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ORIGINAL ARTICLE

Association of Ischemia Modified Albumin and Carbonylated Proteins with Glycated Hemoglobin Levels in Type II Diabetes Patients

Yashasvi Gautam

Associate Professor, Department of General Medicine, Hamdard Institute of Medical Sciences and Research, New Delhi, India

ABSTRACT:

Background: Oxidative stress significantly contributes to the progression and complications associated with type II diabetes mellitus (T2DM). Ischemia Modified Albumin (IMA), and protein carbonyls are emerging biomarkers indicative of oxidative stress-induced protein damage in chronic hyperglycemic conditions. **Aim:** To determine oxidative stress by measuring Ischemia Modified Albumin (IMA) and protein carbonyl levels and assessing their association with glycated hemoglobin (HbA1c) in type II diabetes patients. **Material and Methods:** This cross-sectional observational study included 80 participants (40 controls and 40 type II diabetic patients). IMA levels were estimated using the Albumin Cobalt Binding assay, protein carbonyls by spectrophotometric DNPH assay, insulin via chemiluminescence immunoassay, and HbA1c using Bio-Rad HPLC. Statistical analyses involved independent t-tests and correlation studies. **Results:** Significantly elevated mean values of IMA (0.317 ± 0.139 OD), protein carbonyls (1.82 ± 0.53 µmol/ml), and HbA1c (79.58 ± 18.96 mmol/mol) were observed in diabetic patients compared to controls ($p < 0.001$). Protein carbonyl and IMA levels strongly correlated with HbA1c values ($p < 0.001$). **Conclusion:** IMA and carbonyl protein effectively indicate oxidative stress in T2DM, correlating positively with HbA1c. Routine assessment of these markers may help predict oxidative damage and guide therapeutic strategies in diabetes management.

Keywords: Ischemia Modified Albumin; Protein Carbonyls; Type II Diabetes Mellitus

Corresponding author: Yashasvi Gautam, Associate Professor, Department of General Medicine, Hamdard Institute of Medical Sciences and Research, New Delhi, India

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INTRODUCTION

Type II diabetes mellitus (T2DM) represents one of the most significant global public health challenges of the 21st century, characterized by chronic hyperglycemia resulting from insulin resistance and impaired insulin secretion [1]. The persistent hyperglycemic state in T2DM accelerates oxidative stress, contributing significantly to diabetic complications, including cardiovascular diseases, nephropathy, neuropathy, and retinopathy [2,3]. Oxidative stress results from an imbalance between the production of reactive oxygen species (ROS) and antioxidant defense mechanisms, leading to molecular damage in carbohydrates, lipids, proteins, and nucleic acids [4].

Among various oxidative stress markers, Ischemia Modified Albumin (IMA) has emerged as an important biomarker. Initially associated with myocardial ischemia, IMA reflects structural modifications in albumin molecules due to oxidative stress and has recently gained attention as a promising indicator of generalized oxidative injury in diabetic patients [5,6]. Elevated IMA levels in diabetes suggest a potential role as an early marker for oxidative stress-mediated vascular complications [7].

Similarly, protein oxidation, specifically indicated by protein carbonylation, is another crucial marker highlighting oxidative damage in diabetes mellitus. Protein carbonylation results from oxidative modification of proteins, often impairing their function and stability [8]. Elevated protein carbonyl levels have been positively correlated with chronic hyperglycemia, further emphasizing their utility in evaluating oxidative protein damage and subsequent diabetic complications [9].

Glycated hemoglobin (HbA1c) is a well-established marker used to assess glycemic control over an extended period. Previous studies demonstrated an association between poor glycemic control (elevated HbA1c) and increased oxidative stress markers, including IMA and protein carbonyls [6,10]. However, detailed studies exploring the association between these specific oxidative stress markers and HbA1c in type II diabetes mellitus, particularly in the Indian context, remain relatively scarce.

Thus, the present study aims to evaluate oxidative stress in patients with type II diabetes mellitus by analyzing Ischemia Modified Albumin (IMA) and protein carbonyl levels and exploring their association with glycated hemoglobin (HbA1c). This study will provide valuable insights into the role of oxidative stress markers in predicting the risk of protein damage and related diabetic complications.

MATERIAL AND METHODS

This cross-sectional observational study was conducted at the Department of Medicine in a tertiary care hospital.

A total of 80 participants diagnosed with type II diabetes mellitus (T2DM), attending outpatient and inpatient departments, were enrolled through purposive sampling. Participants with known cardiovascular disease, renal impairment, severe hepatic dysfunction, acute infection, malignancy, or those receiving antioxidant supplements were excluded from the study to avoid potential confounders.

Approval from the Institutional Ethical Committee was obtained prior to initiation. Written informed consent was taken from each participant after explaining the aims, procedures, potential risks, and benefits of the study.

After an overnight fast of at least 8 hours, 3 ml of venous blood samples were collected aseptically into EDTA-containing vacutainers. Immediately after collection, samples were gently mixed to prevent clotting. A portion of whole blood was aliquoted for the measurement of glycated hemoglobin (HbA1c), while the remaining blood was centrifuged at 3500 g for 15 minutes at 4°C to obtain clear plasma, which was promptly stored at -80°C until further analysis.

Laboratory Investigations:

1. **Measurement of Glycated Hemoglobin (HbA1c):** Glycemic control was assessed by measuring HbA1c levels using the Bio-Rad Variant II high-performance liquid chromatography (HPLC) method, which offers high specificity and accuracy.
2. **Estimation of Plasma Insulin:** Plasma insulin concentrations were quantified by Chemiluminescence Immunoassay (CLIA) technique, using an automated immunoassay analyzer, ensuring precise detection and minimal cross-reactivity.
3. **Measurement of Protein Carbonyls:** Protein carbonylation, indicative of oxidative damage to proteins, was evaluated using an extremely sensitive spectrophotometric assay based on the reaction of protein carbonyl groups with 2,4-dinitrophenylhydrazine (DNPH), forming stable 2,4-dinitrophenyl hydrazone adducts. This assay was performed spectrophotometrically by measuring absorbance at 370 nm, as previously standardized.
4. **Estimation of Ischemia Modified Albumin (IMA):** Ischemia Modified Albumin (IMA) levels were measured using the Albumin Cobalt Binding (ACB) assay. In this assay, cobalt binds specifically to the N-terminal region of human serum albumin; modifications due to oxidative stress result in decreased cobalt-binding capacity. The absorbance was read spectrophotometrically, providing reliable quantification of IMA levels.

Statistical Analysis

Collected data were analyzed using SPSS software version 26. Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), based on the distribution pattern. Pearson or Spearman correlation coefficients were calculated to assess the association between oxidative stress markers (IMA, protein carbonyls) and HbA1c levels. A p-value <0.05 was considered statistically significant.

RESULTS

Table 1 shows the comparison of mean values ± SD for Ischemia Modified Albumin (IMA), Protein Carbonyl, Insulin, and Glycated Hemoglobin (HbA1c) between the Control and Type II Diabetes groups. Significant increases in IMA (0.317 ± 0.139 vs. 0.065 ± 0.052; $p < 0.001$), Protein Carbonyl (1.82 ± 0.53 vs. 0.58 ± 0.28; $p < 0.001$), and HbA1c (79.58 ± 18.96 vs. 32.17 ± 5.42; $p < 0.001$) were observed in diabetic patients compared to controls. However, insulin levels did not differ significantly (12.67 ± 6.14 vs. 8.41 ± 2.65; $p = 0.061$).

Figure 1 illustrates the distribution and variability of Protein Carbonyl levels in patients with Type II Diabetes and controls. There is a notable increase in protein oxidation, represented by higher protein carbonyl concentrations, among diabetic patients compared to the control group.

Figure 2 depicts variations in Ischemia Modified Albumin (IMA) between Type II Diabetes and controls. The trend line indicates a significant rise in IMA levels among diabetic individuals, highlighting increased oxidative stress and potential hypoxic risk associated with chronic hyperglycemia.

Figure 3 visually summarizes the mean variations of IMA, Protein Carbonyls, HbA1c, and Insulin. Notably elevated mean values of Protein Carbonyls, IMA, and HbA1c in the Type II Diabetes group underscore the heightened oxidative stress and poor glycemic control characteristic of diabetic pathology compared to healthy controls. Insulin shows a moderate but non-significant increase.

Table 1: Indicating the Mean and SD of IMA, Protein Carbonyl,HbA1c, insulin, parameters in type II diabetes and controls groups

Groups	IMA (OD)	Protein Carbonyl (µmol/ml)	Insulin (mcu/ml)	HbA1c (mmol/mol)
Controls	0.065 ± 0.052	0.58 ± 0.28	8.41 ± 2.65	32.17 ± 5.42
Type II Diabetes	0.317 ± 0.139	1.82 ± 0.53	12.67 ± 6.14	79.58 ± 18.96
p-value	<0.001**	<0.001**	0.061 NS	<0.001**

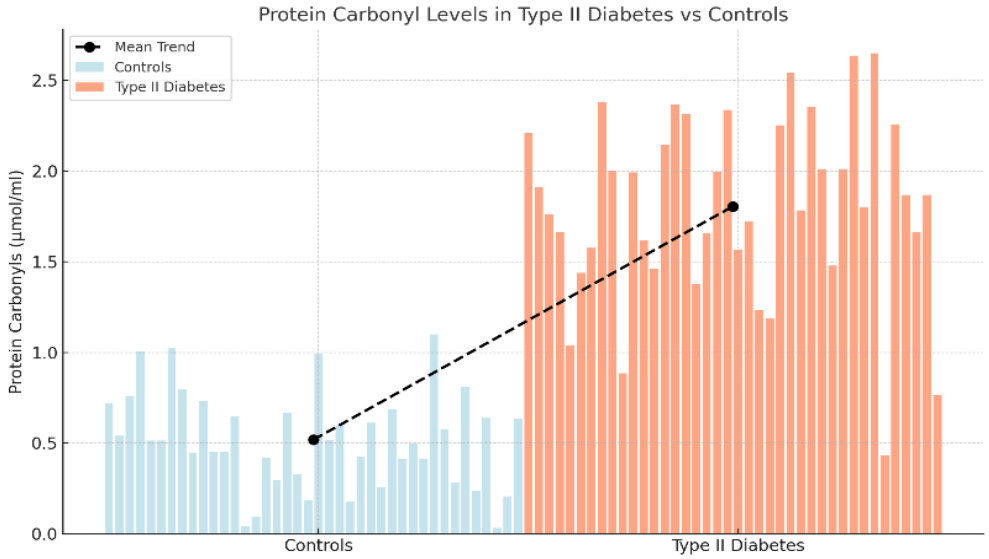

Figure 1: The series of variations with protein damage through protein carbonyls in type II diabetes Vs. Control

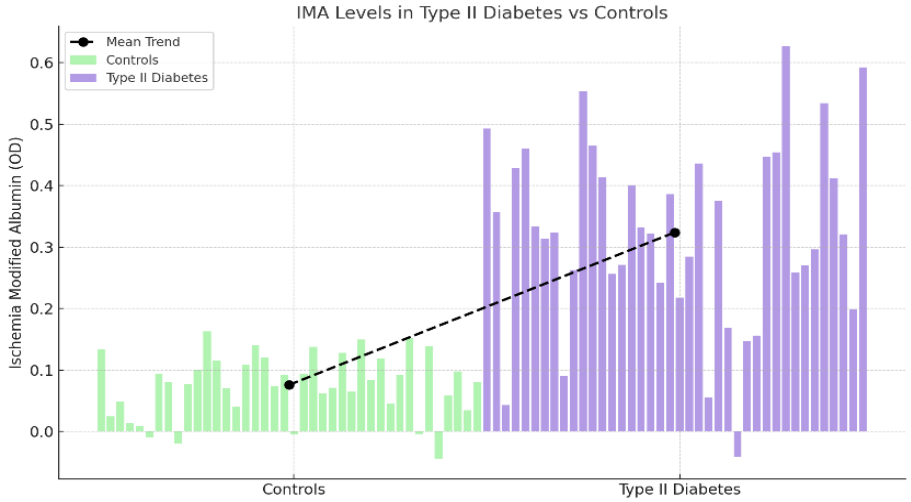

Figure 2: The series of variations with generation of hypoxic risk in Hyperglycemia condition via IMA in type II diabetes when compared to the Controls.

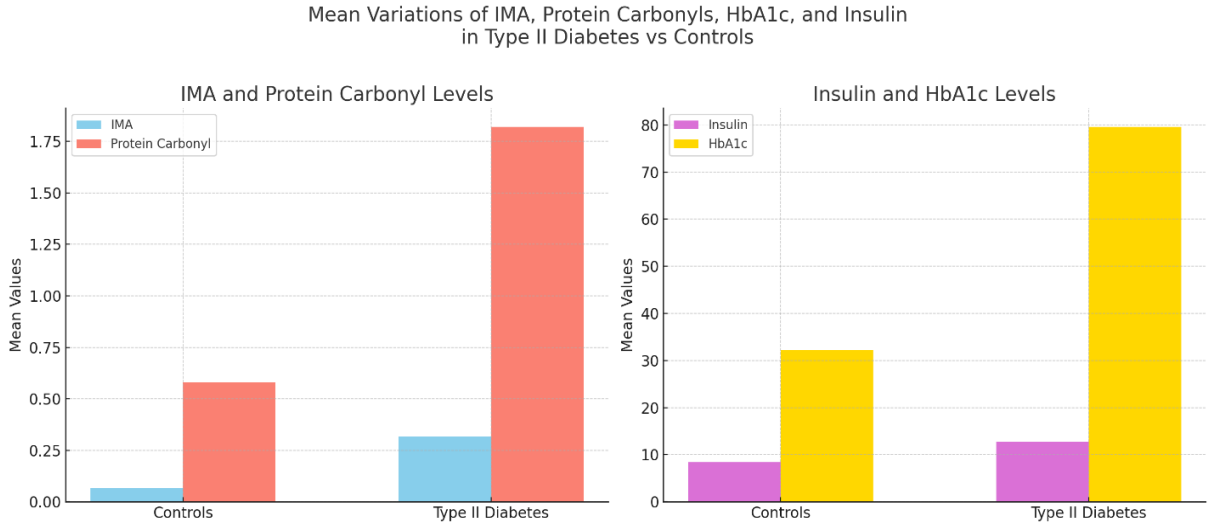

Figure 3: The Mean variations of IMA, Protein Carbonyls,HbA1c and Insulin in type II diabetes when compared with controls.

DISCUSSION

In the present study, significantly increased levels of oxidative stress markers, specifically Ischemia Modified Albumin (IMA) and protein carbonyls, were observed in type II diabetic patients compared to healthy controls. These findings strongly suggest enhanced oxidative stress and subsequent protein damage occurring in the diabetic milieu. Elevated oxidative stress markers have been previously associated with hyperglycemia-induced metabolic derangements, contributing significantly to diabetic complications [11].

The notable increase in IMA observed in diabetic patients aligns well with recent literature indicating that oxidative modifications of albumin occur under hyperglycemic conditions, leading to altered cobalt-binding capacities [12]. These modifications render IMA a potent indicator of oxidative injury beyond its traditional use in ischemic cardiac diseases, expanding its potential application in chronic metabolic disorders such as diabetes mellitus [13].

Similarly, protein carbonyls, indicative of oxidative protein damage, were significantly elevated in the diabetic group. Protein carbonylation represents irreversible protein modifications leading to loss of protein function, stability, and altered cellular processes [14]. Previous studies have reported strong correlations between protein carbonyl levels and the severity of diabetic complications, emphasizing their role as reliable biomarkers for assessing chronic oxidative stress-induced tissue damage [15].

An important observation was the highly significant correlation between oxidative markers (IMA and protein carbonyls) and glycated hemoglobin (HbA1c). Elevated HbA1c reflects poor glycemic control and prolonged hyperglycemia, which accelerates the generation of reactive oxygen species (ROS) [16]. Persistent hyperglycemia promotes non-enzymatic glycation and glycoxidation reactions, which contribute directly to oxidative stress, consequently augmenting protein carbonylation and modifications of albumin [17].

Although insulin levels appeared slightly elevated in diabetic patients, this increase was statistically insignificant. This observation may suggest insulin resistance without marked insulin deficiency, a common scenario in early to moderate type II diabetes. However, chronic hyperinsulinemia could indirectly enhance oxidative stress, emphasizing the complex interplay between insulin metabolism and oxidative damage [11].

This study's findings reinforce the potential clinical utility of evaluating oxidative stress markers, particularly IMA and protein carbonyls, alongside traditional glycemic markers like HbA1c. Such biomarkers can effectively predict oxidative protein damage, thus identifying individuals at higher risk for diabetic complications and guiding targeted therapeutic strategies aimed at reducing oxidative injury.

CONCLUSION

The present study underscores the significance of oxidative stress markers, specifically Ischemia Modified Albumin (IMA) and protein carbonyls, in type II diabetes mellitus. Elevated levels of these markers strongly correlate with glycated hemoglobin (HbA1c), highlighting the role of persistent hyperglycemia in oxidative protein damage. These findings advocate for the routine monitoring of oxidative stress biomarkers in diabetic patients to better anticipate the risk of complications and inform clinical management strategies, ultimately improving patient outcomes.

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