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Dissecting the Intricate Relationship Between Oxidative Stress and Blood Sugar Levels in Middle-Aged Indian Populations: A cross-sectional Study

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ABSTRACT

Introduction: The global prevalence of diabetes mellitus, particularly type 2 diabetes mellitus (T2DM), has reached alarming proportions, transforming into a major public health crisis. Among these mechanisms, oxidative stress has emerged as a pivotal factor influencing glucose metabolism and diabetic complications. The majority of studies examining oxidative stress biomarkers in diabetes have been conducted in Western populations, and there is a paucity of data from India, particularly among middle-aged individuals who are at high risk of developing metabolic disorders due to a combination of genetic, lifestyle, and environmental factors. Our study was conceptualized to bridge this crucial knowledge gap by exploring the association between oxidative stress markers and blood sugar levels in the middle-aged Indian population

Materials and Methods: We enrolled 300 age-matched participants in the current study and examined them for their serum malondialdehyde (MDA) levels, serum nitric oxide (NO) levels, fasting blood sugar (FBS) levels, post-prandial

blood sugar (PPBS) levels, and HbA1C levels. Through convenience sampling, participants were divided into two groups according to their FBS and PPBS levels. Group-1 consisted of 150 participants with normoglycemia, and group-2 consisted of 150 participants with diabetes. The statistical analysis of the data was performed by using SPSS software version 27.

Results: We observed a significantly ($p < 0.001$) higher value of oxidative stress marker in Group-2 individuals when compared with Group-1 individuals. Our data also revealed a positive correlation of markers of blood glucose with serum MDA and a negative correlation with serum NO.

Conclusion: The study concludes by highlighting a significant positive correlation between oxidative stress and diabetes in the middle-aged Indian population. Elevated MDA levels and reduced NO levels in diabetic participants point towards oxidative stress as a central mediator in the disease process.

Keywords: *oxidative stress, diabetes, malondialdehyde, blood glucose, nitric oxide*

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1. INTRODUCTION

Non-communicable diseases (NCDs) are the most common causes of morbidity and mortality across the globe. Among all NCDs, diabetes mellitus holds a major share, especially when it comes to developing countries such as India. The global prevalence of diabetes mellitus, particularly type 2 diabetes mellitus (T2DM), has reached alarming proportions, transforming into a major public health crisis. According to the International Diabetes Federation (IDF), over 537 million adults worldwide were living with diabetes in 2021, and this number is projected to rise to 643 million by 2030 [1]. In parallel with the rising incidence of diabetes, there is growing interest in the pathophysiological mechanisms underlying its onset and progression. Among these mechanisms, oxidative stress has emerged as a pivotal factor influencing glucose metabolism and diabetic complications. In individuals with diabetes or prediabetes, hyperglycemia-induced oxidative stress has been implicated in the pathogenesis of insulin resistance, β-cell dysfunction, and the development of microvascular and macrovascular complications [2].

The relationship between blood glucose levels and oxidative stress is bidirectional and complex. Hyperglycemia promotes ROS generation through multiple pathways, including glucose autoxidation, the polyol pathway, advanced glycation end-product (AGE) formation, and protein kinase C activation [3]. Conversely, oxidative stress impairs insulin signaling and exacerbates insulin resistance, thereby worsening glycemic control [4]. This cyclical interplay creates a self-perpetuating loop that accelerates metabolic deterioration in susceptible individuals.

In recent years, biomarkers of oxidative stress have garnered significant attention in diabetes research. Among these, malondialdehyde (MDA) has been extensively studied as a reliable indicator of oxidative damage in vivo. Elevated serum levels of MDA have been reported in individuals with T2DM and correlate positively with fasting blood glucose [5]. Despite these findings, the majority of studies examining oxidative stress biomarkers in diabetes have been conducted in Western populations. There is a paucity of data from India, particularly among middle-aged individuals who are at high risk of developing metabolic disorders due to a combination of genetic, lifestyle, and environmental factors.

Middle-aged populations represent a critical demographic in the Indian context. This age group is often exposed to a unique convergence of risk factors, including sedentary lifestyles, high-calorie diets, central obesity, psychosocial stress, and inadequate healthcare access. Moreover, cultural factors often delay health-seeking behavior, allowing silent metabolic changes to persist undiagnosed for years. As a result, many individuals in this age group are either undiagnosed diabetics or are on the verge of developing metabolic syndrome [6]. Given the asymptomatic nature of early oxidative stress and glucose dysregulation, early identification of oxidative stress markers in this group could play a vital role in preventive strategies.

Our study was conceptualized to bridge this crucial knowledge gap by exploring the association between oxidative stress markers and blood sugar levels in middle-aged Indian population.

2. MATERIALS AND METHODS

Study Design: The present study is cross-sectional in design, which follows the STROBE guidelines, and prospective in nature, which was conducted in the Department of Physiology of Teerthanker Mahaveer Medical College & Research Centre, Moradabad, India.

Ethical Considerations: The study was conducted after prior approval from the Institutional Ethics Committee (Ref No: TMU/IEC/2024-25/FACULTY/01 Dated: 10/JUNE/2024). All the enrolled participants in this study were informed regarding the study, and written voluntary consent was taken.

Sample size: With an anticipated correlation coefficient between MDA and FBS at a 95% confidence level and 90 power in the study [7], the minimum sample size of each study group was determined to be 142. Hence, the total sample size was calculated as 142+142 = 284. To increase the sensitivity of the total sample, we continued enrollment of more study participants till each group reached 150 participants consisting each group. For the smooth conduct of the study, we opted for a convenient sampling.

Study duration: The data was planned to be collected till the 300 participants are finished. The data of the first participant was collected on 15th June 2024, and the data of the 300th participant was collected on 19th March 2025.

Study participants: Total study participants were divided into 2 groups in which each group consisted gender ratio of 1:1. Group-1 consisted of participants who belonged to normoglycemia (FBS 70 - 100 mg/dl, PPBS 70 - 140 mg/dl, n = 150,) whereas Group-2 consisted of the diabetic individuals (FBS ≥ 140 mg/l, PPBS ≥200 mg/dl, n = 150).

Inclusion & Exclusion criteria: All individuals of the age group of 35 – 50 years having no history of any chronic diseases were included in the current study. We excluded individuals with any recent history of infections, surgeries, or hospital admissions, history of smoking or alcohol use, intake of vitamin supplements or antioxidant therapy within the past six months. We also did not include the prediabetic individuals in the current study.

Assessment of variables: Venous blood (5 mL) was collected following all aseptic and antiseptic precautions after overnight fasting from all the participants. The fasting blood sugar (FBS), serum nitric oxide (NO) and the serum MDA levels were estimated. The participants were provided oral glucose, and post-prandial blood sugar (PPBS) was estimated. We also analyzed the Serum Creatinine to rule out involvement of any renal diseases and serum triglyceride to rule out involvement of any cardiovascular diseases. We also analyzed HbA_1C levels for a better understanding of the blood sugar levels.

Statistical Analysis: Data were analyzed using SPSS Statistics version 27. Continuous variables were expressed as mean ± standard deviation (SD). Student's t-test was employed to compare mean differences between the groups. Spearman's correlation coefficient was used to examine the association between the variables. A p-value < 0.05 was considered statistically significant.

3. RESULTS

Analysis of the demographics of the participants: The demographic characteristics of the study population were comparable between both the groups. The average age was 41.8 ± 4.2 years in Group 1 and 41.3 ± 4.6 years in Group-2. We did not find any difference in regard to the socioeconomic status of the participants. Although when compared with the clinical profiles of the participants, it indicated that Group-2 had more sedentary lifestyles.

Comparison of variables between groups: We not only found a significantly ($p < 0.05$) higher value of serum MDA, but also observed a significantly ($p < 0.05$) lower value of serum NO in Group-2 participants when compared with Group-1 participants, as evident from Table-1. It is also evident from table-1 that the proposed study design was properly followed. We observed that the pgroup-2 participants also share higher HbA1C levels than the group-1 participants.

Table-1: Comparison of the variables among study participants

Variables	Group-1 (mean ± SD), n = 150	Group-2 (mean ± SD), n = 150	p-value
Serum FBS (mg/dl)	88.3 ± 9.4	158.7 ± 16.1	<0.0001
Serum PPBS (mg/dl)	108 ± 14.3	288 ± 36.3	<0.0001
Serum HbA_1C (%)	5.7 ± 0.3	7.3 ± 1.1	<0.0001
Serum MDA (µmol/L)	2.5 ± 0.3	4.9 ± 0.7	<0.0001
Serum NO (µmol/L)	9.562 ± 1.21	3.546 ± 1.01	<0.0001
Serum Creatinine (mg/dl)	0.09 ± 0.02	0.09 ± 0.03	NS
Serum Triglyceride (mg/dl)	143 ± 6.1	142 ± 5.3	NS

p-value <0.05 is considered statistically significant; FBS, fasting blood glucose; PPBS, post-prandial blood glucose; HbA_1C, glycated hemoglobin; MDA, malondialdehyde; NO, nitric oxide; NS, not significant.

Correlation Between the variables: Spearman's correlation analysis revealed a positive correlation of FBS, PPBS, and HbA1C with serum MDA level and a negative correlation with serum NO level, indicating that as glucose levels rise, oxidative stress increases significantly. The analytical report of these correlations is depicted in Table-2.

Table-2: Spearman's Correlation between the variables

Variable (n = 300)	Serum FBS (mg/dl)	Serum PPBS (mg/dl)	Serum HbA_1C (%)
Serum MDA (µmol/L)	r = 0.63, p <0.001	r = 0.79, p <0.001	r = 0.43, p <0.001
Serum NO (µmol/L)	r = -0.57, p <0.001	r = -0.66, p <0.001	r = -0.73, p <0.001

r, correlation coefficient; p-value <0.05 is considered statistically significant; FBS, fasting blood glucose; PPBS, post-prandial blood glucose; HbA_1C, glycated hemoglobin; MDA, malondialdehyde; NO, nitric oxide.

Analysis of variables between genders: We did not find any significant difference (p >0.05) when analysis of the study variables was conducted between the genders.

4. DISCUSSION

Our study demonstrates significantly higher oxidative stress markers in diabetic individuals, which suggests that hyperglycemia-induced oxidative damage is an early and critical event in the pathogenesis of diabetes. By examining serum MDA and serum NO concentrations, the established markers of lipid peroxidation and oxidative stress, alongside fasting and post-prandial blood sugar levels, this study offers critical insights into the biochemical interplay that potentially underpins the onset and progression of type 2 diabetes mellitus (T2DM) in this high-risk population. Findings from our study corroborate with previous reports and also add to the existing literature [8, 9].

Mechanistic pathways of the observed results: The possible mechanistic pathways of the observed results can range from increased mitochondrial ROS production, glucose auto-oxidation, to activation of NADPH oxidase pathways. The by-products of these processes not only damage pancreatic β-cells but also impair insulin signaling in peripheral tissues. MDA, being a terminal product of lipid peroxidation, serves as a reliable indicator of such damage. NO, a potent vasodilator, was reported to have antioxidant functions in various studies. Hence, the lower serum NO levels in the diabetic population supports these mechanistic processes [9]. The clinical implications from the findings of our study may be suggestive of monitoring the oxidative stress markers like MDA and NO for early detection of diabetes-related complications. Furthermore, it can be advisable to the general population that lifestyle interventions, including antioxidant-rich diets, regular physical activity, could play a role in mitigating oxidative stress [10].

It is also crucial to consider the broader impact of oxidative stress on systemic inflammation, endothelial dysfunction, and insulin resistance, all of which are intricately linked to the complications of diabetes [11]. Our results emphasize the potential of antioxidant therapy as an adjunct to glycemic control. Moreover, the statistically significant positive correlation found between blood glucose and MDA levels in our study population reinforces the hypothesis that hyperglycemia and oxidative stress exist in a mutually reinforcing cycle. This feedback loop wherein hyperglycemia increases oxidative stress and oxidative stress impairs insulin signaling could be a key factor driving the early stages of insulin resistance and β-cell dysfunction. This has been supported by prior research showing that ROS directly inhibits insulin-stimulated glucose uptake by modulating insulin receptor substrate (IRS) signaling pathways [12, 13].

Increased oxidative stress is not only associated with increased blood sugar or obesity but also with increased morbidity and mortality from various non-communicable diseases, especially due to cardiovascular diseases. Thus, reducing oxidative stress might help reduce mortality due to non-communicable diseases [14, 15, 16].

It is also worth noting that environmental and lifestyle factors prevalent in the Indian subcontinent may exacerbate oxidative stress in this population. Urbanization, increased exposure to air pollution, dietary shifts toward processed and high-glycemic-index foods, and sedentary behavior all contribute to a heightened pro-oxidative state [17]. These environmental stressors compound the inherent genetic predisposition of South Asians, who are known to develop insulin resistance at lower body mass indices and younger ages compared to Western populations [18, 19]. The observation of significantly higher MDA levels in our diabetic participants may therefore reflect not just hyperglycemia-induced oxidative stress but also the cumulative effect of environmental and epigenetic factors.

Limitations of the current study: Despite the valuable insights provided, the study is not without limitations. Firstly, the cross-sectional design precludes establishing causality. While the association between oxidative stress and blood glucose

is evident, longitudinal studies are required to determine the temporal relationship and whether elevated oxidative stress precedes the onset of hyperglycemia or vice versa. Secondly, the study population was limited to individuals aged 35–50 years, which may limit the generalizability of the findings to other age groups. While MDA is a well-recognized biomarker of lipid peroxidation, assessing additional markers such as superoxide dismutase (SOD), glutathione peroxidase (GPx), catalase, and 8-isoprostanes could provide a more comprehensive picture of the oxidative status. Lastly, dietary intake, antioxidant consumption, and physical activity levels, all of which influence oxidative stress, were not controlled for in this study. Inclusion of these parameters in future investigations would help delineate confounding effects and identify modifiable risk factors.

5. CONCLUSION

The present study highlights a significant positive correlation between oxidative stress and diabetes in middle-aged Indian populations. Elevated MDA levels and reduced NO levels in diabetic participants point towards oxidative stress as a central mediator in the disease process. Early assessment and management of oxidative stress could serve as a valuable strategy in diabetes prevention and care. Further large-scale longitudinal studies are warranted to confirm these findings and investigate potential interventions targeting oxidative stress.

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