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Evaluation of Plasma Malondialdehyde among Sudanese Type 2 Diabetic Patients

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Abstract

Background and objectives: Diabetes is a chronic multifactorial disease which requires a variety of strategies to reduce its epidemic. Type 2 diabetes (T2MD) is the most common form of diabetes which results from inefficiency of insulin secretion or resistance to insulin action, both of which lead to chronic hyperglycemia. Lipid peroxidation is an oxidative stress process that involve in T2DM complications. This study aimed to 1) determine plasma malondialdehyde (MDA) levels as a biomarker for lipid peroxidation in Sudanese patients with T2DM, and 2) assess the associations between MDA and diabetes-related variables. **Material and Methods**: This case-control study was conducted from November 2022 to June 2023 at the National University, Sudan. It included 100 participants, of whom 50 were T2DM patients and 50 were healthy controls. Data on demographics, clinical characteristics, and biochemical markers (FBS, HbA1c, and MDA) were collected. The NycoCard HbA1c method and the GOD-POD Method were used for HbA1c and glucose measurement, respectively. MDA was determined by the thiobarbituric acid reactive substances method. The data were analyzed using SPSS Version. **Results**: Significant differences were observed between T2DM patients and healthy controls in FBS ($P = 0.000$), HbA1c ($P = 0.000$), and MDA ($P = 0.010$), with T2DM patients exhibiting higher levels. The study revealed a strong positive correlation between MDA levels and the duration of diabetes ($r = 0.69$, $P = 0.00$), while other variables, including age, BMI, and glucose control, did not significantly correlate with MDA levels. **Conclusion**: Findings revealed elevated MDA levels in Sudanese T2DM patients, with a positive correlation between MDA and diabetes duration. These findings emphasize the importance of oxidative stress in T2DM pathogenesis and call for

the need for targeted strategies to mitigate oxidative damage and improve diabetes care.

Keywords

Lipid Peroxide, Malondialdehyde, Hyperglycemia, Type 2 Diabetes Mellitus, Sudanese

1. Introduction

Diabetes mellitus (DM) is a chronic, multifactorial health disorder that results from either inadequate insulin secretion or impaired insulin utilization [1]. DM is caused by genetic and/or environmental factors [2]. The prevalence of DM, as reported by the International Diabetes Federation, is anticipated to increase from 10.5% in 2021 to 11.3% by 2030 and 12.2% by 2040 [3]. According to the 2019 Global Burden of Diseases, Injuries, and Risk Factors Study (GBD), DM was ranked in the eighth position for causes leading to mortality and morbidity worldwide [4].

Type 2 diabetes mellitus (T2DM), also known as "noninsulin-dependent diabetes" or "adult-onset diabetes," accounts for around 90% - 95% of all occurrences of DM [5]. T2DM has substantial economic and social consequences [6]. Microvascular and macrovascular complications are both more likely in patients with T2DM [7]. Around 54% of diabetics in Africa went undiagnosed, and 416 thousand deaths in 2021 were caused by diabetes-related complications [8].

Lipid peroxidation is a chemical process that occurs when free radicals or other reactive substances combine with polyunsaturated fatty acids leading to the production of lipid peroxyl radicals and hydroperoxides which damage the human cells [9]. Cell damage induced by oxidative stress ultimately results in complications of diabetes [10]. Malondialdehyde (MDA), a lipid peroxidation byproduct, is a reliable biomarker for oxidative stress [11].

In the Sudanese population diagnosed with T2DM, there was limited research that explored biomarkers of oxidative stress. Therefore, we aimed to 1) assess plasma MDL levels as a biomarker for lipid peroxidation in Sudanese patients with T2DM, 2) examine the relationships between MDA levels and selected variables associated with type 2 diabetes.

2. Materials and Methods

2.1. Study Design

An age- and sex-matched hospital-based, case-control study was conducted at the National University, Faculty of Medical Laboratory Sciences in Khartoum, Sudan, from November 2022 to June 2023.

2.2. Study Population and Data Collection

One hundred Sudanese individuals were enrolled. They were divided into two

groups: the case group consisted of 50 type 2 diabetic patients, and the control group consisted of 50 healthy individuals. The patients were recruited from the diabetes center at Yastabshiron Hospital in Khartoum, Sudan, whereas healthy individuals were randomly selected from the community. Inclusion criteria: ambulatory type 2 diabetic patients, male or female, do not have any diabetic complications. Exclusion criteria: patients with type 1 diabetes or patients with type 2 diabetes who had comorbidities, renal impairment, metabolic abnormalities, smoking habits, liver illness, or other diabetes-related complications.

Patients with T2DM were diagnosed according to guidelines from the World Health Organization (WHO). Diabetes was established when an overnight fasting plasma glucose level of ≥126 mg/dL [12].

A structured questionnaire was developed with the purpose of gathering both personal and medical information, such as the participant's age, gender, disease duration, and current undertaken medication for diabetes.

2.3. Blood Sampling & Plasma Preparation

5 ml of fasting venous blood was collected from each subject in heparin vacutainers. To extract the plasma, whole blood in the heparin vacutainers was centrifuged at 3000 RPM for 15 minutes. The plasma was placed in a sterile container and stored at 8˚C until starting the experiments.

2.4. Anthropometric Measures

The weight and height of each subject were carefully assessed and documented. Weight was measured using an electronic weighing scale, and height measurement was recorded using a stadiometer. We computed body mass index (BMI) as body weight in kilograms divided by height in meters squared. Participants with a BMI equal to 25 - 29.9 kg/m^2 were defined as overweight, while those with a BMI ≥ 30.0 kg/m^2 were defined as obese according to the WHO definition.

2.5. Estimation of Biochemical Parameters

The glucose oxidase-peroxidase (GOD-POD) method was used to measure plasma glucose levels on a COBAS INTEGRA 400 using kits purchased from Roche Diagnostics. Briefly, the glucose in the samples was oxidized by glucose oxidase to produce gluconic acid and hydrogen peroxide. The hydrogen peroxide was broken down into oxygen and water by a peroxidase enzyme. The oxygen then reacted with the oxygen acceptor orthotoluidine, which converted into a colored compound, the amount of which was measured colorimetrically.

The NycoCard HbA1c method was employed to determine the levels of glycated hemoglobin (HbA1c). Briefly, a monoclonal antibody binds to HbA1c, resulting in the formation of an immune complex whose intensity of color change is directly proportional to the HbA1c concentration.

Plasma malondialdehyde (MDA) was estimated by the spectrophotometric method using an MDA commercial kit purchased from a Bio diagnostic compa-

ny. MDA was assessed by the thiobarbituric acid reactive substances (TBARS) method. Briefly, thiobarbituric acid (TBA) reacts with MDA in acidic medium at a temperature of 95˚C for 30 min to form a pink thiobarbituric acid reactive product (TBARS) which was measured at 534 nm using a spectrophotometer.

2.6. Data Analysis

The Statistical Package for Social Science (SPSS Inc., Chicago, Illinois, USA) version 25.0 software was utilized for data analysis. Continuous data were presented as mean ± SD (range), while categorical data were expressed as the number (%). A comparison of variables between patients and healthy controls was performed with an unpaired t-test for continuous data and a chi-square for categorical data. The Pearson coefficient correlation was used to examine the relationship between MDA and selected variables. The level of significance was considered when the P-value < 0.05.

2.7. Ethical Considerations

The National University Research Ethics Committee (NU-REC) at the National University in Khartoum, Sudan, gave its approval for the study under approval number NU-REC/13-022/10.

The study was conducted according to the principles of the Helsinki Declaration. Participation was voluntary, and verbal consent was obtained from each participant. The confidentiality of all participants was maintained as no names were requested.

3. Results

3.1. Characteristics of Study Participants

Data analysis (Table 1) indicates that there was no significant difference in age, gender, weight, and BMI distributions between the cases and healthy controls, as indicated by P-values of 0.104, 0.423, 0.924, and 0.213, respectively. However, a significant difference was observed in height, where the control group exhibited a significantly lower mean height compared to the case group (P = 0.021). The duration of diabetes in the case group had a mean of 13.33 years, with a range from 1 to 27 years. A significant number of the diabetic patients were on antidiabetic tablets for treatment, and a small percentage were on insulin.

3.2. Measurement of Biochemical Markers

Significant differences in the key biochemical markers between the case and control groups were documented (Table 2). Firstly, FBS levels in the case group were significantly higher, with a mean of 156.66 mg/dL, compared to the control group's mean of 82.64 mg/dL (P = 0.000). This difference indicates impaired glucose control in the case group, which is a characteristic feature of diabetes. Additionally, the average HbA1c percentage was significantly elevated in the case group, with a mean of 8.56%, while the control group displayed 4.97% (P = 0.000). The

Table 1. Demographic characteristics of diabetic and control participants.

	Cases (n = 50)	Controls (n = 50)	p-value
M:F ratio	26:24	22:28	0.423
Age; years	52.92 ± 8.7 (40 - 74)	50.28 ± 7.9 (38 - 70)	0.104
Weight, Kg	74.06 ± 6.1	74.18 ± 6.4	0.924
Height, cm	163.50 ± 5.5	161.04 ± 5.1	0.021*
BMI; kg/m²	27.52 ± 3.0 (18.8 - 33.1)	28.36 ± 3.0 (23 - 31)	0.213
Duration DM; years	13.33 ± 6.9 (1 - 27)	-	-
Treatment; n (%)		-	-
Insulin	3 (6)	-	0.000*
Tablets	34 (68)	-	-
Tablets + insulin	13 (26)	-	-

BMI, body mass index; DM, diabetes mellitus; F, female; M, male. Data presented as mean ± SD (min-max) for continuous variables or number (%) for categorical variables; *P value less than 0.05 was considered statistically significant.

Table 2. Biochemical characteristics of diabetic and control participants.

	Case	Control	P-value
FBS; mg/dL	157.660 ± 68.5	82.64 ± 24.1	0.000*
HbA1c; %	8.56 ± 1.8	4.97 ± 1.6	0.000*
MDA, nmol/ml	1.83 ± 0.3	1.01 ± 0.2	0.010*

FBS, fasting blood sugar; HbA1c, glycosylated haemoglobin; MDA, malondialdehyde. Data presented as mean ± SD; *P value less than 0.05 was considered statistically significant.

elevated HbA1c levels in the case group reflect the prolonged hyperglycemia, which is a hallmark of poor glycemic control in diabetes. Moreover, plasma MDA levels, a marker of oxidative stress, were significantly higher in the case group with a mean of 1.83 nmol/ml, compared to the control group's mean of 1.01 nmol/ml (P = 0.000). This elevated MDA suggests increased oxidative stress in diabetic patients, likely resulting from the metabolic disturbances associated with diabetes.

3.3. Relation between MDA and Selected Variables

As presented in Table 3, the Pearson coefficient analysis revealed a significant strong positive correlation between the duration of diabetes and plasma MDA levels (r = 0.69, P = 0.00). This finding highlights that, with the prolonged duration of diabetes, there is a significant increase in oxidative stress, as evidenced by elevated MDA levels. Conversely, other variables, including age, height, weight, BMI, and markers of short-term glucose control such as FBG and HbA1c, did not demonstrate significant correlations with MDA levels. These findings highlight the substantial impact of chronic diabetes on oxidative stress and underscores

Table 3. Correlation between malondialdehyde (MDA) and age, Body max index (BMI), duration of disease, fasting blood glucose (FBG) and glycosylated haemoglobin (HbA1c) in all participants.

Variable	MDA
Age	r = −0.282
	P = 0.470
Height	r = 0.057
	P = 0.693
Weight	r = 0.236
	P = 0.099
BMI	r = −0.190
	P = 0.180
Duration of disease	r = 0.69
	P = 0.00*
FBG	r = −0.122
	P = 0.58
HbA1c	R = 0.210
	P = 0.32

FBS, fasting blood sugar; HbA1c, glycosylated haemoglobin; MDA, malondialdehyde; BMI, body mass index. *Correlation is significant at the 0.05 level (2-tailed).

the role of chronic hyperglycemia as a significant factor in enhancing oxidative stress in patients with diabetes.

4. Discussion

Findings from this study reveal significantly elevated plasma MDA levels in Sudanese patients with type 2 diabetes compared to healthy individuals. This aligns with various published research conducted among different populations worldwide. There was a significant increase (P = 0.004) in MDA levels observed in South African individuals with type 2 diabetes (n = 57) compared to healthy controls (n = 41), with respective measurements of 4.33 μM and 3.43 μM [13]. Moreover, a case-control study conducted on an Indonesian population revealed higher MDA levels in diabetes patients (n = 40) with median values of 2.43 μM compared to non-diabetic individuals (n = 40) with median values of 1.69 μM, respectively (P = 0.000) [14]. In a study of Iraqi Arab females with type 2 diabetes mellitus (n = 51) and control subjects (n = 31), serum MDA was significantly elevated in diabetic patients at 6.78 ± 1.21 nmol/ml compared to controls at 3.82 ± 0.77 nmol/ml (p < 0.001) [15]. Among Indian participants, MDA levels were significantly higher in type 2 diabetic patients (n = 100) compared to non-diabetic individuals (n = 100), with measurements of 5.9 ± 1.6 μmol/L and 1.8 ± 0.6 μmol/L, respectively (P = 0.029) [16]. Another study involving 139 Nigerian men and women found that serum malondialdehyde levels were elevated

in type 2 diabetes patients, measuring 2.1 ± 0.1 μmol/L, compared to control subjects at 0.7 ± 0.0 μmol/L (P = 0.01) [17]. Additionally, in Iranian population; female patients exhibited significantly higher MDA levels (2.57 ± 1.38 nmol/ml) than their male counterparts (2.10 ± 0.67 nmol/ml), whereas male patients showed increased MDA levels (2.10 ± 0.67 nmol/ml) compared to male controls (1.14 ± 0.7 nmol/ml). Similarly, female patients displayed significantly higher MDA levels (2.57 ± 1.38 nmol/ml) compared to female controls (1.07 ± 0.39 nmol/ml) [18]. These findings collectively emphasize the association between MDA and type 2 diabetes across diverse populations.

Furthermore, the study documented a strong positive correlation between MDA levels and the duration of the disease, indicating that as diabetes advances, oxidative stress increases. This supports the concept that extended exposure to high blood sugar levels increases the likelihood of oxidative damage [19]. The lack of a significant correlation between MDA levels and fasting blood glucose and HbA1C might be surprising. Although high blood glucose is recognized for its role in oxidative stress, the complex relationship between glucose control and oxidative stress may not consistently result in a direct correlation. Other variables, like dietary habits and individual variation, could independently impact MDA levels [20] [21].

The clinical implications of the elevated MDA levels observed in diabetic patients are important. As indicated by an elevated MDA, oxidative stress is linked to a variety of diabetic microvascular and macrovascular complications. For example, it exerts a substantial influence on the progression and onset of microvascular complications, including diabetic nephropathy, retinopathy, and neuropathy [22]. Furthermore, increased MDA levels may worsen insulin resistance, resulting in a vicious cycle that may have an adverse effect on glycemic control and overall health [23] [24]. Chronic hyperglycemia causes oxidative stress, which in turn causes lipid peroxidation by promoting the production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) [25]. When lipid peroxidation begins, it sets off a sequence of chain reactions that continue until termination byproducts are produced, one of which is lipid hydroperoxide. These hydroperoxides subsequently break down into aldehydes, such as MDA [9]. The rise in MDA levels among patients with type 2 diabetes in this study can be attributed to the elevated production of lipid peroxides and their release into the bloodstream.

5. Conclusion

In conclusion, this study highlights the elevated MDA levels in Sudanese patients with type 2 diabetes and the correlation between the raised MDA levels and disease duration, especially in patients who have had the disease for a longer period of time. These findings underline the need for diabetes care techniques to reduce oxidative stress which has a crucial role in the pathogenesis of diabetes complications.

6. Limitation

We did not measure parameters of lipid profile, including total cholesterol, LDL, HDL, and triglycerides. Specific lipid alterations can influence the production of reactive oxygen species, potentially impacting MDA levels. Future studies may consider including lipid profile assessments to gain a more comprehensive understanding of oxidative stress mechanisms in type 2 diabetes.

Conflicts of Interest

The authors declare no conflicts of interest.

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