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Oxidative Stress and Glycaemic Control in Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: There is growing evidence that excess generation of highly reactive free radicals largely due to hyperglycaemia cause oxidative stress which further exacerbates the development and progression of type 2 diabetes mellitus and its complications.

Objective: This study aims to assess glycaemic status and oxidative stress in type 2 diabetes mellitus patients.

Methods: Forty confirmed Type 2 diabetes mellitus patients registered with the General Medicine department of Mamata General Hospital, Khammam, Andhra Pradesh were selected for the study. Based on HbA_1c levels these patients were subdivided into two groups one with HbA_1c levels >8.5% was considered poor glycaemic control and the other with HbA_1c levels ≤8.5% was considered as good glycaemic control. Malondialdehyde and total antioxidant capacity were measured among the cases and controls.

Results: This study reveals the comparison of glycated haemoglobin, malondialdehyde, and total antioxidant capacity in 40 confirmed cases of Type 2 Diabetes Mellitus, which included 19 good glycaemic control and 21 poor glycaemic control. Firstly, the comparison of HbA1C (P value: 0.01), MDA (P value: 0.02) and TAC (P value: 0.04) revealed the significant difference between good glycaemic control and poor glycaemic control. Moreover, the Pearson correlation revealed a significant positive correlation of HbA1C with MDA (+0.72, 0.02) and a negative correlation with TAC (-0.01, 0.7) which was not statistically significant.

Conclusions: It is observed that poor glycaemic control has resulted in increased oxidative stress and decreased antioxidant capacity which can ultimately lead to complications. Antioxidant supplementation may help the patients in overall improvement and may delay the complications.

Keywords: Diabetes mellitus; glycated Haemoglobin; malondialdehyde; oxidative Stress; total antioxidant capacity

INTRODUCTION

Diabetes mellitus (DM) is a major health problem throughout the world. It is a group of metabolic disorders characterized by hyperglycaemia and glycosuria with disturbances in carbohydrate, fat and protein metabolism resulting from either an absolute or relative deficiency of insulin secretion or

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action.[1,2]Type 2 DM has been linked to oxidative stress through a single unifying mechanism of superoxide radical production include glucose autoxidation, protein glycation, advanced glycated end products formation and activation of polyol pathway, ultimately resulting in oxidative stress in a variety of tissues.[3]

These radicals cause peroxidative damage to cell membrane and DNA, leading to the increase in the plasma levels of some of the end products like Malondialdehyde (MDA). This is the common pathogenic factor leading to insulin resistance, B-cell dysfunction, impaired glucose tolerance and ultimately type 2 DM.[4] The absence of suitable compensatory mechanisms from endogenous antioxidant systems causes a redox imbalance and leads to the activation of stress-sensitive intracellular signalling pathways.[5]Hence, oxidative stress may be implicated in the pathogenesis of diabetes.

Oxidative stress, defined as a measure of steady levels of reactive oxygen species (ROS) or oxygen radicals in the biological system plays an important role in the aetiology of diabetic complications as it may be a common pathway linking the diverse mechanism for the pathogenesis of diabetic complications. Increased oxidative stress has been observed in diabetic patients as there is increased production of free radicals like superoxides and hydrogen peroxides. This increase, in the free radicals, is countered by various antioxidant enzymes like superoxide dismutase, glutathione reductase, catalases and protein thiolase. Diabetic patients have increased oxidative damage due to an increase in the production of oxygen free radicals and a deficiency in antioxidant defence mechanisms.[6-7]Lipids are among the primary targets of oxidative stress.[8]The present study was conducted to assess glycaemic status and oxidative stress in type 2 DM.

METHODS

It is a hospital-based cross-sectional observational study which is a part of my previous study conducted from 2011 to 2012 A.D in the Department of Biochemistry, Mamata Medical College and General Hospital, Khammam, Andhra Pradesh, India. 40 confirmed Type 2 DM patients registered with the General Medicine department of Mamata General Hospital, Khammam, Andhra Pradesh were selected for the study. Based on HbA1c levels these patients were subdivided into two groups: one with HbA1c levels >8.5% and the other with HbA1c levels ≤8.5%.[2]

Five milliliters of whole blood was collected after an overnight fast, 2 ml into an EDTA vial for HbA1c and 3 ml was allowed to clot. The serum was separated within an hour and used for MDA & TAC estimation.

The chromatographic-spectrophotometric ion exchange method was used for HbA1c. The spectrophotometric method was used for MDA (measured as thiobarbituric acid reacting substances-TBARS) and Total Antioxidant Capacity using the FRAP (Ferric Reducing Ability of Plasma) assay.

RESULTS

The current study was conducted on forty confirmed cases of diabetes mellitus, which included 19 good glycaemic control and 21 poor glycaemic control. In our study, male participants were more in comparison to female participants as illustrated in table 1.

Table 1: Age and Gender wise distribution of the study population (n=40).

Parameters	Good glycaemic control (n=19)	Poor glycaemic control (n=21)
Males	10 (52.6%)	11 (52.4%)
Females	9 (47.4%)	10 (47.6%)
Age (years)	41±1.2	49±3

An increase in mean MDA and a decrease in mean TAC levels were observed in patients with poor glycaemic control when compared with patients with good glycaemic control. The glycated haemoglobin and malondialdehyde were found to be more in poor glycaemic control as compared to good glycaemic control and the total antioxidant capacity (TAC) was found to be more in good glycaemic control as compared to poor glycaemic control groups, which were statistically significant as depicted in the table 2.

Table 2: Comparison of HbA1c, MDA, and TAC between good and poor glycaemic control population (n=40)

Parameters	Good glycaemic control (n=19)	Poor glycaemic control (n=21)	P – Value
HbA1c (%)	7.55 ±0.78	10.17 ±1.27	0.0001
MDA(nmol/ml)	2.81 ±1.90	4.29 ±2.10	0.0257
TAC(µmol/ml)	0.84 ±0.18	0.69 ±0.26	0.0423

[P value <0.05 was considered statistically significant]

A significant positive correlation was observed between HbA1c and MDA and a negative correlation was observed between HbA1c and TAC though it was not significant as shown in the table 3.

Table 3: Correlation of HbA1C with MDA and TAC

Parameters	R-Value	P –Value
MDA(nmol/ml)	+0.72	0.02
TAC(µmol/ml)	-0.01	0.7

[P value <0.05 was considered statistically significant]

DISCUSSION

Diabetes affects lipid metabolism profoundly and this effect is directly related to the control of their plasma glucose levels. Diabetics who have poor glycaemic control are at more risk of developing micro and macrovascular complications. De Zwart et al proposed that oxidative stress may be associated with the pathogenesis of NIDDM complications, particularly cardiovascular diseases.[9] Free radicals are known to be produced in excess in diabetic mellitus due to several factors, including hyperglycaemia, which results in oxidative stress. This oxidative stress

accelerates the onset, progression, and consequences of diabetes.[10] Hyperglycaemia causes the production of free radicals in several ways. Firstly, it can lead to auto-oxidation of glucose resulting in the formation of α-hydroxy-aldehyde that can form an enediol and subsequently produce superoxide radicals, hydroxyl radicals, and hydrogen peroxide.[11]

In type 2 diabetics, if glycaemic control improves, the oxidative stress indicators such as MDA will partially decrease.[12] This study reveals a positive correlation between glycated haemoglobin and MDA. Secondly, glycated haemoglobin and the total antioxidant capacity were negatively correlated. A study by Goodarzi MT et al had shown increased lipid peroxidation and oxidative stress in the Type 2 Diabetes mellitus patients in agreement with our study. They also revealed a positive correlation between the degree of hyperglycaemia and oxidative stress.[13]

The current study investigated the higher MDA level in Diabetic patients having poor glycaemic control, which indicates the greater oxidative stress in those patients. A study by Slatter DA et al. mentioned the disturbance of lipid metabolism, formation of the advanced glycation end products and the proteins including collagen get glycated. Thus, formed sugar adducts stimulate the formation of malondialdehyde. MDA has higher reactivity and binds to the proteins modifying their function.[14]

The present study also investigated the decreased total antioxidant capacity in diabetic poor glycaemic control patients. TAC represents the sum of endogenous and exogenous antioxidant system. In T2DM patients due to elevated oxidative stress the total antioxidant capacity is decreased. A study done in Chennai India by Rani AJ and Mythily SV revealed the findings similar type of findings.[15]

If glycaemic management in type 2 diabetics improves, oxidative stress markers like MDA will partially decline. There is growing evidence that excess generation of highly reactive free radicals, largely due to hyperglycaemia causes oxidative stress, which further exacerbates the development and progression of type 2 diabetes and its complications.[16]

CONCLUSIONS

This study concludes that poor glycaemic control has resulted in increased oxidative stress and decreased antioxidant capacity which may lead to complications that can result in increased morbidity and mortality. Antioxidant supplementation may help in overall improvement and can delay complications. It is thus suggested to include antioxidant supplementations to hypoglycaemic agents in the management of diabetes, which might go a long way in the reduction of associated complications.

Large-scale randomized controlled trials are needed to validate this suggestion.

Conflict of Interest: None

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