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Micronutrient Profiles and Oxidative Stress in Metabolic Syndrome: A Comparative Analysis and Cardiovascular Risk Assessment

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ABSTRACT

Background: Metabolic syndrome, a complex condition with multifaceted origins, is closely linked to heightened cardiovascular risk. This investigation focused on the intricate relationship between micronutrient levels, oxidative stress, metabolic syndrome (MetS), and their combined influence on factors contributing to cardiovascular risk. **Objectives:** The main goal was to examine and contrast the levels of micronutrients and markers of oxidative stress in individuals with MetS against a healthy control group. Additionally, the research sought to analyze novel markers indicative of cardiovascular risk in these cohorts and to determine how these biochemical factors correlate with standard markers of MetS. **Methods:** In this cross-sectional comparative study, 200 individuals were equally divided into groups of MetS patients and healthy controls at MES Medical College and Hospital in Kerala. The study involved measuring anthropometric variables and assessing serum concentrations of micronutrients like Magnesium, Zinc, and Copper alongside oxidative stress indicators (Malondialdehyde [MDA] and Vitamin C) and newly recognized markers of cardiovascular risk (LpPLA2 and hs-CRP). Established markers of MetS were also evaluated. **Results:** Individuals with MetS showed notably higher

body mass index (BMI) and waist circumference than the control group. Analysis of micronutrients indicated diminished levels of Zinc and Copper in the MetS cohort. Markers of oxidative stress, namely elevated MDA and decreased Vitamin C levels, were observed in the MetS group. Additionally, the MetS patients exhibited increased levels of LpPLA2 and hs-CRP, signaling heightened cardiovascular risk. The research further noted intricate interrelations between these biochemical markers and traditional indicators of MetS.

Conclusion: This research emphasizes the vital link between obesity and metabolic syndrome, highlighting the critical role of micronutrient deficiencies and oxidative stress in the underlying mechanisms of the disease. The increased levels of LpPLA2 and hs-CRP among MetS patients point to a greater risk of cardiovascular complications, underscoring the necessity for an inclusive management approach for MetS. These findings support the integration of micronutrient and oxidative stress evaluation into the routine clinical assessment of MetS, in conjunction with monitoring established and emerging cardiovascular risk markers. Future studies should adopt longitudinal designs to delve deeper into the cause-and-effect relationships and assess the impact of specific interventions targeting these areas**.**

Keywords: Metabolic Syndrome, Micronutrients, Oxidative Stress, Cardiovascular Risk, LpPLA2, hs-CRP.

Introduction

Metabolic Syndrome (MetS) has garnered growing attention as a significant public health issue, primarily because of its escalating prevalence worldwide and its association as a precursor to numerous cardiovascular diseases and type 2 diabetes [1]. This multifaceted disorder is distinguished by a range of risk factors that include insulin resistance, hypertension, obesity, and dyslipidemia [2]. The intricate interplay of these factors heightens the risk of developing serious health conditions and presents significant challenges in understanding and managing MetS. The burgeoning interest in the role of micronutrients in MetS has opened new avenues for research. Micronutrients, vital for numerous metabolic processes, have considerably impacted metabolic disorders [3]. Their role in modulating insulin action, glucose metabolism, and inflammation suggests a significant influence on the development and progression of MetS [4]. Conversely, oxidative stress, defined by an imbalance between the generation of reactive oxygen species and the body's antioxidant defenses, has been identified as a factor that worsens MetS [5]. This imbalance plays a significant role in the progression and severity of the syndrome. The oxidative stress response in MetS is believed to contribute to endothelial dysfunction, inflammation, and insulin resistance, further complicating the syndrome's pathophysiology [6].

Despite growing research in these areas, there remains a notable gap in comprehensive studies that simultaneously evaluate the status of micronutrients and oxidative stress markers in MetS [7]. Most existing studies have focused on these elements in isolation, overlooking their potential combined impact on cardiovascular risk associated with MetS. This study addresses this gap by conducting a detailed comparative analysis of micronutrient profiles and oxidative stress markers in cases with MetS and those in a control group. Our objectives are to investigate the status of key micronutrients and oxidative stress markers in both groups, examine conventional attributes of MetS, and explore the correlations among these factors. Our specific focus is to meticulously examine the association between the apoB100/apoA1 ratio and the atherogenic index and to explore the impact that imbalances in micronutrients and oxidative stress have on these factors in individuals afflicted with MetS.

The importance of this research is multifaceted. Through an in-depth analysis of micronutrient levels and oxidative stress indicators within the framework of MetS, our objective is to gain a deeper understanding of the fundamental mechanisms driving this syndrome. Such insights could enhance our approaches in forecasting, averting, and treating cardiovascular conditions linked to MetS. We anticipate that our findings will contribute valuable insights into the pathophysiology of MetS and associated cardiovascular risks, thereby enriching the broader narrative of metabolic health management. As we delve into the methodology and results, this study seeks to underscore critical factors that could influence the clinical approach to MetS and its related complications, highlighting the need for a multifaceted perspective in understanding and managing this multifactorial syndrome.

Materials and Methods

Study Design and Setting: A comparative cross-sectional study was conducted at the diabetic clinic of MES Medical College and Hospital, Perinthalmanna. The study spanned from January 2021 to December 2022, focusing on patients with MetS.

Study Participants: Participants were patients with MetS attending the clinic. Inclusion criteria were age 25-75 years and willingness to participate, excluding individuals with serious illnesses such as liver diseases, kidney diseases, endocrine disorders, or malignancy. A control group of healthy subjects within the same age range and without clinical evidence of significant conditions was also selected. To guarantee consistency and dependability in the comparison analysis, the research meticulously matched the issues based on age and sex.

Data Collection & Biochemical Analysis: The demographic information, baseline lipid profiles, and other critical biochemical markers were systematically collected and documented throughout the data-collecting process. In addition, anthropometric parameters such as age, sex, Body Mass Index (BMI), and blood pressure were assessed to fully understand each participant's health state. In biochemical analysis, we used a cutting-edge, totally automated analyzer. The use of this advanced apparatus was pivotal in accurately quantifying the wide range of essential variables in the investigation. The device effectively measured blood glucose levels and offered a thorough analysis of lipid components, encompassing Total Cholesterol (TC), Triglycerides (TG), High-Density Lipoprotein (HDL), and Low-Density Lipoprotein (LDL). Furthermore, it proficiently evaluated specific indicators such as Lipoprotein-associated phospholipase A2 (Lp-PLA2) and high-sensitivity C-Reactive Protein (hs-CRP). The device again demonstrated consistent measurement of Apolipoprotein A1 (Apo-A1), Apolipoprotein B (Apo B), and crucial serum minerals such as

Magnesium (Mg) and Zinc (Zn), therefore guaranteeing the precision and reliability of our biochemical assessments.

The approach selection for analyzing each parameter in this research was carefully made based on considerations of accuracy and dependability. The glucose oxidase-peroxidase (GOD-POD) reaction, an exact enzymatic endpoint approach, was used to detect serum glucose levels. Similarly, total cholesterol levels were quantified in blood using an enzymatic endpoint approach that included the cholesterol oxidase (CHOD) - peroxidase (POD) reaction. This method is well-known for its accuracy in measuring cholesterol. The estimation of serum triglycerides was also performed using an enzymatic endpoint method. Endpoint homogeneous assays involving cholesterol oxidase-peroxidase reaction were used to assess HDL and LDL cholesterol, known for their precision in lipid profiling. The serum apolipoproteins A1 and B concentrations were measured using a liquid-phase immunoprecipitation assay with a nephelometric endpoint, a technique known for its sensitivity.

To guarantee specificity and accuracy, the quantitative measurement of Lp-PLA2 in serum and plasma was carried out using photometric equipment and a particular diagnostic reagent. Malondialdehyde (MDA) levels were measured using ELISA, based on MDA's interaction with thiobarbituric acid (TBA) to generate an MDA-TBA2 adduct. An enzyme immunoassay that targets IgG and IgM class autoantibodies against oxidized LDL in human blood was used to quantify oxidized LDL. This technology is very exact in recognizing oxidative stress indicators. Key micronutrient concentrations, such as Vitamin C, Copper, Zinc, and Magnesium, were determined spectroscopically using suitable chemical procedures to fully examine micronutrient levels. High-sensitivity C-reactive protein (hs-CRP) was detected through a sandwich immunometric assay in the solid phase, recognized for its sensitivity and specificity in identifying inflammatory markers. The selection of each analytical method was guided by its appropriateness for accurately measuring the respective biochemical parameters, thereby establishing a robust and dependable foundation for the study's findings.

Results

The study comprehensively analyzed the micronutrient profiles, oxidative stress markers, and conventional and emerging markers of metabolic syndrome (MetS) in a sample of patients attending a diabetic clinic. By comparing these patients with a control group, the study aimed to unearth significant differences and correlations that could provide deeper insights into the nature and management of MetS.

Demographic and Anthropometric Analysis: The age distribution indicated a higher prevalence of MetS in middle-aged individuals, particularly in the 41-50 age group. There was a nearly equal distribution of males and females in both test and control groups, suggesting that MetS affects both genders similarly. Significant differences in weight, waist circumference, and BMI between MetS patients and controls highlighted the association of obesity with MetS.

Table A: Demographic and Anthropometric Comparison

Parameter	MetS Patients	Control Group	P-value

Age (41-50 years)	High Prevalence	Lower Prevalence	-
Gender Distribution	Nearly Equal	Nearly Equal	-
BMI (Mean)	Higher	Lower	<0.001
Waist Circumference (Mean)	Higher	Lower	<0.001

Micronutrient and Oxidative Stress Markers: MetS patients showed lower Zinc and Copper levels than the control group. This finding aligns with other research indicating micronutrient deficiencies in MetS patients. Elevated MDA and lower Vitamin C levels in MetS patients suggested increased oxidative stress.

Table B: Micronutrient and Oxidative Stress Markers

Marker	MetS Patients	Control Group	P-value
Magnesium (Mean)	Comparable	Comparable	0.549
Zinc (Mean)	Lower	Higher	0.001
Copper (Mean)	Lower	Higher	<0.001
MDA (Mean)	Higher	Lower	<0.001
Vitamin C (Mean)	Lower	Higher	<0.001

Conventional & Emerging MetS Markers: Differences in BMI, blood pressure, HbA1c, fasting blood sugar (FBS), and lipid profiles between the groups confirmed these as reliable indicators of MetS. Elevated levels of LpPLA2 and hs-CRP in MetS patients pointed towards an increased cardiovascular risk associated with MetS.

Correlations: The study found mixed correlations between micronutrients and conventional/emerging MetS markers, indicating a complex interplay. Oxidative stress markers showed significant correlations with emerging MetS markers, particularly Ox LDL.

Table C: Correlation of Markers with MetS

Marker	Correlation with MetS Components	Significance
Micronutrients (Zinc, Copper)	Mixed	Varies
Oxidative Stress (MDA, Vitamin C)	Significant with Ox LDL	<0.05
Emerging Markers (LpPLA2, hs-CRP)	Positive for Cardiovascular Risk	<0.001

Interpretation

The results suggest a significant association of MetS with obesity, micronutrient deficiencies (particularly Zinc and Copper), and increased oxidative stress. The emerging markers (LpPLA2, hs-CRP) provide new avenues for understanding the cardiovascular risks associated with MetS. Though complex, the correlations between these markers and MetS components point towards multifactorial interactions in the disease's pathophysiology. This study underscores the need for holistic approaches in managing MetS, considering both nutritional and oxidative stress aspects alongside conventional markers.

Discussion

The study revealed several critical insights into MetS. Firstly, a significant association between obesity and MetS was observed, evidenced by higher BMI and waist circumference in MetS patients compared to the control group. MetS patients have substantial deficits in key micronutrients, particularly zinc and copper. Furthermore, there was a significant increase in oxidative stress among MetS patients, as seen by higher MDA levels and reduced Vitamin C levels. Finally, new indicators such as LpPLA2 and hs-CRP were considerably raised in MetS patients, indicating that the syndrome is linked with a greater cardiovascular risk.

The results of this study are consistent with previous research that linked obesity to MetS. Studies such as Fisher et al., 2019 have similarly reported high BMI and waist circumference in MetS patients [8]. The micronutrient deficiencies observed in this study, particularly in Zinc and Copper, resonate with Shi et al., 2020, who noted similar deficiencies in MetS patients [9]. However, the extent of these deficiencies varies from other studies like Dominguez et al., 2022, possibly due to differences in dietary patterns and genetic predispositions [10]. The elevated oxidative stress markers align with the study by Kargar et al., 2021, supporting the theory that oxidative stress plays a significant role in MetS [11]. The high levels of LpPLA2 and hs-CRP align with recent studies such as Panteghiniet et al., 2016, which underscore their potential as indicators of cardiovascular risk in MetS [12].

One of the key strengths of this study is its comprehensive approach, evaluating both conventional and emerging markers of MetS alongside micronutrient profiles and oxidative stress markers. The matched control group adds to the reliability of the findings. However, the study has limitations. The cross-sectional design limits the ability to infer causality between observed associations. Additionally, the study's findings are specific to the demographic and geographic context of the sample, which may limit their generalizability to other populations.

Future research, benefiting from a longitudinal approach and incorporating a broader spectrum of participants, could significantly enhance the generalizability of these findings. This study contributes robust evidence connecting obesity, micronutrient deficits, heightened oxidative stress, and increased levels of novel markers with metabolic syndrome. It underscores the complex characteristics of MetS and emphasizes the need for a comprehensive strategy in its diagnosis and management. The results support the integration of micronutrient and oxidative stress evaluations in the clinical assessment of MetS and the monitoring of traditional and emerging indicators. Subsequent studies should clarify the cause-and-effect relationships and investigate specific interventions to address these elements in management.

Conclusion

The comprehensive investigation conducted on MetS has yielded crucial findings, augmenting our understanding of this intricate disorder. There is a notable association between obesity and MetS, as shown by elevated BMI and waist circumference in those afflicted [13]. The aforementioned association highlights the imperative need for proficient management of obesity as a fundamental element in preventing and treating MetS, whereby weight regulation assumes a pivotal position [14]. The research findings indicated significant insufficiencies in essential micronutrients, particularly Zinc and Copper, in people diagnosed with MetS. This discovery implies that the imbalances of micronutrients influence the

pathophysiology of MetS, which may affect its development and progression. Therefore, evaluating and rectifying these deficits in micronutrients are crucial components within a comprehensive approach to the management of MetS. Furthermore, the study revealed a heightened state of oxidative stress in individuals diagnosed with MetS, as seen by raised levels of MDA and lower concentrations of Vitamin C. The discovery indicates that oxidative stress plays a significant role in developing MetS and emphasizes the potential efficacy of antioxidant therapies in its therapy. The research further revealed elevated levels of developing cardiovascular risk indicators, namely LpPLA2 and hs-CRP, in individuals diagnosed with MetS. These markers are indicative of an increased susceptibility to cardiovascular complications. Using these indicators in regular clinical assessments can improve the timely detection and management of cardiovascular risks associated with MetS. In brief, the research provides insight into the complex characteristics of MetS, which encompasses several elements such as obesity, deficiencies in micronutrients, oxidative stress, and emerging cardiovascular risk indicators. A complete treatment strategy is required for MetS, which involves integrating conventional risk factor management, nutritional evaluation, and reduction of oxidative stress. The findings derived from this study have significant value in influencing clinical practices and directing future research endeavors, particularly in designing tailored therapies to address the identified deficits and stress factors associated with MetS. Enhancing our comprehension of these intricate relationships is essential to developing more efficacious treatments for managing MetS and mitigating its concomitant health hazards.

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