ORIGINAL ARTICLE

Oxidative stress among subjects with metabolic syndrome in Sokoto, North-Western Nigeria

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Abstract

Background: Oxidative stress is known to play a role in the pathophysiology of metabolic syndrome and its components. Racial differences may exist in the level of markers of oxidative stress and antioxidants in patients with metabolic syndrome.
Aim: The aim of this study was to determine the oxidative stress and antioxidants status in subjects with metabolic syndrome in Sokoto, North-Western Nigeria.
Methods: A cross-sectional community-based study was carried out. Two hundred subjects (96 males and 104 females) were recruited for the study using a multi-stage sampling technique. Demographic data were obtained from the participants. Evaluation of anthropometric variables, blood pressure, blood glucose levels, lipid profiles, plasma insulin levels, total antioxidant status, and oxidative stress markers was performed.
Results: The subjects with metabolic syndrome had significantly higher malondialdehyde as compared to those without metabolic syndrome (236.4 [92.2] vs. 184 [63.2] nmol/l). The antioxidant enzymes (superoxide dismutase, glutathione peroxidase and catalase) were significantly lower in subjects with metabolic syndrome than in those without metabolic syndrome (11.3 [4.2] vs. 13.9 [4.1] U/ml, 160[42] vs. 220[32] U/ml, and 2.12 [0.2] vs. 2.42 [0.2] U/ml, respectively). Similarly, the antioxidant Vitamins (A, C, and E) levels were significantly lower in subjects with metabolic syndrome than in those without metabolic syndrome (7.1 [4.1] vs. 7.7 [4.2] μmol/L, 225 [55.3] vs. 227.6 [62.3] μmol/L, and 75.9 [13.9] vs. 82.8 [18.6] mg/dl, respectively). There was a positive correlation between components of metabolic syndrome and free radicals.
Conclusion: Significantly increased oxidative stress and diminished antioxidant defenses were found among Nigerians with metabolic syndrome.

Key words: Antioxidants, metabolic syndrome, oxidative stress

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Introduction

Oxidative stress is known to play a role in the pathophysiology of metabolic syndrome and its components.[1-4] Reactive oxygen species (ROS) are highly reactive molecules formed as natural products of normal oxygen metabolism. They have important roles in cell signaling and homeostasis. ROS are normally maintained at an optimal level by a balance between the production and elimination by enzymes (superoxide dismutase [SOD], glutathione peroxidase [GPx], and catalase) and antioxidants Vitamins (A, C, and E). The

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components of metabolic syndrome can cause increase production of ROS and the impairment of antioxidant enzymatic defenses such as SOD and GPx.[4-6] It has been postulated therefore that antioxidants could have a beneficial effect of lowering the risk of metabolic syndrome, however, the results are inconclusive.[7-9] Metabolic syndrome is a cluster of metabolically related cardiovascular risk factors, the core components of which comprise of central obesity, insulin resistance, dyslipidemia, and hypertension.[10] Racial differences are known to exist in the level of antioxidants in patients with metabolic syndrome.[11] However, there is a lack of data on oxidative stress and antioxidant status among patients with metabolic syndrome in sub-Saharan Africa.

The aim of this study was to determine the markers of oxidative stress and antioxidants status in subjects with metabolic syndrome in Sokoto, Nigeria.

Methods

Study location

The study was conducted in Sokoto metropolis in the Sudan savannah zone of North-Western Nigeria. The state had a population of 3.69 million according to the 2006 census figures over 90% of whom are Muslim Fulani and Hausas.[12]

Participants

Consenting adults (above 18 years of age) were recruited. Trained research assistants administered questionnaires and obtained the measurements including a collection of blood samples.

Ethical consideration

The study protocol was approved by the Research and Ethics Committee of Sokoto State, Nigeria.

Study design

A cross-sectional community-based study was carried out. Two hundred subjects (96 males and 104 females) were recruited for the study. Using a multi-stage sampling technique, two districts of Gidan Igwai and Arkilla were selected. The first stage involved random sampling selection of some districts; while the second stage involved selection of some households using clustered sampling technique from the districts selected. Pretested questionnaire was administered by trained research assistants. Demographic and the lifestyle data were obtained from the participants. Evaluation of anthropometric variables and blood pressure measurement was performed.

Laboratory analysis

About 10 ml fasting blood was drawn from the antecubital vein for the determination of fasting blood glucose, lipid profiles, total antioxidant status, oxidative stress, and insulin assay.

Serum glucose was determined by glucose oxidase method of Trinder.[13] Serum total cholesterol (TC), high-density lipoprotein (HDL), and triglyceride (TG) were determined by enzymatic methods using various determination kits according to manufacturer's instructions. Low-density lipoprotein (LDL) cholesterol was calculated using Friedwald's formula.[14]

Vitamin A was measured after ultraviolet irradiation according to the modified method of Neild and Pearson.[15] Vitamin C was estimated using dinitrophenylhydrazine.[16] Vitamin E was measured by spectrophotometry using bathophenanthroline assayed according to the micro method described by Quaife *et al.*[17] The activity of SOD was assayed using SOD assay kit.[18] GPx activity was assayed according to the method of Paglia and Valentine.[19] Malondialdehyde (MDA) was estimated using the MDA assay kit.[20] The assay is based on the reaction of MDA with thiobarbituric acid (TBA), forming an MDA-TBA_2 adducts that absorbs at 532 nm. Insulin was estimated by ELISA and insulin resistance was determined by homeostasis model assessment method (HOMA-IR):[21]

HOMA-IR = fasting plasma insulin (μiU/ml) × fasting plasma glucose (mmol/l) 22.5.

Operational definitions

The classification of metabolic syndrome was based on the National Cholesterol Education Program Adult Treatment Panel III guidelines [Table 1].[10] Metabolic syndrome was diagnosed when any three features were present: Fasting glucose ≥100 mg/d, blood pressure ≥130/85 mm Hg, TGs ≥150 mg/dl, HDL cholesterol (HDL-C) <40 mg/dl in men or <50 mg/dl in women, waist circumference ≥102 cm in men or ≥88 cm in women.

Data management and statistical analysis

Statistical analysis was performed using Epi Info version 3.3.4. The significance of differences between group means was assessed using Student's *t*-test while Chi-squared statistic was employed to determine significance of results of the comparison of proportions between groups. Linear relationships were determined using Pearson's correlation coefficients (*r*). The level of statistical significance is set at $P < 0.05$.

Results

Sociodemographic characteristics

The mean (standard deviation [SD]) age of the sample population was 33.6 (13.6) years. Fifty-four (27%) subjects

Table 1: Anthropometric characteristics of the study participants

Variable	All (*n*=200)	Metabolic syndrome (*n*=54)	Nonmetabolic syndrome (*n*=146)	*P*
Weight (kg)	65.4 (12.3)	68.5 (13.5)	64.3 (11.7)	0.03
Height (cm)	163.1 (9.2)	163.0 (8.4)	163.1 (9.5)	0.95
BMI (kg/m^2)	24.1 (4.5)	25.4 (5.5)	23.5 (4.1)	0.013
WC (cm)	81.6 (11.8)	85.2 (11.9)	80.3 (11.5)	0.009
SBP (mmHg)	133.6 (25.9)	135.7 (30.3)	132.9 (24.2)	0.49
DBP (mmHg)	79.5 (14.2)	82.1 (15.3)	78.6 (13.8)	0.12

BMI=Body mass index, DBP=Diastolic blood pressure, SBP=Systolic blood pressure, WC=Waist circumference

Table 2: Metabolic profile of research participants

Variable	All (*n*=200)	Metabolic syndrome (*n*=54)	Nonmetabolic syndrome (*n*=146)	*P*
FBG (mmol/l)	5.9 (1.7)	7.4 (1.9)	5.4 (0.8)	0.001
TC (mg/dL)	146.3 (52.8)	173.8 (52.9)	136.2 (49.3)	0.001
HDL-C (mg/dL)	49.3 (13.6)	46.9 (16.9)	50.7 (12.7)	0.48
LDL-C (mg/dL)	92.6 (17.1)	107.7 (23.4)	86.9 (16.2)	0.001
TG (mg/dL)	113.4 (24.8)	124.6 (25.4)	109.3 (19.6)	0.08
Insulin (U/ml)	14.6 (9.7)	23.7 (15.3)	11.2 (7.7)	0.001
HOMA-IR	2.32 (2.59)	4.44 (5.1)	1.54 (1.36)	0.001

FBG=Fasting blood glucose, TC=Total cholesterol, HDL-C=High-density lipoprotein cholesterol, LDL-C=Low density lipoprotein cholesterol, TG=Triglyceride, HOMA-IR=Homeostasis model assessment of insulin resistance

Table 3: Oxidative stress markers and antioxidant levels of the research participants

Variable	All (*n*=200)	Metabolic syndrome (*n*=54)	Nonmetabolic syndrome (*n*=146)	*P*
Catalase (U/ml)	2.32 (0.3)	2.12 (0.2)	2.42 (0.2)	0.82
GPx (U/ml)	176.5 (39)	160 (42)	220 (32)	0.033
SOD (U/ml)	12.3 (4.1)	11.3 (4.2)	13.9 (4.1)	0.042
MDA (nmol/L)	198.4 (77.5)	236.4 (92.2)	184 (63.2)	0.006
Vitamin A (μmol/l)	7.5 (4)	7.1 (4.1)	7.7 (4.2)	0.05
Vitamin C (μmol/l)	263.6 (55.2)	225 (55.3)	277.6 (62.3)	0.036
Vitamin E (mg/dL)	80.9 (17.8)	75.7 (13.9)	82.8 (18.6)	0.49

GPx=Glutathione peroxidase, SOD=Superoxide dismutase, MDA=Malondialdehyde

had metabolic syndrome while 146 (73%) did not fulfill the criteria for metabolic syndrome. The mean (SD) age of subjects with metabolic syndrome was 35.6 (14.4) years, and that of the subject without metabolic syndrome was 32.9 (13.3) years ($P = 0.21$). Table 1 shows the comparison of the anthropometric parameters between the subjects with metabolic syndrome and nonmetabolic syndrome subjects.

The subjects with metabolic syndrome had significantly higher weight, body mass index and waist circumference.

Metabolic profile

The metabolic profile of the research participants is shown in Table 2.

The subjects with metabolic syndrome had significantly higher fasting blood glucose, TC, LDL, plasma insulin, and HOMA-IR. The HDL-C was found to be lower in subjects with metabolic syndrome but not statistically significant ($P = 0.48$).

Antioxidant levels

The oxidative stress markers and antioxidant levels of the research participants are shown in Table 3. The subjects with metabolic syndrome had significantly higher levels of oxidative stress marker (MDA). The antioxidant enzymes (GPx and SOD) and antioxidant Vitamins (A and C) levels were significantly lower in subjects with metabolic syndrome than in those without metabolic syndrome. Vitamin E and catalase levels were also lower in subjects with metabolic syndrome but not statistically significant ($P = 0.49$ and 0.82, respectively).

Oxidative stress and components of metabolic syndrome

The correlation between markers of oxidative stress and components of metabolic syndrome is seen in Table 4.

There was a positive correlation between HOMA-IR and free radicals.

Table 4: Correlation between markers of oxidative stress and components of metabolic syndrome

Variable	FBS	TG	HDL	HOMA-IR	WC	SBP	DBP
MDA	0.67*	0.14	−0.15	0.31*	0.24	0.65*	0.33
SOD	0.21*	0.24*	−0.19	0.26	0.39*	0.54	0.56*
Catalase	0.17	0.36	0.12*	0.56	0.51*	0.23*	0.16
GPx	0.05	0.44*	−0.7	0.21	0.19	0.34	0.43*
Vitamin A	−0.064	−0.11	−0.22	−0.28	−0.24*	−0.33*	0.04
Vitamin C	−0.14*	0.08	−0.4*	−0.32	0.09	0.32	−0.23*
Vitamin E	0.05	0.09	−0.9	0.02	−0.08	0.04	0.05

*Significant difference $P<0.05$. GPx=Glutathione peroxidase, SOD=Superoxide dismutase, MDA=Malondialdehyde, DBP=Diastolic blood pressure, SBP=Systolic blood pressure, WC=Waist circumference, FBS=Fasting blood sugar, HDL=High-density lipoprotein, TG=Triglyceride, HOMA-IR=Homeostasis model assessment of insulin resistance

Discussion

In this study, we found subjects with metabolic syndrome had significantly lower antioxidant Vitamins (A, C and E) and decreased antioxidant enzymes (SOD, catalase, and GPx) as compared to subjects without metabolic syndrome. There was also high MDA level indicative of oxidative stress in subjects with metabolic syndrome as compared to subjects without metabolic syndrome. The low levels of antioxidant vitamins and enzymes would have led to the imbalance between their protecting effects and the damaging effects of the free radicals hence the increased oxidative stress. Some other previous studies have found a similar pattern of significantly low levels of Vitamin A, C, and E and significantly increased oxidative stress in subjects with metabolic syndrome.[3,4,22]

Ford *et al*.[4] suggested that the low levels of antioxidant vitamins in subjects with metabolic syndrome could be attributed to the increased use of antioxidants by the tissues and decreased intake of fruits and vegetables rich in antioxidants found in subjects with metabolic syndrome. Bilbis *et al*.[23] found out that supplementation with antioxidants played a vital role in prevention and management of metabolic syndrome in rat models. Several studies have also shown the importance of diet on oxidative status. Esposito *et al*.[24] found Mediterranean-style diet intervention (increased intake of whole grains, fruits, vegetables, nuts, and olive oil) resulted in decreased oxidative stress as well as improved insulin resistance. The benefit of the dietary intervention is greater in subjects with metabolic syndrome because some studies reported only a small increase in antioxidant concentration with increased consumption of fruit and vegetables in the diet of healthy individuals.[25] Wali *et al*.[26] also found significantly lower antioxidants vitamins among patients with diabetes mellitus as compared to subjects without diabetes mellitus in Sokoto, Nigeria. However, some researchers did not find any difference in the level in the antioxidant vitamins between the subjects with metabolic syndrome and those without metabolic syndrome.[27]

The components of metabolic syndrome correlated positively with the markers of oxidative stress. Hyperglycemia, as seen in metabolic syndrome, is known to cause protein glycation and glucose auto-oxidation with the resultant effect of increased production of ROS.[28] Dyslipidemia seen in patients with metabolic syndrome further leads to increased production of free fatty acids that are substrates for ROS.[29] The oxidized form of LDL and TGs are known to play important roles in the pathogenesis of atherosclerosis and increased predisposition to oxidative stress. On the contrary, HDL has antioxidant properties and has a protective role against oxidation. The oxidative changes of lipoprotein metabolism, therefore, plays an important role in the development of cardiovascular diseases.[30] Obesity also correlated positively with markers of oxidative stress. Molnár *et al*.[31] found markedly decreased antioxidant vitamin levels to be important characteristics of metabolic syndrome. Some studies have shown that weight reduction through dietary restriction and moderate-intensity exercise in obese patients has been shown to improve markers of oxidative stress and other markers of cardiovascular risk associated with metabolic syndrome.[32] The improvement is a due reduction in oxidative stress through exercise-mediated improvement in endothelial function and nitric oxide production.[33]

Conclusion

Oxidative stress is emerging as a major underlying mechanism in the metabolic syndrome. The significantly low levels of antioxidant vitamins/enzymes and significantly increased oxidative stress in subjects with metabolic syndrome was also found among Nigerians with metabolic syndrome. There is, therefore, the need to educate the community that apart from lifestyle modification (diet, exercise, and weight reduction) and medications there may be a need to include antioxidants in the management of metabolic syndrome.

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Conflicts of interest
There are no conflicts of interest.

References

1. Cavalca V, Veglia F, Squellerio I, Marenzi G, Minardi F, De Metrio M, *et al*. Glutathione, Vitamin E and oxidative stress in coronary artery disease: Relevance of age and gender. Eur J Clin Invest 2009;39:267-72.
2. Halliwell B. Antioxidants and human disease: A general introduction. Nutr Rev 1997;55 (1 Pt 2):S44-9.
3. Roberts CK, Barnard RJ, Sindhu RK, Jurczak M, Ehdaie A, Vaziri ND. Oxidative stress and dysregulation of NAD (P) H oxidase and antioxidant enzymes in diet-induced metabolic syndrome. Metabolism 2006;55:928-34.
4. Ford ES, Mokdad AH, Giles WH, Brown DW. The metabolic syndrome and antioxidant concentrations: Findings from the Third National Health and Nutrition Examination Survey. Diabetes 2003;52:2346-52.
5. Rösen P, Nawroth PP, King G, Möller W, Tritschler HJ, Packer L. The role of oxidative stress in the onset and progression of diabetes and its complications: A summary of a Congress Series sponsored by UNESCO-MCBN, the American Diabetes Association and the German Diabetes Society. Diabetes Metab Res Rev 2001;17:189-212.
6. Perticone F, Ceravolo R, Candigliota M, Ventura G, Iacopino S, Sinopoli F, *et al*. Obesity and body fat distribution induce endothelial dysfunction by oxidative stress: Protective effect of Vitamin C. Diabetes 2001;50:159-65.
7. Lonn E, Bosch J, Yusuf S, Sheridan P, Pogue J, Arnold JM, *et al*. Effects of long-term Vitamin E supplementation on cardiovascular events and cancer: A randomized controlled trial. JAMA 2005;293:1338-47.
8. Knekt P, Ritz J, Pereira MA, O'Reilly EJ, Augustsson K, Fraser GE, *et al*. Antioxidant vitamins and coronary heart disease risk: A pooled analysis of 9 cohorts. Am J Clin Nutr 2004;80:1508-20.

9. Meagher EA, Barry OP, Lawson JA, Rokach J, FitzGerald GA. Effects of Vitamin E on lipid peroxidation in healthy persons. JAMA 2001;285:1178-82.
10. Grundy SM, Brewer HB Jr, Cleeman JI, Smith SC Jr, Lenfant C; American Heart Association; National Heart, Lung, *et al*. Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation 2004;109:433-8.
11. Morris AA, Zhao L, Patel RS, Jones DP, Ahmed Y, Stoyanova N, *et al*. Differences in systemic oxidative stress based on race and the metabolic syndrome: The Morehouse and Emory Team up to Eliminate Health Disparities (META-Health) study. Metab Syndr Relat Disord 2012;10:252-9.
12. National Population Commission. 2006 National Population Census. Federal Republic of Nigeria Official Gazette. Vol. 94 (4); 2007. p. 196.
13. Trinder P. Determination of blood glucose using an oxidase-peroxidase system with a non-carcinogenic chromogen. J Clin Pathol 1969;22:158-61.
14. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972;18:499-502.
15. Neild C, Pearson S. Spectrophotometric determination of serum antioxidants. Ann Clin Biochem 1967;9:42-50.
16. Moeslinger T, Brunner M, Volf I, Spieckermann PG. Spectrophotometric determination of ascorbic acid and dehydroascorbic acid. Clin Chem 1995;41 (8 Pt 1):1177-81.
17. Quaife ML, Scrimshaw NS, Lowry OH. A micromethod for assay of total tocopherols in blood serum. J Biol Chem 1949;180:1229-35.
18. McCord JM, Fridovich I. Superoxide dismutase. An enzymic function for erythrocuprein (hemocuprein). J Biol Chem 1969;244:6049-55.
19. Paglia DE, Valentine WN. Studies on the quantitative and qualitative characterization of erythrocyte glutathione peroxidase. J Lab Clin Med 1967;70:158-69.
20. Ohkawa H, Ohishi N, Yagi K. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. Anal Biochem 1979;95:351-8.
21. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: Insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412-9.
22. Skalicky J, Muzakova V, Kandar R, Meloun M, Rousar T, Palicka V. Evaluation of oxidative stress and inflammation in obese adults with metabolic syndrome. Clin Chem Lab Med 2008;46:499-505.
23. Bilbis LS, Muhammad SA, Saidu Y, Adamu Y. Effect of Vitamins A, C, and E supplementation in the treatment of metabolic syndrome in albino rats. Biochem Res Int 2012;2012:678582.
24. Esposito K, Marfella R, Ciotola M, Di Palo C, Giugliano F, Giugliano G, *et al*. Effect of a mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: A randomized trial. JAMA 2004;292:1440-6.
25. John JH, Ziebland S, Yudkin P, Roe LS, Neil HA; Oxford Fruit and Vegetable Study Group. Effects of fruit and vegetable consumption on plasma antioxidant concentrations and blood pressure: A randomised controlled trial. Lancet 2002;359:1969-74.
26. Wali U, Jogana MU, Zarummai AL, Saidu Y. Antioxidant Vitamins and Trace Elements Status of Diabetics in Sokoto, Nigeria. Niger J Basic Appl Sci 2011;19:130-4.
27. Veigas NM, Dharmalingam M, Marcus SR. Oxidative stress in obesity and metabolic syndrome in Asian Indians. J Med Biochem 2011;30:115-20.
28. Nowotny K, Jung T, Höhn A, Weber D, Grune T. Advanced glycation end products and oxidative stress in type 2 diabetes mellitus. Biomolecules 2015;5:194-222.
29. de Oliveira J, Hort MA, Moreira EL, Glaser V, Ribeiro-do-Valle RM, Prediger RD, *et al*. Positive correlation between elevated plasma cholesterol levels and cognitive impairments in LDL receptor knockout mice: Relevance of cortico-cerebral mitochondrial dysfunction and oxidative stress. Neuroscience 2011;197:99-106.
30. Demircan N, Gurel A, Armutcu F, Unalacak M, Aktunc E, Atmaca H. The evaluation of serum cystatin C, malondialdehyde, and total antioxidant status in patients with metabolic syndrome. Med Sci Monit 2008;14:CR97-101.
31. Molnár D, Decsi T, Koletzko B. Reduced antioxidant status in obese children with multimetabolic syndrome. Int J Obes Relat Metab Disord 2004;28:1197-202.
32. Rector RS, Warner SO, Liu Y, Hinton PS, Sun GY, Cox RH, *et al*. Exercise and diet induced weight loss improves measures of oxidative stress and insulin sensitivity in adults with characteristics of the metabolic syndrome. Am J Physiol Endocrinol Metab 2007;293:E500-6.
33. Roberts CK, Won D, Pruthi S, Kurtovic S, Sindhu RK, Vaziri ND, *et al*. Effect of a short-term diet and exercise intervention on oxidative stress, inflammation, MMP-9, and monocyte chemotactic activity in men with metabolic syndrome factors. J Appl Physiol 2006;100:1657-65.