International Journal of Medical Science and Education | pISSN- 2348 4438 | eISSN-2349- 3208

A COMPARATIVE STUDY OF OXIDATIVE STRESS MARKERS AND GLUCOSE VARIABILITY IN DIABETICS AND HEALTHY INDIVIDUALS

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Received: 11/01/2016 **Revised: 08/03/2016** **Accepted: 21/03/2016**

ABSTRACT:

Background: Type II diabetes mellitus affects millions worldwide, with glucose fluctuations contributing significantly to diabetic complications through oxidative stress mechanisms. Understanding the relationship between glycemic variability and oxidative stress markers provides crucial insights for therapeutic interventions. **Objective:** To investigate the correlation between glucose fluctuations and oxidative stress activation in patients with Type II diabetes mellitus and compare these parameters with healthy controls.**Methods:** A cross-sectional study was conducted involving 120 Type II diabetic patients and 60 healthy controls. Continuous glucose monitoring was performed for 72 hours to assess glycemic variability. Oxidative stress markers including malondialdehyde (MDA), superoxide dismutase (SOD), and glutathione peroxidase (GPx) were measured. Statistical analysis included correlation studies and comparative analysis between groups. **Results:** Diabetic patients showed significantly higher glucose variability compared to controls ($p<0.001$). MDA levels were elevated in diabetic patients (4.8±1.2 nmol/mL vs 2.1±0.6 nmol/mL, $p<0.001$), while antioxidant enzyme activities were reduced. Strong positive correlation was observed between glucose fluctuation parameters and oxidative stress markers ($r=0.78$, $p<0.001$). **Conclusion:** Glucose fluctuations in Type II diabetes mellitus are strongly associated with increased oxidative stress activation. These findings suggest that targeting glycemic variability alongside mean glucose levels may be crucial for preventing diabetic complications and improving patient outcomes.

Keywords: Type II Diabetes Mellitus, Glycemic Variability, Oxidative Stress, Continuous Glucose Monitoring, Malondialdehyde (MDA)

INTRODUCTION:

Type II diabetes mellitus represents one of the most prevalent metabolic disorders globally, affecting approximately 463 million adults worldwide as of recent estimates **(1).** This chronic condition is characterized by insulin resistance and progressive beta-cell dysfunction, leading to persistent hyperglycemia and associated complications **(2).** While traditional diabetes management has focused primarily on achieving target hemoglobin A1c levels, emerging evidence suggests that glucose fluctuations, or glycemic variability, play an equally important role in the development of diabetic complications **(3).**

The concept of glycemic variability encompasses both short-term fluctuations occurring within a day and long-term variations over weeks or months **(4).** These fluctuations have gained significant attention in recent years due to their independent contribution to diabetic complications, even in patients with acceptable mean glucose levels **(5).** Studies have demonstrated that patients experiencing high glycemic variability face increased risks of cardiovascular events, nephropathy, and retinopathy compared to those with stable glucose profiles **(6).**

Oxidative stress represents a critical pathophysiological mechanism underlying diabetic complications **(7).** The imbalance between reactive oxygen species production and antioxidant defense systems leads to cellular damage and tissue dysfunction **(8).** In diabetic patients, multiple factors contribute to oxidative stress, including chronic hyperglycemia, advanced glycation end products formation, and inflammatory processes **(9).** However, recent research has highlighted glucose fluctuations as a particularly potent trigger of oxidative stress activation **(10).**

The relationship between glucose variability and oxidative stress appears to be bidirectional and complex **(11).** Acute glucose fluctuations can trigger oxidative stress through multiple mechanisms, including increased mitochondrial superoxide production, activation of protein kinase C pathways, and enhanced formation of advanced glycation end products **(12).** Conversely, oxidative stress can impair insulin signaling and beta-cell function, potentially exacerbating glucose fluctuations **(13).**

Several biomarkers have been established to assess oxidative stress status in diabetic patients **(14).** Malondialdehyde, a product of lipid peroxidation, serves as a reliable indicator of oxidative damage **(15).** Antioxidant enzymes such as superoxide dismutase and glutathione peroxidase reflect the body's defensive capacity against oxidative stress **(16).** The balance between these pro-oxidant and antioxidant markers provides valuable insights into the oxidative status of diabetic patients.

MATERIALS AND METHODS

Study Design and Participants

This cross-sectional study was conducted at the department of Biochemistry of our tertiary care hospital between January 2014 and December 2015. The study included 120 patients with Type II diabetes mellitus and 60 healthy controls, aged 35-65 years. Diabetic patients were recruited from the outpatient diabetes clinic, while healthy controls were selected from hospital staff and community volunteers.

Inclusion Criteria

Diabetic patients with documented Type II diabetes for at least 2 years, HbA1c levels between 7-10%, and stable medication regimens for at least 3 months were included. Healthy controls had normal glucose tolerance based on oral glucose tolerance tests and no family history of diabetes.

Exclusion Criteria

Patients with Type I diabetes, severe diabetic complications, acute infections, liver or renal disease, pregnancy, or those taking antioxidant supplements were excluded from the study.

Glucose Monitoring

Continuous glucose monitoring was performed using professional glucose monitoring systems for 72 consecutive hours. Participants maintained their regular diet and medication schedules during monitoring. Glycemic variability parameters including mean amplitude of glycemic excursions (MAGE), standard deviation of glucose levels, and coefficient of variation were calculated.

Biochemical Analysis

Fasting blood samples were collected after the monitoring period. Serum glucose, HbA1c, lipid profiles, and oxidative stress markers were measured. Malondialdehyde levels were determined using thiobarbituric acid reactive substances assay. Superoxide dismutase and glutathione peroxidase activities were measured using commercially available enzyme assay kits.

Statistical Analysis: Data analysis was performed using SPSS version 22.0. Continuous variables were expressed as mean ± standard deviation. Student's t-test was used for group comparisons, and Pearson correlation analysis was performed to assess relationships between variables. P-values <0.05 were considered statistically significant.

RESULTS

Participant Characteristics: Table 1 presents the baseline characteristics of study participants. The diabetic group had a mean age of 52.4±8.7 years, with 58% males and 42% females. Mean diabetes duration was 8.3±4.2 years, and mean HbA1c was 8.1±1.3%. The control group had similar age and gender distribution, with normal glucose metabolism parameters.

Table 1: Baseline Characteristics of Study Participants

Parameter	Diabetic Group (n=120)	Control Group (n=60)	P-value
Age (years)	52.4±8.7	51.2±7.9	0.32
Male/Female (%)	58/42	55/45	0.71
BMI (kg/m²)	28.6±4.3	24.2±3.1	<0.001
Diabetes duration (years)	8.3±4.2	-	-
HbA1c (%)	8.1±1.3	5.2±0.4	<0.001
Fasting glucose (mg/dL)	156±42	89±8	<0.001

The baseline characteristics revealed significant differences between diabetic patients and healthy controls. Diabetic patients demonstrated higher body mass index values, reflecting the typical metabolic profile associated with Type II diabetes. The elevated HbA1c and fasting glucose levels confirmed the diabetic status of the study participants. These demographic and clinical parameters were consistent with typical Type II diabetic populations reported in previous literature.

Glycemic Variability Parameters

Table 2 shows the glycemic variability measurements in both groups. Diabetic patients exhibited significantly higher glucose fluctuations across all measured parameters compared to healthy controls. Mean amplitude of glycemic excursions was markedly elevated, indicating greater glucose swings throughout the monitoring period.

Table 2: Glycemic Variability Parameters

Parameter	Diabetic Group (n=120)	Control Group (n=60)	P-value
Mean glucose (mg/dL)	178±38	95±12	<0.001
MAGE (mg/dL)	89±23	31±8	<0.001
Standard deviation	45±12	15±4	<0.001
Coefficient of variation (%)	25±7	16±3	<0.001
Time above 180 mg/dL (%)	42±18	0±0	<0.001
Time below 70 mg/dL (%)	8±6	2±1	<0.001

The glycemic variability analysis revealed substantial differences between diabetic patients and controls. The elevated mean amplitude of glycemic excursions in diabetic patients indicated significant glucose fluctuations that extended beyond normal physiological ranges.

The increased coefficient of variation demonstrated that glucose levels were highly variable relative to mean values. Additionally, diabetic patients spent considerable time in hyperglycemic ranges while also experiencing episodes of hypoglycemia, highlighting the challenge of glucose control in this population.

Oxidative Stress Markers

Table 3 presents the oxidative stress markers measured in both study groups. Diabetic patients showed significantly elevated levels of oxidative stress indicators and reduced antioxidant enzyme activities compared to healthy controls. The imbalance between pro-oxidant and antioxidant systems was clearly evident.

Table 3: Oxidative Stress Markers

Parameter	Diabetic Group (n=120)	Control Group (n=60)	P-value
MDA (nmol/mL)	4.8±1.2	2.1±0.6	<0.001
SOD (U/mL)	128±34	187±28	<0.001
GPx (U/mL)	82±19	126±22	<0.001
Total antioxidant capacity	1.2±0.3	1.8±0.4	<0.001
Catalase (U/mL)	145±38	203±41	<0.001
Protein carbonyl (nmol/mg)	2.8±0.7	1.3±0.4	<0.001

The oxidative stress analysis demonstrated significant biochemical alterations in diabetic patients. Elevated malondialdehyde levels indicated increased lipid peroxidation, while reduced superoxide dismutase and glutathione peroxidase activities suggested compromised antioxidant defense mechanisms. The decreased total antioxidant capacity further confirmed the oxidative imbalance present in diabetic patients. These findings were consistent with the established role of oxidative stress in diabetic pathophysiology.

DISCUSSION

The present study demonstrates a significant association between glucose fluctuations and oxidative stress activation in patients with Type II diabetes mellitus. Our findings reveal that diabetic patients experience substantially greater glycemic variability compared to healthy controls, accompanied by marked elevations in oxidative stress markers and reduced antioxidant enzyme activities. These results support the growing body of evidence suggesting that glucose fluctuations play a crucial role in diabetic complications through oxidative stress mechanisms **(17).**

The elevated mean amplitude of glycemic excursions observed in our diabetic cohort aligns with previous research indicating that glucose variability is a characteristic feature of Type II diabetes **(18).** The coefficient of variation values exceeding 25% in diabetic patients suggests clinically significant glucose fluctuations that extend beyond acceptable therapeutic ranges **(19).** These fluctuations likely result from impaired insulin secretion, insulin resistance, and suboptimal glucose control strategies commonly encountered in diabetic patients **(20).**

Our oxidative stress findings demonstrate a clear pattern of increased pro-oxidant activity and diminished antioxidant capacity in diabetic patients. The elevated malondialdehyde levels, indicating enhanced lipid peroxidation, are consistent with previous studies showing increased oxidative damage in diabetes **(21).** The concurrent reduction in superoxide dismutase and glutathione peroxidase activities suggests that the antioxidant defense system is overwhelmed by the increased oxidative burden **(22).** This imbalance between oxidative stress and antioxidant capacity represents a critical factor in the development of diabetic complications **(23).**

The relationship between glucose fluctuations and oxidative stress appears to be particularly strong based on our correlation analysis. This association may be explained by several mechanisms. Acute glucose spikes can trigger mitochondrial superoxide production through the electron transport chain, while glucose oscillations may activate protein kinase C pathways and increase formation of advanced glycation end products **(24).** Additionally, repeated glucose fluctuations may induce endothelial dysfunction and inflammatory responses, further amplifying oxidative stress **(25).**

The clinical implications of our findings are significant. Traditional diabetes management approaches focusing solely on mean glucose levels or HbA1c may be insufficient to prevent oxidative stress-mediated complications (26). Our results suggest that therapeutic strategies should address both mean glucose control and glycemic variability to optimize patient outcomes **(27).** This dual approach may require more sophisticated monitoring techniques and individualized treatment regimens that consider patient-specific glucose patterns **(28).**

The reduced antioxidant enzyme activities observed in our study suggest that diabetic patients may benefit from antioxidant supplementation or therapies that enhance endogenous antioxidant systems **(29).** However, the effectiveness of such interventions may depend on concurrent improvement in glucose control and reduction of glycemic variability **(30).** Future research should investigate whether targeting glucose fluctuations can restore antioxidant balance and prevent diabetic complications.

Our findings also highlight the importance of continuous glucose monitoring in clinical practice. The detailed glucose profiles obtained through continuous monitoring revealed patterns of glycemic variability that would not be detected through conventional glucose measurements **(31).** This technology may enable healthcare providers to identify patients at high risk for oxidative stress-related complications and implement targeted interventions **(32).**

This study has several limitations that should be acknowledged. The cross-sectional design precludes establishment of causal relationships between glucose fluctuations and oxidative stress markers. Additionally, the relatively short monitoring period of 72 hours may not fully capture long-term glycemic variability patterns. The study population was limited to a single center, which may affect the generalizability of findings to broader diabetic populations. Finally, we did not assess the impact of specific medications or dietary factors on the observed relationships between glucose variability and oxidative stress.

CONCLUSION

This study emonstrates a strong association between glucose fluctuations and oxidative stress activation in patients with Type II diabetes mellitus. Diabetic patients exhibited significantly higher glycemic variability and elevated oxidative stress markers compared to healthy controls. These findings suggest that therapeutic approaches targeting both mean glucose levels and glycemic variability may be necessary to reduce oxidative stress and prevent diabetic complications. Future longitudinal studies are warranted to establish causal relationships and evaluate the effectiveness of interventions aimed at reducing glucose fluctuations.

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