumption of vegetables, fruit, and berries showed a protective effect toward metabolic syndrome, it was not statistically significant and was not included in the multivariate analysis. There was no significant association between HIV serostatus or ART and metabolic syndrome in our sample.

Discussion

The result of this study indicates that metabolic syndrome is a common comorbidity among the general medical outpatient

Table 2 Frequency distribution of various combinations of components of metabolic syndrome among the participants (N=291)

Combinations of metabolic syndrome components	n (%)	Cumulative (%)
0 or <3 components	212 (72.9)	72.9
Low HDL + TRI + high BP	4 (1.4)	74.2
Low HDL + TRI + central obesity	9 (3.1)	77.3
Low HDL + TRI + central obesity + high BP	17 (5.8)	83.2
Low HDL + TRI + central obesity + high BP + FG	1 (0.3)	83.5
Low HDL + central obesity + high BP	38 (13.1)	96.6
Low HDL + central obesity + FG	1 (0.3)	96.9
TRI + central obesity + high BP + FG	1 (0.3)	99.3
Central obesity + FG + High BP	1 (0.3)	99.7
Total	291 (100)	100

Note: Central obesity, mean waist circumference >88 cm in females and >102 cm in males.

Abbreviations: BP, blood pressure; FG, fasting glucose; HDL, high-density lipoprotein; TRI, hypertriglyceridemia.

population in Botswana. The prevalence was 27.1% based on NCEP-ATP III criteria. A triad of central obesity, low HDL-C, and elevated BP was the most prevalent (13.1%) combination of CVD risk factors constituting the syndrome in this population. This was followed by a combination of four CVD risk factors, namely central obesity, low HDL-C,

Table 3 Univariate and multivariate analyses of demographic and clinical risk factors for metabolic syndrome

Characteristics	Proportions (%)	Unadjusted OR (95% CI)	P-values	Adjusted OR (95% CI)	P-values
Female	74.2	1			
Male	25.8	1.67 (0.89–3.18)	0.109	2.38 (0.94–6.06)	0.68
Age groups, years					
<45	35.4	1		1	
45–54	33	2.26 (1.15–4.43)	0.018	1.26 (0.56–2.84)	0.58
55–64	19.2	3.04 (1.41–6.56)	0.005	2.26 (0.89–5.72)	0.09
>64	12.4	2.66 (1.14–6.21)	0.024	1.45 (0.52–4.05)	0.48
Body mass index, kg/m ²					
<25	36.4	1		1	
25–30	28.2	4.88 (1.20–11.95)	0.01	1.77 (0.58–5.43)	0.32
>30	35.4	12.24 (5.16–29.06)	<0.001	2.62 (0.84–8.23)	0.1
Waist circumference (females), cm					
<94 (<80)	27.5	1		1	
94–102 (80–88)	19.2	0.88 (0.23–11.95)	0.8	0.73 (0.17–3.13)	0.67
>102 (>88)	53.3	11.05 (4.53–26.99)	<0.001	6.66 (1.87–23.76)	0.004 ^b
Abnormal waist to hip ratio ^a	48.8	3.33 (1.92–5.82)	<0.001	1.5 (0.75–2.97)	0.25
Family history of diabetes mellitus					
First-degree family	17.5	1.96 (1.03–3.75)	0.042	1.55 (0.70–3.43)	0.28
Second-degree family	14.4	0.95 (0.44–2.07)	0.9	0.67 (0.27–1.67)	0.39
Daily physical activity	38.1	0.7 (0.42–1.18)	0.19	–	
Daily consumption of vegetables, fruits, or berries	13.1	0.59 (0.29–1.20)	0.15	–	
Regular antihypertensive use	46.4	3.23 (1.88–5.57)	<0.001	2.36 (1.23–4.51)	0.01 ^a

Notes: ^aWaist to hip ratio defined abnormal if >0.94 for males and >0.8 for females. ^bP-value statistically significant.

Abbreviations: CI, confidence interval; OR, odds ratio.

elevated triglycerides, and elevated BP found in 5.8% of the total participants. Despite the preponderance of the female population in our samples, the prevalence of metabolic syndrome was not statistically different between the sexes; however, individuals aged ≥ 45 years were at increased risk of developing the syndrome. Our findings also suggest that history of regular hypertensive medications use and increased WC were independently associated with the syndrome.

This is the first report of a systematic screening for metabolic syndrome among general medical outpatients in Botswana. Malangu in 2013 examined HIV population at PMH using the same criteria and found a lower rate of 11%.¹⁴ Based on the same criteria in the Eastern Cape Province of South Africa, a comparable overall prevalence of 26.6%, with no significant variation among antiretroviral-naïve individuals (15.7%) and HIV-negative groups (21.9%) were reported.¹⁵

Reports from community survey of health care workers aged 22–65 years in Botswana using the same criteria found a higher prevalence of 34%.¹⁶ Community surveys from other sub-Saharan African countries reported a lower prevalence, ranging from 12.5% to 15% among general workers in Ethiopia and palm oil workers in Ghana, respectively.^{17,18} These findings are evidence of increasing burden of CVD risk factors and metabolic syndrome in sub-Saharan African urban populations being fueled by changes in lifestyle and nutrition

factors against a backdrop of a high burden of chronic HIV infection in the region.

Our results also show that increased WC was independently predictive of the metabolic syndrome (adjusted OR 6.66, 95% CI 1.87–23.76). This finding is particularly important in resource-limited settings like sub-Saharan African countries where screening programs for CVD risk factors are not a priority due to the high burden of infectious diseases. WC correlates closely with both body mass index and waist–hip ratio and consistently predicts insulin resistance, CVD, hypertension, and stroke.^{19–21} Although, the level of risk varies between population groups, recent data suggest that WC is a better correlate of abdominal visceral adipose tissue accumulation than waist–hip ratio²² and body mass index.²³ In our findings, more than half of the participants had increased WC, of whom >90% were females, which mirrors the reports from similar settings in the South African region.²⁴ More than one-third of the participants were overweight, and a similar proportion of individuals were obese, with females being significantly affected. We found low rates of physical activity and daily consumptions of vegetables, fruit, and berries among the participants, which could explain the high burden of overweight and obesity. However, the reason for the sex differences in obesity apart from genetics might also be related to the positive attitudes and cultural values attached to being

overweight in some African societies. Being overweight is culturally accepted as a sign of wealth and beauty and in some communities, young girls are specially fed to gain weight in preparations for marriage.²⁵ It is therefore imperative that culturally sensitive intervention programs are designed to prevent the rising epidemic of obesity in the region.

This study further indicates that a history of regular anti-hypertensive medications is independently associated with metabolic syndrome (adjusted OR 2.36, 95% CI 1.23–4.51). In hypertensive subjects, metabolic syndrome amplifies cardiovascular risk associated with high BP, independent of the effect of several traditional cardiovascular risk factors,²⁶ which requires targeted intervention by the treating physician.

Metabolic syndrome is a chronic heterogeneous disease and most of its risk factors are interrelated and share the underlying pathogenic factors, including genetic and dietary patterns. In addition, most of its risk factors are themselves considered components in the definition of the syndrome.^{27,28} It is hence not surprising that these components were the most significant in our multivariate analysis, and therefore these findings underscore the importance of history of hypertension and high WC as key determinants of prevalent metabolic syndrome and can be used to identify at-risk individuals in resource-limited settings. Moreover, according to the consensus document of the European Society of Hypertension working group on hypertension and cardiovascular risk in low resource settings, screening and treatments programs ought to be based on cardiovascular risk stratification, rather than focusing on the single risk factor such as untreated hypertension.²⁹ Thus in a clinical setting, the history of hypertension or being on treatment and increased WC are highly predictive of metabolic syndrome in this population and should prompt clinicians to assess for other related CVD risk factors in the same patient.

This study has several limitations. First, the cross-sectional nature of the study does not establish the causality between metabolic syndrome and the risk factors analyzed. Second, this was a clinic-based survey, and the fact that it was conducted in only two urban-based settings further limits its generalizability to the wider population. Third, the predominantly female population also limits its generalization. However, this is not unique to our study as most surveys in the medical outpatients in general and in this region in particular have also reported female predominance.¹⁵

Conclusion

Our study clearly shows that metabolic syndromes are highly prevalent in the general outpatient populations in the urban

settings of Botswana. These findings support the need to equip health care facilities to routinely assess anthropometric indices and identify the most important determinants of metabolic syndrome for case diagnosis and consider preventive intervention programs such as dietary advices and lifestyle changes as well as pharmacotherapy for specific elements of the syndrome.

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Disclosure

The authors report no conflicts of interest in this work.

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