Metabolic syndrome using national cholesterol education program criteria in black patients with arterial hypertension

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Résumé

Objectif: évaluer la prévalence et les déterminants du syndrome métabolique chez les patients porteurs d'une hypertension artérielle essentielle.
Méthodes: la présente analyse transversale porte sur 100 patients noirs (53 hommes et 47 femmes, âge moyen 49 ± 10 ans, IMC 27 ± 5 Kg/m², PAS 155 ± 19 mmHg, PAD 101 ± 11 mmHg) porteurs d'une hypertension artérielle essentielle, recrutés de manière consécutive dans une étude cas-témoins sur les lipides et les lipoprotéines aux Cliniques Universitaires de Kinshasa. L'évaluation des facteurs de risque lipidiques et non lipidiques a été sur base de l'examen clinique, des tests biologiques et de l'électrocardiogramme. Les critères du NCEP-ATP III ont été utilisés pour définir le syndrome métabolique (SM). La comparaison entre groupes a été faite, selon le cas, à l'aide des tests t de Student, non paramétrique de Mann Whitney ou Chi carré. La régression logistique a été utilisée pour évaluer les déterminants indépendants du risque de SM.
Résultats: 31 patients hypertendus (31%), 23 hommes et 8 femmes, avaient rempli les critères du NCEP-ATP III définissant le syndrome métabolique. Hormis les variables définissant le SM, la proportion des fumeurs (13% vs 3%, p ≤ 0,05) et le rapport TC/HDL-c (4,44 ± 2,40 vs 3,79 ± 1,82 ; p ≤ 0,05) étaient significativement plus élevés ; la proportion d'HVG était, paradoxalement, plus basse (39% vs 52%, p ≤ 0,05) chez les patients avec SM comparativement à ceux sans SM. Les deux groupes étaient comparables pour l'âge, le sexe, la durée de l'HTA, le niveau d'activité physique, le status thérapeutique et les autres variables biologiques.
Conclusion: le SM est une entité clinico-biologique fréquemment rencontrée dans la présente série des patients Congolais avec HTA essentielle. Il était positivement associé au tabagisme, à la dyslipidémie et, paradoxalement, à une faible proportion d'HVG suggérant le phénomène d'épidémiologie inverse des facteurs de risque traditionnels.

Mots clé: syndrome métabolique, prévalence, déterminants, Noirs, hypertension essentielle.

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Summary

Objective: to assess the prevalence and correlates of the metabolic syndrome (MS) in black patients with essential hypertension.
Methods: A total of 100 consecutive essential hypertensives (53 men and 47 women, mean age 49 ± 10 years, BMI 27 ± 5 Kg/m², SBP 155 ± 19 mmHg, DBP 101 ± 11 mmHg) attending the University of Kinshasa outpatient hypertension clinic and included in a case-control study of lipids and lipoproteins were considered for the present cross sectional analysis. All patients underwent clinical, laboratory and electrocardiographic investigations searching for lipid and lipid cardiovascular risk factors. NCEP-ATP III criteria were used to define the MS. Between group comparisons were made with the Student t test, Mann Whitney U test or Chi square as appropriate.
Results: 31 hypertensive patients (33%), 23 men and 8 women, fulfilled the NCEP-ATP III criteria of the MS. In univariate analysis, aside the variables defining the MS, patients with the MS had a significantly higher TC/HDL-c ratio (4.44 ± 2.40 vs 3.79 ± 1.82; p ≤ 0.05) and proportion (13% vs 3%, p ≤ 0.05) of smokers; they paradoxically showed lower proportion (39% vs 52%, p ≤ 0.05) of left ventricular hypertrophy (LVH) in comparison to those without the MS. The two groups were similar for age, sex distribution, duration of hypertension, physical activity, treatment status, BP and other biological variables. Multivariate logistic regression analysis was used to determine the independent contribution of risk factors to the risk of MS.
Conclusion: MS is common among Congolese patients with essential hypertension and seems to be paradoxically associated with less pronounced cardiac damage probably due to the phenomenon of reverse epidemiology of traditional cardiovascular risk factors.

Key words: metabolic syndrome, prevalence, correlates, blacks, essential hypertension.

Introduction

The clustering of cardiovascular risk factors such as elevated blood pressure (BP), dyslipidaemia and hyperglycaemia associated or not to obesity in the same individual appears to confer a substantial cardiovascular risk additional to the sum of the risk associated with each abnormality(1).

A multiple set of risk factors that commonly appears together is now termed the metabolic syndrome (MS) and increases the morbidity and mortality of cardio-vascular disease (CVD) (1). The third report of the National Cholesterol Education Program Adult Treatment Panel (NCEP-ATP III) has recommended appropriate measures to identify individuals with the MS and to manage their care prior to development of cardiovascular compli-cations (2). Hypertension commonly occurs in conjunction with insulin resistance and other components of the MS (3) which could contribute to enhanced cardiovascular risk seen in hypertensives. A relationship between the MS and left ventricular hypertrophy (LVH) as a measure of subclinical target organ damage has already been reported (4). This relationship is of utmost importance in blacks in whom both the MS and LVH are very common (5).

In the Democratic Republic of the Congo (DRC), hypertension is reported to afflict about 30% of adults (6). Coronary heart disease (CHD) remains of marginal occurrence whereas stroke of both haemor-rhagic and ischemic subtypes, LVH (7) and subsequent congestive heart failure (CHF) and CKD are the deadly complications of the hypertensive process (8, 9). Despite the growing evidence concerning the impact of the MS on cardiovascular and renal disease, little is known about the MS and its correlates in hypertensive patients. Thus, the major aim of the present study was to determine the prevalence of the MS and its correlates in black patients with essential hypertension seen at the University of Kinshasa Hospital.

Patients and methods

Cross sectional analysis for the presence of the MS and associated risk factors of data from 100 consecutive black patients with essential hypertension enrolled in a case-control study of lipid and non lipid risk factors, described in details elsewhere (12). Available lifestyle data included self reported physical activity and smoking habits. Data were also available for the duration of hypertension and current antihypertensive medication. Measures of adiposity included body mass index (BMI) and waist circumference. All patients had the following measurements after 12 h fasting: total cholesterol (TC), high density lipoprotein-cholesterol (LDL-c), trigly-cerides, glucose, uric acid, fibrinogen, and creatinine. Low density lipoprotein-cholesterol (LDL-c) and creatinine clea-rance (CrCl) were calculated according to Friedewal (10) and Cockcroft and Gault (11) equations respectively. Electrocardio-graphic left ventricular hypertrophy (ECG-LVH) was defined according to Cornell voltage index as R wave in lead aVL ≥ 13 mm (12). All patients gave informed consent and research and ethic committee approved data collection.

MS was defined according to NCEP-ATP III criteria (2) as in addition to hypertension, two of the following: waist circumference > 88 cm in women and > 102 cm in men, TG ≥ 1.69 mmol/L, HDL-c < 1.30 mmol/L in women and < 1.04 mmol/L in men, glucose ≥ 6.11 mmol/L.

Data were expressed as mean ± standard deviation (SD) or relative frequency in percent. The distribution of duration of hypertension and triglycerides being positively skewed, non parametric test (Mann Whitney) was used for these variables. Chi square and Student t tests were used for comparing categorical and continuous variables normally distributed, respectively. P value ≤ 0.5 defined statistical significance. All statistical analyses were performed with SPSS for Windows version 10.0 at the Department of Epidemiology and Biostatistics of the Kinshasa School of Public Health.

Results

Clinical and biological characteristics of the whole group and patients with and without the MS are summarized in tables 1 and 2.

Table 1. Clinical characteristics of the whole group and hypertensives with and without metabolic syndrome

Characteristic	Whole group (n = 100)	Without MS (n = 69)	With MS (n = 31)
Gender: M/F	53/47	45/24	23/8
Age, years	49 ± 10	49 ± 10	49 ± 10
DHT, months	66 ± 72	64 ± 69	70 ± 82
Treatment, %	50	51	49
Smoking, %	10	3	13*
Alcohol, %	16	16	16
Physical inactivity, %	93	93	94
LVH, %	49	52	39*
BMI, Kg/m^2	27 ± 5	26 ± 4	28 ± 5
Waist, cm	94 ± 12	91 ± 12	96 ± 11*

SBP, mmHg	155 ± 19	156 ± 19	154 ± 18
DBP, mmHg	101 ± 9	101 ± 9	101 ± 10
PP, mmHg	54 ± 14	54 ± 14	52 ± 14
Heart rate, b/min	79 ± 11	78 ± 11	80 ± 11

Data are expressed as mean ± SD or relative frequency in percent.
Abbreviations: M, male F, female DHT, duration of hypertension BMI, body mass index WHR, waist hip ratio SBP, systolic blood pressure DBP, diastolic blood pressure PP, pulse pressure b, beat *$p \leq 0.05$ **$p \leq 0.01$ ***$p \leq 0.001$.

Table 2. Biological characteristics of the whole group and hypertensives with and without metabolic syndrome

Characteristic	Whole group (n = 100)	Without MS (n = 69)	With MS (n = 31)
TC, mmol/L	5.01±1.49	5.16±1.42	4.67 ± 1.60
LDL-c, mmol/L	3.36±1.31	3.48±1.26	3.10 ± 1.31
HDL-c, mmol/L	1.27±0.38	1.36±0.38	1.05±0.31***
TG, mmol/L	1.07±0.67	0.92±0.36	1.37 ± 1.00
TC/HDL-c	4.24±2.23	3.79±1.82	4.44 ± 2.40*
Glucose, mmol/L	5.05±0.77	4.88±0.72	5.55±0.83***
Uric acid, mmol/L	393 ±112	389±124	399 ±104
Fibrinogen, g/L	2.8 ± 0.8	2.74±0.79	2.95 ± 0.79
Creatinine, µmol/L	85 ± 16	103 ± 32	106 ± 30
CrCl, mL/min	97 ± 16	83 ± 36	77 ± 30

Data are expressed as mean ± SD
Abbreviations: TC, total cholesterol LDL-c, low-density lipoprotein-cholesterol male
HDL-c, high-density lipoprotein-cholesterol TG, triglycerides CrCl, creatinine clearance mL/min *p ≤ 0.05 **p ≤ 0.01 ***p ≤ 0.001

A total of 100 consecutive hypertensive patients (47 women) were examined. Their mean age was 49 ± 10 years and average levels of BMI and BP were 27 ± 5 Kg/m^2 and 155 ± 19/101 ± 10 mmHg, respectively. Fifty patients (50%) were receiving antihypertensive medication as mono-therapy (n = 27) or combined therapy (two drugs, n = 27; three drugs, n = 3); treatment consisted of calcium channel blockers, diuretics, angiotensin converting enzyme inhibitors, central acting drugs and beta blockers in 42%, 30%, 24%, 24% and 16% of patients, respectively.

Overall, 31 patients (33%, 23 men) fulfilled the NCEP-ATP III criteria for the MS and 13 of them (39%) had in addition LVH. In univariate analysis, aside the variables defining the MS, patients with the MS had significantly higher (13% vs 3%, $p \leq 0.05$) proportion of smokers, and paradoxically lower (39% vs 52%, $p \leq 0.05$) proportion of LVH in comparison to patients without this metabolic abnormality. The two groups were similar for age, sex distribution, duration of hypertension, physical activity, treatment status and other biological variables. In multivariate analysis, the strength of the association noted in univariate analysis did not persist for the two variables.

Discussion

The key finding of the present study was a high prevalence of the MS among hypertensive patients and its paradoxical association with LVH.

One third of hypertensive patients in the present case series had the MS. This observation agrees with previous studies reporting a high prevalence of the MS in

hypertensive patients (4, 13). The pathogenesis of the MS in hypertension is complex and so far incompletely understood; but the interaction of obesity, sedentary lifestyle, and dietary and genetic factors are known to contribute to its development (3) Among all these factors, obesity, mainly of central type, appears to play a central role in the development of the MS through mediators such as tumor necrosis factor alpha, adiponectin, leptin and resistin secreted by adipocytes (14, 15).

LVH was observed in nearly 40% of patients in the present study. The most important dimension of the MS is its association with the risk of developing diabetes mellitus and atherosclerotic CVD (16). In hypertensives, nearly half of CV events in men and 68% in women are attributable to the presence of two or more risk factors (17). A 5 fold increase in CV risk has been associated with the presence of the MS (13, 18). Furthermore, a relationship between LVH, a more powerful predictor of CVD than cigarette smoking or dyslipidaemia, and the MS has been already reported (4, 19, 20) and could be the link between the MS and CV risk in hypertensive patient (13). The relationship between LVH and the MS is likely to be of particular importance in Blacks in whom these risk factors are very common (5). Therefore, effective management of the MS could help to prevent the development and progression of LVH and consequently to reduce CV risk in hypertensives (21). Several mechanisms have been evoked to explain the high CV risk associated with the MS and include the clustering of multiple metabolic abnormalities mainly insulin resistance / hyperinsulinaemia (18), the overactivity of the sympathetic nervous and renin angiotensin aldosterone (RAA) systems (3, 22) with subsequent endothelial dysfunction (23).

However, compared with patients without the MS, those bearing this metabolic abnormality had paradoxically lesser cardiac damage. This paradoxical association has been already reported for individual components of the MS such as obesity, hypertension and lipids (24) and is thought to relate, aside of methodological issues, to the so-called phenomenon of reverse epidemiology of traditional risk factors observed in chronic diseases (25). Time differentials of competing risk factors with over nutrition acting as a long term killer but short term protective versus under nutrition as a short term killer as well as malnutrition-inflammation complex Syn-drome (MICS) have been evoked as potential explanatory mechanisms of reverse epidemiology (26).

MS was positively associated with smoking in the present study. Smoking is a major risk factor for CVD. It has been reported to reduce insulin sensitivity or induce insulin resistance and enhance CV risk factors such as elevated plasma triglycerides, decreased HDL-c and hyperglycaemia (26). Further-more, several studies have shown that smoking is associated with metabolic abnormalities and increases the risk of MS (27). In this regard, subjects who habitually smoked tobacco had a 1.07- to 1.66-fold risk of developing MS compared to non-smoking subjects; the quantity of tobacco smoked had a dose-dependent relationship with the severity of MS (29). Of note, subjects with both smoking and MS have been reported to experience increased hazard ratio (HR 3.56 (1.89 - 6.72) for CVD incidence compared to non-smoking subjects without MS (28). Patients with MS had higher TC/HDL-c ratio. Elevated TC/HDL-c ratio

is a well-known risk factor for CVD; it has been reported to better predict CV risk in comparison to TC and HDL-C (29).

The cross sectional design of the present work precludes clear establishment of a causal relationship between MS and associated risk factors. Furthermore, the sample size could not allow sufficient power to detect additional associations. One wonders to what extent the conclusions of the present clinical based study could be extrapolated to the general population given the bias in the referral of patients. The findings of the present study bear however some clinical implications for the identification of the MS and its correlates in hypertensive patients.

Conclusion

The present study has shown that the MS is common among Congolese hypertensive patients and appears to be paradoxically associated with less cardiac damage (Cornell indices) in comparison to patients without MS. This paradoxical association could be linked to the so-called phenomenon of "reverse epidemiology" of traditional risk factors in chronic diseases. Interventions aimed to identify and manage the MS should be encouraged in hypertensive patients.

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