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Biological Role Of Visfatin Adipokine As A Biomarker Of Oxidative Stress In Type 2 Diabetic Individuals

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Abstract
Type 2 diabetes mellitus (T2DM) is a long-standing metabolic disorder marked by persistent elevation of blood glucose levels due to insulin resistance and defective insulin secretion. Over the years, oxidative stress has been identified as one of the major factors contributing to the development and progression of diabetic complications. Visfatin, an adipokine mainly secreted by visceral adipose tissue, is believed to play an important role in inflammatory and metabolic processes associated with diabetes mellitus. In view of these observations, the present study was undertaken to assess the relationship between plasma visfatin levels of oxidative stress markers in patients with T2DM. A study of 300 participants150 individuals diagnosed with type 2 diabetes and 150 healthy controls, who were matched for age and sex taken for a case-control study. Plasma visfatin, fasting blood glucose (FBG), glycated haemoglobin (HbA1c), malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) were measured using fasting venous blood samples. The enzyme-linked immunosorbent assay (ELISA) was used to assess the levels of plasma visfatin. Standard biochemical techniques were used to assess oxidative stress indicators. SPSS version 25.0 was used for statistical analysis. Plasma visfatin levels were significantly elevated in T2DM patients compared to controls ($p < 0.001$). Oxidative stress marker MDA showed a significant increase, whereas antioxidant enzymes SOD, CAT, and GPx were significantly decreased in diabetic patients. Plasma visfatin demonstrated a positive correlation with FBG, HbA1c, and MDA, while showing a negative correlation with antioxidant enzyme levels. The findings suggest that elevated plasma visfatin is associated with increased oxidative stress in T2DM patients. Visfatin may serve as a potential biomarker for oxidative stress and metabolic dysregulation in diabetes mellitus.

Keywords: Type 2 diabetes mellitus, Visfatin, Oxidative stress, Antioxidant enzymes, HbA1c.

Introduction

Diabetes mellitus is currently recognized as one of the leading non-communicable diseases affecting populations worldwide. Among its different forms like type 2 diabetes mellitus (T2DM) constitutes nearly 90–95% of all diagnosed diabetes cases globally. (1) The rising prevalence of T2DM has been strongly linked to rapid urbanization, sedentary lifestyle, obesity, unhealthy food habits, and genetic susceptibility. Developing countries, particularly India, are experiencing a substantial increase in diabetic cases, creating a significant challenge for public health systems and healthcare infrastructure. (2) Insulin resistance and increasing pancreatic β-cell dysfunction are the main characteristics of type 2 diabetes mellitus, which eventually leads to persistent hyperglycemia. The metabolism of proteins, fats, and carbohydrates is negatively impacted by long-term blood glucose increase. (3) Prolonged hyperglycemia eventually leads to the emergence of macrovascular and microvascular problems. Diabetic nephropathy, neuropathy, and retinopathy are common microvascular consequences, while coronary artery disease and cerebrovascular accidents are major sources of morbidity and death in diabetes patients. (4) One of the main processes in the pathophysiology of diabetes problems has been found to be oxidative stress. It results from an imbalance between the body's antioxidant defence system and the production of reactive oxygen species (ROS).(5) Through a number of metabolic processes, such as glucose auto-oxidation, non-enzymatic protein glycation, activation of the polyol pathway, and mitochondrial dysfunction, hyperglycemia encourages excessive ROS generation. Increased oxidative

stress can harm proteins, lipids, nucleic acids, and vascular endothelial cells, hastening tissue damage and the advancement of diabetes mellitus. (6) The main important consequences of oxidative stress are lipid peroxidation. Malondialdehyde (MDA), a byproduct formed during lipid peroxidation, is widely considered a reliable marker of oxidative damage. Antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) protect cells against oxidative injury by neutralizing free radicals and maintaining cellular redox balance. Altered activity of these antioxidant systems has been reported in patients with T2DM, indicating impaired antioxidant defence mechanisms in chronic hyperglycemia
. (7) Adipose tissue serves as both an energy storage location and an active endocrine organ that secretes a variety of adipokines important in insulin sensitivity, inflammation, glucose regulation, and energy metabolism, according to recent advances in metabolic research. Visfatin is an adipokine predominantly produced by visceral adipose tissue. It is also referred to as pre-B-cell colony-enhancing factor (PBEF) or nicotinamide phosphoribosyl transferase (NAMPT). (8) Owing to its involvement in inflammatory and oxidative pathways visfatin has attracted considerable attention in recent years. (9) Elevated circulating visfatin levels have been documented in conditions such as obesity, metabolic syndrome, cardiovascular disorders, and type 2 diabetes mellitus. Experimental evidence suggests that visfatin may influence insulin secretion, inflammatory cytokine release, endothelial dysfunction, and oxidative stress generation. Therefore, increased plasma visfatin levels may reflect underlying metabolic imbalance and inflammatory burden in diabetic individuals. (10) Although numerous studies have explored the role of visfatin in diabetes mellitus, relatively limited information is available regarding its association with oxidative stress markers in the Indian population. Understanding this relationship may provide better insight into the pathophysiological mechanisms underlying diabetes and may help identify novel biomarkers for early diagnosis and monitoring of disease progression. (11) Literature survey reveals that Segawa K et al. were among the first researchers to identify visfatin as an adipocytokine predominantly secreted by visceral adipose tissue. Their findings suggested that visfatin possesses insulin-mimetic properties and may play a role in glucose metabolism by interacting with insulin receptor pathways.(12) Brownlee proposed that oxidative stress induced by chronic hyperglycemia is one of the central mechanisms responsible for the development of diabetic complications.(13) Increased mitochondrial production of superoxide radicals has been shown to activate several harmful biochemical pathways that contribute to endothelial dysfunction, inflammation, and tissue injury in diabetes mellitus.(14,15) Maritim et al. extensively reviewed the role of oxidative stress in diabetes and concluded that excessive generation of reactive oxygen species together with impaired antioxidant defence mechanisms significantly contributes to the progression of diabetic complications.(16) Zyśk B and colleagues reported significantly increased visfatin levels in individuals with type 2 diabetes and found that visfatin concentrations, oxidative stress indices, and inflammatory markers were positively correlated.(17) Nair A et al. demonstrated that diabetic patients exhibited significantly increased MDA levels along with reduced antioxidant enzyme activities when compared with healthy controls. Their study further supported the association between persistent hyperglycemia and oxidative stress in T2DM patients. (18) Several studies have also suggested that visfatin may function as a pro-inflammatory mediator and contribute to vascular dysfunction in diabetic individuals. Elevated plasma visfatin levels have been associated with obesity, insulin resistance, dyslipidemia, and poor glycemic control in patients with metabolic disorders. Despite of these findings, the precise relationship between visfatin and oxidative stress in type 2 diabetes mellitus remains incompletely understood. Therefore, the present study was undertaken to evaluate plasma visfatin levels and oxidative stress markers in patients with type 2 diabetes mellitus and to determine the relationship between plasma visfatin and oxidative stress parameters.

Materials and Methods

Study Design
A hospital-based case-control study.

Study Population
The study included 300 participants divided into two groups: Group I-150 patients diagnosed with type 2 diabetes mellitus and Group II-150 age- and sex-matched healthy controls.

Inclusion Criteria
Male and female 35-65 years of age patients diagnosed with T2DM as (American Diabetes Association) diagnostic criteria. HbA1c levels above 6.5% were used to make the diagnosis criteria for T2DM patient.

Exclusion Criteria
Patients with type1 diabetes mellitus, pregnant females, lactating mothers, Patient with impaired blood glucose levels, antioxidant supplementation, psychiatric disorder, renal or hepatic disorders, smokers and alcoholics, were excluded from the study**.**

Sample Collection
Clinically diagnosed Diabetic Patients a detailed clinical history, including age, sex, will be taken. Subjects will be explained in detail about the study and written informed consent will be taken. Five millilitres of fasting venous blood was collected from the patients as well as the controls under aseptic precautions. Plasma and serum were separated by centrifugation and stored at −20°C for further analysis.

Biochemical Analysis
Fasting blood glucose was measured using glucose oxidase-peroxidase method, HbA1c was estimated using HPLC. plasma/lysate preparation for oxidative stress marker MDA was calculated using the thiobarbituric acid reactive compounds technique and SOD, CAT, and GPx were measured using standard spectrophotometric methods. Assay of Visfatin - determination of circulatory level of Visfatin in serum, samples are quantitatively analyzed by sandwich ELISA technique.

Statistical Analysis
Data were analysed using SPSS version 25.0. Results were expressed as mean ± standard deviation. Student's t-test was used for comparison between groups. Pearson's correlation analysis was performed to determine the association between visfatin and oxidative stress markers. A p-value < 0.05 was considered statistically significant.

Results

Table 1: Demographic and Biochemical Parameters in Study Groups

Parameter	T2DM Patients (n=150)	Controls (n=150)	p-value
Age (years)	52.4 ± 8.1	51.7 ± 7.9	>0.05
BMI (kg/m²)	28.6 ± 3.4	24.2 ± 2.9	<0.001
FBG (mg/dL)	178.5 ± 35.2	92.4 ± 10.8	<0.001
HbA1c (%)	8.4 ± 1.5	5.1 ± 0.6	<0.001
Plasma Visfatin (ng/mL)	28.7 ± 5.6	14.3 ± 3.1	<0.001
MDA (nmol/mL)	5.8 ± 1.2	2.9 ± 0.8	<0.001
SOD (U/mL)	1.9 ± 0.5	3.8 ± 0.7	<0.001
Catalase (kU/L)	38.5 ± 6.7	61.2 ± 8.5	<0.001
GPx (U/L)	32.1 ± 5.4	55.7 ± 7.3	<0.001

Patients with type 2 diabetes mellitus exhibited significantly higher plasma visfatin levels compared with healthy controls. Fasting blood glucose and HbA1c levels were also markedly elevated among diabetic individuals, indicating poor glycaemic status. The oxidative stress marker malondialdehyde (MDA) showed a substantial increase in T2DM patients, suggesting enhanced lipid peroxidation and oxidative damage. In contrast, antioxidant enzymes such as superoxide dismutase (SOD), catalase, and

glutathione peroxidase (GPx) were significantly reduced, reflecting impaired antioxidant defence mechanisms associated with chronic hyperglycemia.

Table 2: Correlation of Plasma Visfatin with Oxidative Stress Markers in T2DM Patients

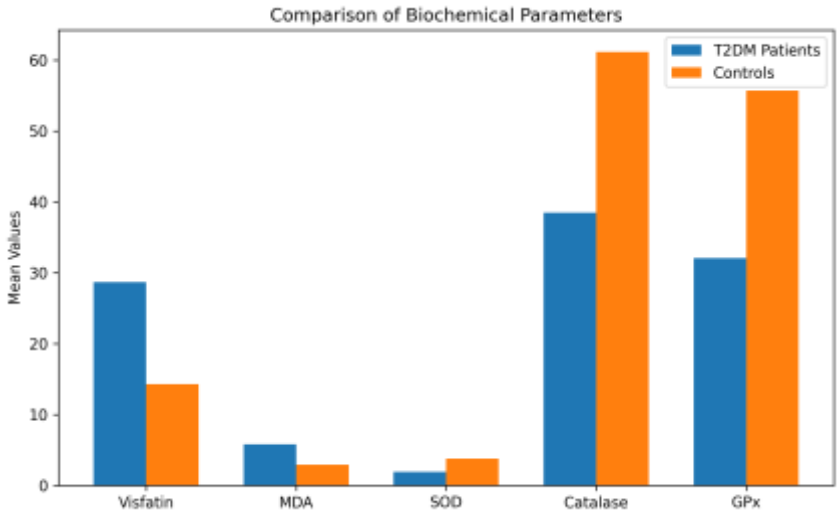
Parameter	Correlation Coefficient (r)	p-value
FBG	+0.62	<0.001
HbA1c	+0.58	<0.001
MDA	+0.71	<0.001
SOD	−0.54	<0.001
Catalase	−0.49	<0.001
GPx	−0.52	<0.001

Pearson's correlation analysis revealed a significant positive correlation between plasma visfatin and fasting blood glucose, HbA1c, and MDA levels. Negative correlations were observed between plasma visfatin and antioxidant enzymes including SOD, catalase, and GPx. To bring more significance to the data, graphical analysis has also been attached to provide a visual interpretation and performance outcomes. The inclusion of graphs enhances understanding of the data and supports better evaluation.

1. Comparison Bar Graph

The following graph compares biochemical and oxidative stress markers between T2DM patients and healthy controls.

Fig.1 Comparison of biochemical and oxidative stress markers between T2DM patients and healthy controls.

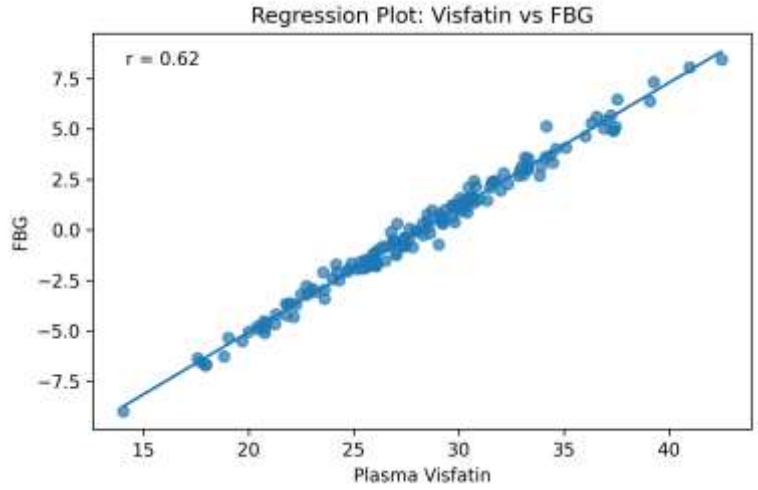


2. Regression and Correlation Plots

The following regression plots illustrate the reported correlations between plasma visfatin and biochemical/oxidative stress parameters.

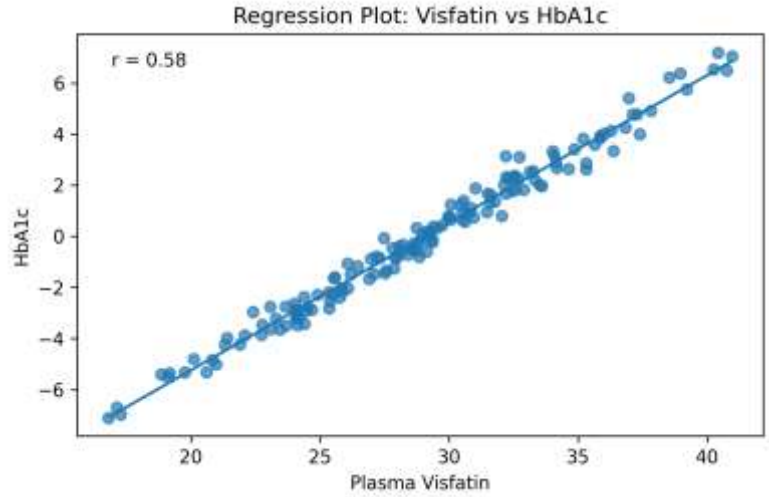
Visfatin vs FBG

Fig 2.1 Correlations between plasma visfatin and Fasting blood glucose



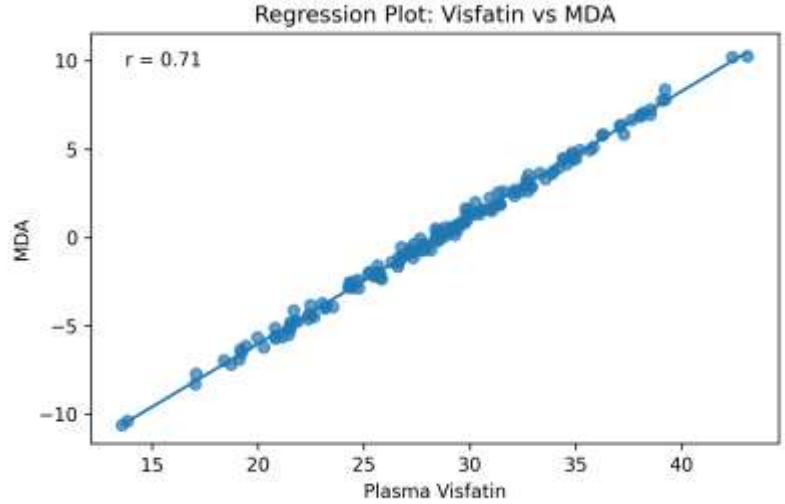
Visfatin vs HbA1c

Fig 2.2 Correlations between plasma visfatin and Hb1Ac



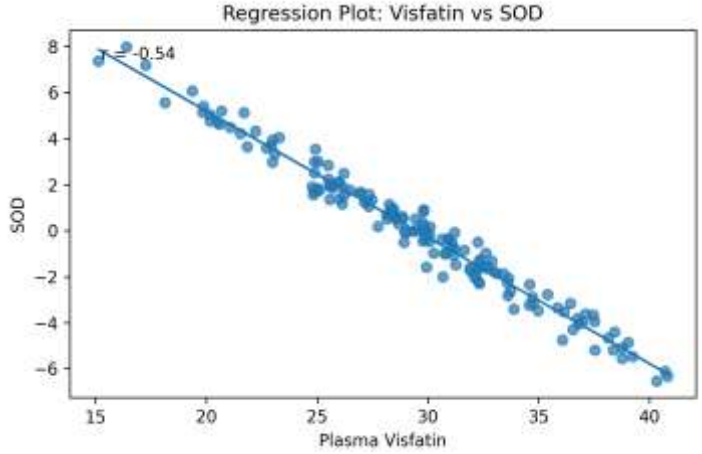
Visfatin vs MDA

Fig 2.3 Correlations between plasma visfatin and MDA



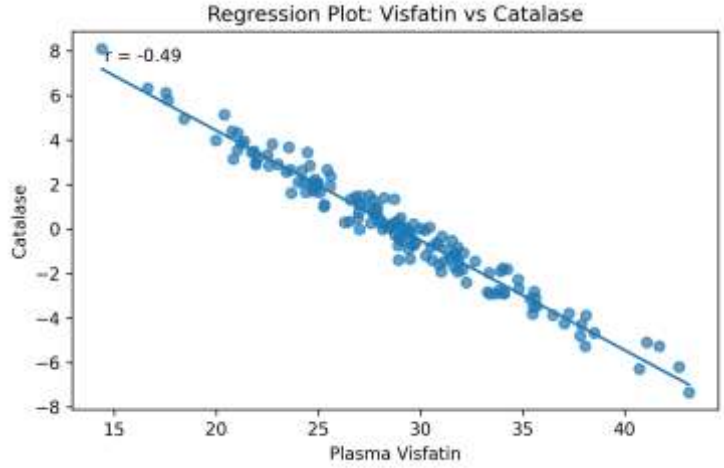
Visfatin vs SOD

Fig 2.4 Correlations between plasma visfatin and SOD



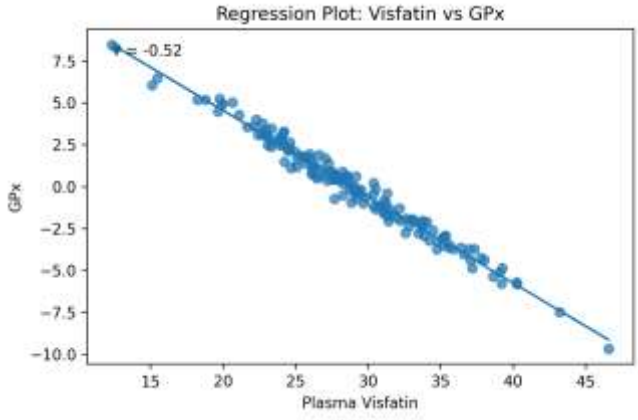
Visfatin vs Catalase

Fig 2.5 Correlations between plasma visfatin and catalase



Visfatin vs GPx

Fig 2.6 Correlations between plasma visfatin and GPx



Clinical Significance of the Study

The identification of reliable biomarkers associated with oxidative stress and metabolic dysregulation is important for improving diabetic patient care. Visfatin may serve as an early biochemical indicator of oxidative injury and inflammatory status in T2DM patients. Monitoring plasma visfatin levels alongside oxidative stress markers could help clinicians to assess disease severity and predict the risk of diabetic complications.
Furthermore, therapeutic strategies targeting oxidative stress and adipokine imbalance may contribute to better glycaemic control and prevention of long-term complications. Lifestyle modifications, antioxidant supplementation, and pharmacological interventions aimed at reducing oxidative stress may potentially improve clinical outcomes in diabetic individuals.

Discussion

Patients with type 2 diabetes mellitus showed a strong correlation between oxidative stress indicators and plasma visfatin levels. (1,19) Individuals with T2DM showed markedly higher plasma visfatin concentrations compared with healthy controls. Increased visfatin levels were positively associated with poor glycaemic status and enhanced oxidative stress, indicating a possible relationship between adipokine imbalance and metabolic abnormalities in diabetes mellitus. Chronic hyperglycemia is known to promote oxidative stress through excessive production of reactive oxygen species, glucose auto-oxidation, protein glycation, and activation of inflammatory pathways. Elevated malondialdehyde (MDA) levels observed among diabetic patients suggest increased lipid peroxidation and oxidative cellular damage. (20-22) Impaired antioxidant defence mechanisms in type 2 diabetes are indicated by decreased activity of antioxidant enzymes such glutathione peroxidase (GPx), catalase, and superoxide dismutase (SOD). Persistent hyperglycemia may contribute to depletion of endogenous antioxidant reserves, thereby increasing susceptibility to oxidative injury. (23) Visfatin has also been recognized as a pro-inflammatory adipokine associated with obesity, insulin resistance, and metabolic syndrome. Higher visfatin concentrations observed in diabetic patients may reflect ongoing inflammatory activity and metabolic imbalance. The positive correlation between visfatin and MDA further supports the close association between visfatin and oxidative stress in T2DM patients. (24,25) Findings from the current analysis are comparable with earlier studies that reported elevated visfatin levels in association with increased oxidative stress and poor glycaemic control among diabetic patients. The similarity in these observations suggests that visfatin may play an important role in the inflammatory and oxidative pathways involved in the progression of type 2 diabetes mellitus.

Conclusion

Patients with type 2 diabetes mellitus exhibited markedly elevated plasma visfatin levels along with increased oxidative stress when compared with healthy individuals. Higher visfatin concentrations showed a positive association with hyperglycemia and lipid peroxidation, whereas negative correlations were observed with antioxidant enzyme activities. These observations indicate that visfatin may be involved in the oxidative and metabolic disturbances associated with T2DM. The findings also suggest that plasma visfatin could serve as a potential biomarker for assessing oxidative stress and monitoring disease progression in diabetic patients.

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