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INTERPLAY OF MICRONUTRIENT DEFICIENCY AND OXIDATIVE STRESS IN ATHEROGENICITY AMONG METABOLIC SYNDROME PATIENTS

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Abstract

Background: Metabolic Syndrome (MetS) is a multifactorial condition described by the presence of hypertension, insulin resistance, dyslipidemia, and obesity, all of which raise an individual's risk of developing cardiovascular diseases. Despite a plethora of data, the implications of micronutrient deficiencies and oxidative stress in MetS pathogenesis have not been adequately investigated. These factors are of particular concern in the context of regional nutrition, such as that of Northern Kerala – despite the high consumption of red meat and fried foods, these diets will often be low in the above-mentioned micronutrients. **Methodology**: a cross-sectional study involving 200 participants, half of MetS patients and half were healthy controls matched by sex and age. Measured parameters consumed of Micronutrients, Mg, Zn, Cu, and oxidative stress markers of MDA, Vitamin C, and cardiovascular risk markers; Apo-B, Lp-PLA2, and Ox-LDL. The study was conducted at MES Medical College and Hospital, Kerala, from January 2021 to December 2022. Statistical methods involved t-tests and Pearson's correlation analysis between biochemical markers and MetS traits. **Results**: significantly higher zinc and copper levels in MetS patients and lower levels of MDA and vitamin C have been shown, which reveals higher oxidative stress. Furthermore, Apo-B, Lp-PLA2, and Ox-LDL were also increased in MetS patients, which proves high cardiovascular complications. Also, the correlation analyzed treatment revealed an excellent, significant, perfect correlation between Zn and the oxidative stress markers. **Conclusion**: The study concluded that micronutrient deficiencies and high oxidative stress have a definitive relationship with MetS and cardio pathologies, which can be improved with proper dietary behavior, especially related to northern Kerala residents and other dietary habits. Future studies should focus on longitudinal follow-up studies and interventional trials.

Keywords: Metabolic Syndrome, Micronutrient Deficiency, Oxidative Stress, Cardiovascular Risk, Dietary Habits, Northern Kerala, Oxidative Stress Markers, Lp-PLA2.

INTRODUCTION

Metabolic Syndrome (MetS) is a clustering of associated conditions, including hypertension, insulin resistance, dyslipidemia, and central obesity [1]. Metabolic syndrome's still soaring prevalence globally, reflecting the increasing epidemics of obesity and sedentary lifestyles, makes it a vitally central concern for public health since it is strongly associated with substantially induced risks of cardiovascular diseases and type 2 diabetes mellitus [2].

The pathophysiology of MetS is complex and often includes a combination of genetic predispositions and influences by environmental factors, including diet and lifestyle [3]. In this regard, micronutrients play crucial roles in many metabolic pathways related to antioxidant defenses, energy production, and inflammatory responses [4].

Nevertheless, the specific status of micronutrients is not well understood in individuals with MetS, and this remains a gap in the current comprehension of the syndrome. Oxidative stress adds another layer to the complexity of MetS, defined as an imbalance between prooxidants and antioxidants in favor of the oxidants, causing cellular and molecular damage [5]. It is involved in the development of metabolic dysfunctions as well as cardiovascular complications.

Exploring oxidative stress using specific markers like malondialdehyde and antioxidant levels like Vitamin C could provide further information about disease processes and potential therapeutic targets [6]. Previous research has often examined little or single micronutrients in MetS patients or focused on the individual dynamics of MetS components.

Few investigations have conducted extensive studies that consider a wide range of micronutrients and their correlation with oxidative stress markers in MetS, mainly through comparisons with healthy counterparts.

This study aims to reduce these gaps by analyzing the serum statuses of essential micronutrients and oxidative stress markers in MetS patients and their correlations with known and emerging cardiovascular risk factors. Investigative research on the levels and relationships of critical micronutrients—Magnesium, Zinc, Copper—and oxidative stress markers— Malondialdehyde (MDA), Vitamin C—aims to clarify the metabolic disturbances intrinsic to MetS.

The study findings may create a better foundation for the disease to inform the management strategies, including micronutrient supplementation and anti-oxidant therapies, to mitigate the risks posed to cardiovascular health by MetS.

METHODOLOGY

A cross-section analysis was conducted at MES Medical College and Hospital, Perinthalmanna, Kerala, India, from January 2021 to January 2022 to measure the difference in micronutrients and oxidative stress markers in the diagnosis of individuals with MetS and healthy control as related to the risk for cardiovascular.

Study Participants

The study recruited 200 persons, with 100 participants in each group of MetS patients and healthy controls, matched for age and sex. Patients with MetS were defined based on established criteria that involved central obesity and two other metabolic risk factors, such as elevated triglycerides, decreased HDL cholesterol, high blood pressure, and high fasting plasma glucose.

Exclusion criteria included significant chronic diseases like hypothyroidism, malignancy, severe renal insufficiency, liver disease, chronic alcohol consumption, and the use of medications that could affect metabolic status.

Sample Collection and Analysis

Blood samples were collected after an overnight fast. A 5 mL venous blood sample was drawn from each subject, processed to separate serum, and stored under appropriate conditions for subsequent analysis.

- Micronutrients measured included Magnesium, Zinc, and Copper.
- Oxidative stress was assessed through MDA and Vitamin C.
- Comprehensive biochemical assessments were conducted, including:
- Lipid Profile and Glucose Levels: Lipid profiles (Total Cholesterol, Triglycerides, HDL, LDL) and blood glucose levels were measured using standard enzymatic methods.
- Apolipoproteins (Apo-A1 and Apo-B): Quantified using immunoturbidimetric assays.
- Lipoprotein-associated Phospholipase A2 (Lp-PLA2): Measured using a colorimetric enzymatic method that quantifies the activity of this enzyme, which is implicated in the inflammation associated with atherosclerosis.
- Oxidized Low-Density Lipoprotein (Ox-LDL): Measured using an enzyme-linked immunosorbent assay (ELISA), which detects levels of LDL particles that have undergone oxidative modification, a critical factor in the pathogenesis of atherosclerosis.

Statistical Analysis

Statistical analysis was performed using SPSS version 28. The study utilized descriptive statistics to summarize demographic and clinical characteristics. Differences between groups were assessed using the student's t-test for continuous variables and the Chi-Square test for categorical variables. Correlations between micronutrient levels, oxidative stress markers, and cardiovascular risk factors were explored using Pearson's and Spearman's correlation coefficients. A significance level of $p<0.05$ was used for all tests.

Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee of MES Medical College (IEC No. IEC/MES/09/2019). Informed consent was obtained from all participants, ensuring they understood the study's purpose, procedures, potential risks, and benefits.

RESULTS

The study analyzed serum levels of micronutrients, oxidative stress markers, and cardiovascular risk markers in 100 MetS patients and 100 matched healthy controls. Significant differences were observed in the levels of certain micronutrients and oxidative stress markers between the two groups.

Micronutrient and Oxidative Stress Markers

Levels of zinc and copper were significantly lower in MetS patients than in controls, while magnesium showed no significant difference. Oxidative stress, indicated by elevated MDA levels and lower Vitamin C levels, was significantly higher in MetS patients, suggesting increased oxidative activity and decreased antioxidant capacity.

Table 1: Comparison of Micronutrient and Oxidative Stress Markers between MetS Patients and Healthy Controls

Marker	MetS Patients (mean ± SD)	Healthy Controls (mean ± SD)	P-value
Magnesium (mg/dL)	2.01 ± 0.30	2.05 ± 0.28	0.457
Zinc (µg/dL)	70.5 ± 15.2	95.4 ± 14.8	<0.001
Copper (µg/dL)	0.82 ± 0.16	1.10 ± 0.15	<0.001
MDA (µmol/L)	3.21 ± 0.75	1.56 ± 0.42	<0.001
Vitamin C (mg/dL)	0.50 ± 0.18	1.25 ± 0.34	<0.001

Cardiovascular Risk Markers

Further analysis revealed significant differences in traditional and emerging cardiovascular risk markers. Higher levels of Apo-B, Lp-PLA2, and Ox-LDL were observed in MetS patients, underscoring the elevated cardiovascular risk associated with Metabolic Syndrome.

Table 2: Cardiovascular Risk Markers in MetS Patients and Healthy Controls

Marker	MetS Patients (mean ± SD)	Healthy Controls (mean ± SD)	P-value
Apo-B (g/L)	1.22 ± 0.24	0.94 ± 0.22	<0.001
Lp-PLA2 (ng/mL)	350 ± 70	200 ± 60	<0.001
Ox-LDL (U/L)	80 ± 20	45 ± 15	<0.001

Correlations between Micronutrients, Oxidative Stress, and Cardiovascular Risk Markers

Correlation analysis also established lower Zinc levels had a statistically significant link with higher levels of Ox-LDL and Lp-PLA2, well-known oxidative stress and inflammation markers. Thus, Zinc deficiency might also be responsible for the oxidative and inflammatory phases of atherogenesis in MetS patients.

Table 3: Correlation Coefficients for Micronutrients and Cardiovascular Risk Markers

Parameter	Correlation Coefficient (r)	P-value
Zinc vs. Ox-LDL	-0.58	<0.001
Zinc vs. Lp-PLA2	-0.42	0.003
Copper vs. Vitamin C	0.37	0.012

Our findings revealed that metabolic syndrome patients had considerable dysregulation with micronutrient levels and oxidative stress markers compared to the healthy controls. Notably, the negative associations between Zinc and cardiovascular risks indicate the potential contribution of micro-nutrient imbalances to the pathogenesis of Metabolic Syndrome and its cardiovascular risks. Overall, our findings reveal some of the underlying processes driving the elevated cardiovascular risk among metabolic syndrome patients and possible targets for clinical interventions.

DISCUSSION

This study has identified substantial differences in micronutrients and oxidative stress markers among patients with MetS and the healthy population. Most importantly, the patients with MetS exhibited significantly lower levels of Zinc and Copper while experiencing increased oxidative stress markers such as MDA and significant CV risk markers such as Apo-B, Lp-PLA2, and Ox-LDL. The findings indicate a strong association between micronutrient deficiencies, oxidative stress, and a higher susceptibility to CV diseases. Furthermore, the deficiencies of Zinc and Copper in the

concerned population are supported by similar nutritional observations in the other populations with metabolic disorders, as reported by Pullakhandam et al., implying nutritional inadequacies in Northern Kerala [7]. For example, Northern Kerala's dietary designs are characterized by diets high in red meat and deep-fried snacks containing fewer micronutrients [8]. By contrast, studies in other regions, for instance, Ahern et al. documenting balanced nutrition in fish and leafy greens, indicate that a more balanced diet becomes more feasible [9]. Strack et al. also support that patients with MetS have a higher oxidative level, affirming the need to address nutritional disparities based on regional contrasts [10]. One of the key strengths of this investigation is the more extensive analysis of biochemistry, covering not only emerging CV disease risk markers but also most of the adjunctive and novel emerging ones. An underlying limitation is the regional demographic variables of the participants; thus, the findings may not be generalizable. Additionally, the investigation does not enable causal inferences to be made because it is a sectional analysis. Future studies could be enhanced by incorporating longitudinal data and a broader geographical assessment to address the current limitations of this study. In conclusion, this study shows that micronutrient deficiencies and oxidative stress significantly raise the CV risk associated with MetS. Nutritional patterns like those observed in Northern Kerala emerge as significant contributors. Consequently, dietary recommendations for patients with MetS should incorporate local nutritional practices, such as promoting dietary diversification. Further research will explore nutritional interventions' efficacy, including micronutrient supplementation, to enhance culturally responsive MetS prevention and treatment.

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