

Increased High Density Lipoprotein Cholesterol and Total Cholesterol Levels in Traders with Metabolic Syndrome in an Apparently Healthy Nigerian Population

Aim: To identify specific alterations of metabolic biomarkers indicated in individuals with metabolic syndrome for early diagnosis, prevention and management of the metabolic syndrome (MS) and its associated diseases.

Study Design: Cohort study

Place and Duration of Study: Department of Chemical Pathology, College of Medicine, University of Ibadan, Ibadan between March, 2010 and August 2010.

Methodology: 534 apparently healthy Nigerian traders aged 18–105 years were participants of a cohort study. The International Diabetes Federation (2005) and the National High Blood Pressure Education Program Coordinating Committee criteria were used for MS and HTN classifications respectively. Anthropometric indices were obtained by standard methods. Plasma glucose, total cholesterol (TC), triglycerides and high density lipoprotein cholesterol (HDL-C) were determined by enzymatic methods, while low density lipoprotein cholesterol (LDL-C) was calculated. Data analysed statistically were significant at $p < 0.05$.

Results: Only 63 (11%) traders had no component of the MS. All the measures of adiposity and biochemical indices tested (including HDL-C and TC) were significantly higher MS and non-MS groups except height and LDL-C. MS was associated with age and blood pressure. The differences were significant ($p < 0.05$). Number of participants with MS increased with increasing decade of age but reduced after 54 years, and increased from hypertension stages-normotension to hypertension.

Conclusion: Metabolic alterations exist in MS and MS was associated with BP and age. The high levels of HDL-C in Nigerians with MS may be cardioprotective. Healthy diet and lifestyle should be promoted as part of African sustainable development programmes.

Keywords: Metabolic syndrome, cardiovascular diseases, measures of adiposity, lipids, type2 diabetes mellitus

1. INTRODUCTION

Escalating overnutrition in the continuing presence of undernutrition characterise many resource poor settings [1] including Nigeria. The prevalence of 16.3% of obesity and 23.4% of metabolic syndrome (MS) have been reported in the face of 3.3% of undernutrition in an apparently healthy market population in Nigeria. The observed MS was associated with female gender and body mass Index [2].

Obesity is a natural consequence of overnutrition and sedentary lifestyle. Persistent obesity dysregulates metabolic processes including action of insulin on glucose-lipid-free fatty acid metabolism and severely affects processes controlling blood glucose, blood pressure, and lipids. The resultant cluster of conditions: dysglycemia, dyslipidemia, hypertension, and procoagulant state known as MS culminates in cardiovascular disease (CVD) and type2 diabetes mellitus (DM2) [1]. A recent study in obese individuals in Nigeria showed dyslipidaemia, hypertension but not dysglycemia [2]. Fabian et al. [3] observed significant correlations between leptin levels and measures of adiposity in individuals with MS. The increased leptin level was postulated as a compensatory mechanism for both the maintenance of blood pressure and weight loss.

Overweight and obesity progress to MS through pathophysiological mechanisms, which are still largely unclear. Recent mechanisms put forward are the inflammatory state and oxidative stress with more complications than were earlier imagined. Firstly, it is hypothesised that overfeeding is the starting signal of obesity, which results in a proinflammatory state starting in the metabolic cells (adipocyte, hepatocyte, or myocyte) and also recruiting immune cells with the

consequent release of inflammatory cytokines (TNF- α , IL-6, adiponectin, etc.). This inflammatory process may lead to complications such as hypertension, atherosclerosis, dyslipidaemia, insulin resistance, and diabetes mellitus which characterize metabolic syndrome [4].

Secondly, oxidative stress, a condition in which an imbalance results between the production and inactivation of reactive oxygen species characterize MS [5], its components and progression [6]. Reactive oxygen species, short-lived molecules are highly reactive derivatives of oxygen metabolism. They play an essential role in multiple physiological systems such as gene expression and signal transduction but contribute to cellular dysfunction under conditions of oxidative stress. Oxidative stress is thought to play a major role in the pathogenesis of ageing and a variety of human diseases, including atherosclerosis, diabetes, hypertension, Alzheimer's disease, kidney disease and cancer [5,6].

These complications of MS are overwhelming and necessitate early identification of specific biomarkers for early diagnosis, prevention and management of the syndrome particularly in a region that is battling with undernutrition and overnutrition in addition to communicable diseases. Reducing the prevalence of MS will reduce the diseases associated with MS. This study is intended to identify specific markers in individuals with and without metabolic syndrome.

2. SUBJECTS AND METHODS

2.1 Study Design

The study was a cross-sectional survey conducted over a period of 6 months and ethical approval was obtained from the Joint Ethical Committee of the University of Ibadan/University College Hospital, Ibadan, Nigeria (UI/UCH).

2.2 Participants

534 (170 males and 364 females) apparently healthy traders from a local market in Bodija, Ibadan aged 18–105 years participated in the study as described by Charles-Davies et al. [2]. They were non-diabetic participants and were not on any type of medication. Methods used were shown elsewhere [2,3,7].

2.3 Classes of Hypertension

Participants were classified into different BP (SBP and/or DSP) groups-normal (BP:<120 and <80mmHg), pre-hypertension (BP:120-139 or 80-90mmHg), stage1 hypertension (BP:140-159 or 90-99mmHg) and stage2 hypertension (BP: $\geq$ 160 or $\geq$ 100mmHg) [8].

2.4 Diagnosis of Metabolic Syndrome

MS was diagnosed using the International Diabetes Federation diagnostic criteria [9]. The criteria include central obesity (WC) (male: $\geq$ 94 cm, female: $\geq$ 80 cm) and any two of raised triglycerides: $\geq$ 150 mg/dL (1.7 mmol/L), reduced HDL cholesterol (males: < 40 mg/dL, females: < 50 mg/dL, raised blood pressure ($\geq$ 130/ $\geq$ 85 mmHg), or raised fasting plasma glucose (FPG) ($\geq$ 100 mg/dL).

2.5 Components of Metabolic Syndrome

These were parameters contained in the International Diabetes Federation diagnostic criteria for metabolic syndrome-waist circumference (WC), triglycerides (TG), high density lipoprotein cholesterol (HDL), blood pressure (BP), and fasting plasma glucose [2,7,9].

2.6 Measures of Adiposity and Lipids

Adiposity measures included: body weight, height, body mass index (BMI), hip circumference (HC), waist hip ratio (WHR), waist height ratio (WHT) and percentage body fat (PBF). Lipids (other than HDLC and TG-components of MS) included total cholesterol (TC) and low density lipoprotein cholesterol (LDLC) [2].

2.7 Sample Collection

6ml of venous blood sample was aseptically obtained by venopuncture from the participants after an overnight fast (10-14 h). 4 ml was dispensed into potassium ethylene diamine tetra acetic acid (K3EDTA) tube for the determination of lipid profile (TC, TG and HDLC). 2 ml was dispensed into fluoride oxalate tube for FPG estimation. All samples were centrifuged at 500 g for 5 min after which plasma/serum were aspirated in small aliquots into clean vials and stored at -20°C until analyses were done.

2.8 Statistical Analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS) software 15.0 version. Student's t-test was used for comparison of quantitative variables. Two-tailed independent t-test of significance at 95% confidence limit with $p < 0.05$ was considered significant for the variables. Chi-Square test (X^2) was used to find relationship between two qualitative variables.

3. RESULTS AND DISCUSSION

Table 1 shows frequency of traders with components of MS. Majority of the traders 229 (42.9%) had 2 components of the metabolic syndrome. Most of the males 69 (40.6%) had only 1 component of the MS while most of the females 182 (50%) had 2 components of the metabolic syndrome. Only (63)11% of traders had no component of the MS. Out of these 42 (66.7%) were males while 21(33.3%) were females. The highest number of components was 4, which were exhibited by 11 (2.1%) of the participants in the study. 2 (18.2%) were males while 9 (81.8%) of them were females.

Table 1 Frequency of Traders with Components of Metabolic Syndrome

Number of MS Components	Female Frequency (%)	Male Frequency (%)	All Frequency (%)
0	21 (5.8)	42 (24.7)	63 (11.8)
1	84 (23.1)	69 (40.6)	153 (28.7)
2	182 (50.0)	47 (27.6)	229 (42.9)
3	68 (18.7)	10 (5.9)	78 (14.6)
4	9 (2.5)	2 (1.2)	11 (2.1)
Total	364 (100.0)	170 (100.0)	534 (100.0)

values in frequency with percentage in parentheses, MS=metabolic syndrome

Table 2 shows the comparison of the age and metabolic variables between participants with and without MS. All the indices tested were different between MS and non-MS groups except height and LDL. Increases were observed in age, BP (Systolic and diastolic), body weight, BMI, WC, HC, WHR, WHT, PBF, TC and TG as well as HDL in MS compared with non-MS. These differences were significant ($p < 0.05$).

Table 3 shows the association of MS with sex, age and BP in traders studied. Sex, age and blood pressure were significantly associated with MS ($p < 0.05$). Number of participants with MS was higher in females than males, increased with increasing decade of age but reduced after 54 years, and increased from hypertensive stages -normotensive to stage 2. 2.3% and 79.3% of traders with MS were normotensive and hypertensive (stages 1 and 2) respectively while 31.5% and 27.9% of traders without MS were normotensive and hypertensive (stages 1 and 2) respectively. 40.5% of traders without MS as against 18.4% of traders with MS were pre-hypertensive. 31.8% and 24.2% of males and females respectively were normotensive while 20.6% of males and 43.6% of females were hypertensive 47.1% of males and 32.1% of females were pre-hypertensive.

The metabolic syndrome is a complex of clinical features leading to an increased risk for CVD and DM2 in both sexes [4]. It is also a useful and simple clinical concept that enhances early detection of DM2, CVD [10], ageing as well as a variety of other complications including atherosclerosis, hypertension, Alzheimer's disease, kidney disease and cancer [5,6].

Visceral obesity and insulin resistance are considered the main features determining the negative cardiovascular profile in metabolic syndrome [4]. The IDF has five components-abdominal (visceral) obesity, blood pressure, low HDLC levels, elevated triglyceride levels and elevated FPG levels in the criteria for MS. Only 63 (11%) traders had no component of the MS. Most of the traders- 229 (42.9%) had 2 components of the metabolic syndrome. The highest number of components was 4, which were exhibited by 11 (2.1%) of the participants in the study. Several approaches including WC have been used to measure obesity. PBF and BMI measure general obesity, HC measures subcutaneous adipose tissue while WC, waist-hip ratio (WHR) and waist-to-height ratio (WHT) measure abdominal fat [2,11,12,13,14].

Table 2 Comparison of Age and Metabolic Variables between Participants with Metabolic Syndrome and Non- Metabolic Syndrome

Group n	Non –MS 447	MS 87	Total 534	t	p
Age (years)	43.12±12.99	47.99±10.39	43.91±12.72	-3.296	0.001*
Systolic Blood Pressure (mmHg)	124.89±20.77	149.71±25.75	128.93±23.50	-9.385	0.000*
Diastolic Blood Pressure (mmHg)	78.70±11.85	89.89±12.87	80.52±12.70	-7.938	0.000*
Height (m)	1.634±0.0945	1.615±0.0786	1.63±0.09	1.742	0.082
Weight (kg)	68.76±13.36	77.54±15.01	70.19±14.01	-5.498	0.000*
Body Mass Index (kg/m ²)	25.78±5.29	29.60±4.75	26.40±5.39	-6.269	0.000*
Waist Circumference(cm)	92.38±13.27	102.91±12.19	94.10±13.65	-6.859	0.000*
Hip circumference(cm)	100.56±10.88	107.60±09.29	101.71±10.94	-5.653	0.000*
Waist: Height Ratio	56.93±10.95	63.81±07.58	58.05±10.77	-5.601	0.000*
Waist: Hip Ratio	0.917±0.066	0.957±0.079	0.923±0.070	-4.925	0.000*
Percentage Body Fat	31.40±11.83	39.83±08.14	32.80±11.72	-6.354	0.000*
Fasting Plasma Glucose (mg/dl)	82.87±20.11	96.42±37.85	85.09±24.41	-4.837	0.000*
Total Cholesterol (mg/dl)	142.14±40.34	156.19±40.35	144.60±40.69	-3.182	0.002*
Triglyceride (mg/dl)	63.85±29.42	79.30±37.18	66.37±31.31	-4.278	0.000*
High density Lipoprotein(mg/dl)	40.38±13.56	52.66±18.86	42.38±15.23	-7.202	0.000*
Low Density Lipoprotein (mg/dl)	88.45±36.96	89.33±36.46	88.60±36.85	-.204	.839

n= number of participants, values are in mean ± s.d, p=probability, t = Student's t-test, *=significant, MS=metabolic syndrome, Non-MS=non-metabolic syndrome

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WHT, an improved index over WC was reported as a simple and practical index for assessing central fat distribution and metabolic risk in men and women [15]. Although BMI, WC, WHR, WHT are independently associated with cardiovascular and metabolic risk, a combination of general and central adiposity has been recommended [11,13,14]. These measures were higher in obese than normal weight traders [2].

We observed increases in all components of MS defined by the IDF criteria in MS compared with non-MS. All measures of general and central obesity indicated in this study were higher in MS than non-MS ($p<0.05$). BP (systolic and diastolic), triglyceride level and FPG level were higher in MS than non-MS. However, HDLC was higher in MS than non-MS. This is inconsistent with previous studies. Low HDLC level is one of the components of metabolic syndrome in the IDF criteria [9] used in this study. Gordon et al. [16] in the Framingham study had long shown the cardioprotective effect of HDLC. The increase observed in HDLC in this study is a novel finding in our region. Our previous study showed similarities in HDLC in overweight and obese groups compared with normal weight individuals [2]. Fresh reports indicate higher HDL levels in MS than non-MS. Yan et al. [17] in China, observed that serum HDLC levels in normotensive participants increased with age, body mass index, blood pressure and fasting glucose levels. Although the reason is not clear, the ineffectiveness of high HDL cholesterol levels in inhibiting the development of atherosclerosis in a mammal with severe hypercholesterolaemia has been demonstrated [18]. The level of TC, a CVD risk factor but a non-MS component by IDF definition of MS was higher in MS compared with non-MS in this present study. New research suggests that risk factors specific to a particular racial or ethnic population may be important [19]. However, all components of the MS in the IDF criteria are not used for MS diagnosis. It is therefore possible that most participants with MS in this study had higher levels of HDLC when compared with participants without MS but requires further studies.

167 **Table 3 Association of Metabolic Syndrome with Sex, Age, Obesity and Blood Pressure in Traders**

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	Non-MS	MS	Total	X ²	P
n (%)	447(83.7%)	87(16.3%)	534		
Age groups					
<25 years	16(100.0%)	0(0%)	16	22.292	0.000*
25-34 years	99(95.2%)	5(4.8%)	104		
35-44 years	154(84.6%)	28(15.4%)	182		
45-54 years	92(74.8%)	31(25.2%)	123		
>54 years	86(78.9%)	23(21.1%)	109		
Blood Pressure					
Normotensive	141(31.5%)	2(2.3%)	143	87.713	0.000*
Prehypertensive	181(40.5%)	16(18.4%)	197		
Stage 1 Hypertensive	77(17.2%)	37(42.5%)	114		
Stage 2 Hypertensive	48(10.7%)	32(36.8%)	80		

n= number of participants, p=probability, *=significant, X2= chi-squared test, MS=Metabolic Syndrome, Non-MS=Non-metabolic syndrome

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170 The similarity in LDLC concentrations in MS and non-MS tends to corroborate previous reports of small LDL particle size
171 implicated in MS [20]. MS was associated with age and BP. The frequency of participants with MS was higher in females
172 than males, increased with increasing decade of age but reduced after 54 years. These observations are consistent with
173 our previous findings in obese traders in same population [2].

Oestrogen is a female hormone and is thought to prevent the development of atherosclerosis through favourable effects on an intact endothelium. However, prothrombotic and possibly proinflammatory effects of estrogens are likely to predominate and prove harmful once the vascular endothelium is damaged [21]. We observed that the frequency of participants with MS increased from hypertension stages -normotensive to hypertension (stages 1 and 2). Hypertension is a very prominent feature of the metabolic syndrome, present in up to 85% of patients. It is frequently undiagnosed until relatively late in its course, leading to a variety of other life-threatening conditions like kidney damage and heart failure (Duvnjak et al., 2008).

4. CONCLUSION

We observed increases in general and abdominal obesity in traders with MS similar to our previous study in obesity. Biochemical measures-FPG, triglycerides, TC and HDLC were increased in MS compared with non-MS. The similarity observed in LDLC in both the MS and non-MS groups may be attributed to small LDL particle size usually observed in MS. Increases observed in age and BP (systolic and diastolic) in MS compared with non-MS as well as associations of MS with BP and age of less than 54 years are consistent with our previous study, increased with increasing decade of age but reduced after 54 years. The finding of only 11% of traders with no component of the MS and most of them- 229 (42.9%) with 2 components of the metabolic syndrome suggests that Nigerians are unhealthy. The observation of high HDLC and TC may be important in MS management. Increase in HDLC may possibly reduce CVD risk in Nigerians with MS. Further characterisation of frequency of specific metabolic components in individuals as well as specific cut-off of the metabolic factors in individuals without any MS component may be needed to identify healthy and unhealthy Nigerians. Further studies should investigate the effect of oestrogen on MS components in pre- and post-menopausal women.

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COMPETING INTERESTS

We declare that no competing interests exist.

AUTHORS' CONTRIBUTIONS

The authors contributed to the intellectual content of this paper and have met the following requirements:

- a) Significant contributions to the concept and design, data acquisition, analysis and interpretation
- b) Drafting and reviewing the article for intellectual content
- c) Final approval of the article for publication.

CONSENT (WHEREEVER APPLICABLE)

We declare that informed consent was obtained from all the participants in the study after detailed explanation of the study.

ETHICAL APPROVAL (WHEREEVER APPLICABLE)

We hereby declare that the study protocol was examined and approved by the University of Ibadan /University College Hospital, Ibadan ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki."

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