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
components of metabolic syndrome can cause increase production of ROS and the impairment of antioxidant enzymatic defenses such as SOD and GPx.\textsuperscript{[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.\textsuperscript{[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.\textsuperscript{[10]} Racial differences are known to exist in the level of antioxidants in patients with metabolic syndrome.\textsuperscript{[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.\textsuperscript{[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.\textsuperscript{[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.\textsuperscript{[14]}

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

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\text{HOMA-IR} = \frac{\text{fasting plasma insulin (µIU/ml) \times 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].\textsuperscript{[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
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.
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.\(^{[13,4,22]}\)

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 have 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.\(^{[12]}\) The improvement is a due reduction in oxidative stress through exercise-mediated improvement in endothelial function and nitric oxide production.\(^{[32]}\)

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.

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