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Evaluation of the Role of Serum Malondialdehyde in the Pathogenesis of Diabetic Retinopathy

DOI: https://doi.org/10.32007/jfacmedbagdad.6431957

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J Fac Med Baghdad
2022; Vol.64, No. 3
Received: Aug,2022
Accepted: Oct, 2022
Published: Oct. 2022

Abstract:

Background: The most typical consequence of diabetes mellitus is diabetic retinopathy. An important part of the etiology of diabetes and diabetic retinopathy is played by oxidative stress. Malondialdehyde is a dialdehyde that is moderately toxic and is frequently used as a marker for oxidative stress as well as lipid peroxidation.

Objectives: To assess the serum malondialdehyde levels in diabetic patients with and those without retinopathy and to compare these levels to controls .In additions to, investigate the relationship between serum malondialdehyde level and long glycemic control, the glycated hemoglobin (HbA1c).

Patients and Methods: This case-control study included (120) individuals from 40 to 70 years of age. They were divided into three groups: Group 1: 40 type 2diabetic patients with retinopathy, Group 2 :40 type 2 diabetic patients without retinopathy, and Group 3 40 controls .The biochemical testes included fasting blood glucose measured by Cobas c 311 systems, glycated hemoglobinHbA1c measured by Cobas c 111 systems, and serum malondialdehyde (MDA) measured by enzyme linked immunosorbent assay (ELISA).

Results: A higer mean value of (MDA) was found serum diabetic patients with and without retinopathy as compared to control (p=0.0001). As well as a significantly higher mean value of serum (MDA) in diabetic patients with retinopathy as compared to those without (p=0.0001).A significant positive correlation was found between serum(MDA) and HbA1C in diabetic patient with retinopathy group (r=0.931,p=0.0001) .

Conclusion: Higher serum levels of malondialdehyde is an indicator of increased lipid peroxidation that may be involved in pathogeneses of retinopathy in uncontrolled type 2 diabetic patients.

Keywords: Oxidative stress, diabetic retinopathy, malondialdehyde

Introduction:

Diabetes mellitus (DM) is a chronic condition that is defined by an elevated blood sugar level. It happens either when the body does not produce enough insulin or whenthe cells do not respond to the insulin that is produced (1,2,3). DMis associated with many complications (4). Retinopathy is one of DM's long-term consequences, which may result in vision loss, Nephropathy, atherosclerotic cardiovascular disease, peripheral neuropathy, arterial disease, as well as cerebral vascular disease are also possible complications of DM (5). Diabetic retinopathy (DR) a known cause of blindness in people in the working age,and is one of the most important pathologic vascular effects of diabetes (6). The pathophysiology of retinal microvascular injury is heavily influenced by hyperglycemia. (7).

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as it accelerates the development of oxidative stress and increases plasma free radical concentration is hyperglycemia (8). Through the production of free radicals, particularly reactive oxygen species (ROS) (4). Vascular leakage, vascular malfunction, and pathological angiogenesis are all indicators of (DR) and are influenced by the overproduction of ROS (9). The ability of biological systems to detoxify (ROS) is out of balance during oxidative stress, which causes these substances to accumulate (10).Oxidative stress, and ROS, can damage DNA, proteins, and lipids, causing adjustments to DNA and proteins as well as lipid peroxidation. (MDA) is a by-product of polyunsaturated fatty acid peroxidation (11). And is an extremely dangerous chemical that develops from lipid peroxidation as a result of free radical damage (9). MDA is associated with oxidative stress and poor antioxidant defense, which promotes the progression of DR (12). Serum MDA level is a sensitive marker of lipid peroxidation that is a useful measure of oxidative stress status (11). Since hyperglycemia is the primary

cause of lipid peroxidation, the rise in serum MDA shows that this rate of MDAhas increased (13).

Cases and Methods:

This case – control study included (120) individuals from 40 to 70 years of age. Participants were old diabetic but new retinopathy included all patients coming to the center of clients of the Diabetic Control Clinic and Diabetes/ Specialized Center for Endocrinology and Ibn- Al Haitham Teaching Hospital in Rusafa city in Baghdad .November 2021 to January 2022 Informed consent was obtained from each participant. The study was approved by the Scientific Committee of the College of Medicine/ University of Baghdad. Individuals were divided into three groups: 40 type 2 diabetics with retinopathy in Group 1, 40 type 2 diabetics with no retinopathy in group2. And 40 controls group three.

Patients with a history of severe eye illness or retinal detachment, type1DM, end-stage renal disease, malignancies, end-stage cardiac disease, immunosuppressive drug usage in the past or present, or IV drug steroid users were excluded from the study. The diagnosis of DM was based on the history of type2 DM, fasting serum glucose (FSB > 126) and glycated hemoglobin (HbA1C > 6.5%) according to the WHO criteria. The diagnosis of DR was made by after an ophthalmologist through history taking clinical and ophthalmological examination which. Included examination of the fundus by a slit lamp bio-microscope and indirect ophthalmoscope with 90-D lens, fundus color photograph centered on the macula, and optical coherence tomography (OCT).

Blood tests included glycated hemoglobin (HbA1C) measured by autoanalzer (cobs) C111, fasting serum glucose (FSG) by autoanalzer (cobs) C311 and serum MDA levels by an enzyme -linked immunoassay (ELISA).

Statistical analysis:

Data analysis was don using SPSS-27(Statistical Packages for Social Sciences- version 27) Simple statistics such as mean, standard deviation, and range were used to describe the groups. When comparing

two independent means, the Students't-test was used, and when comparing more than two means, the ANOVA test was used. A P value ofless than 0.05 was considered asstatistically significan

Results:

The mean values of FBSand HbA1C in the two diabetic patients groups(with and without retinopathy) were significantly higher p= 0.0001 than the controls figures(1 and 2).

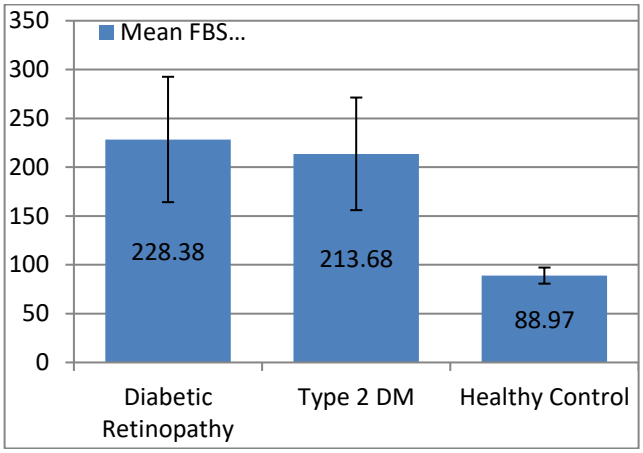

Figure (1): Mean value of FBS in all studied groups.

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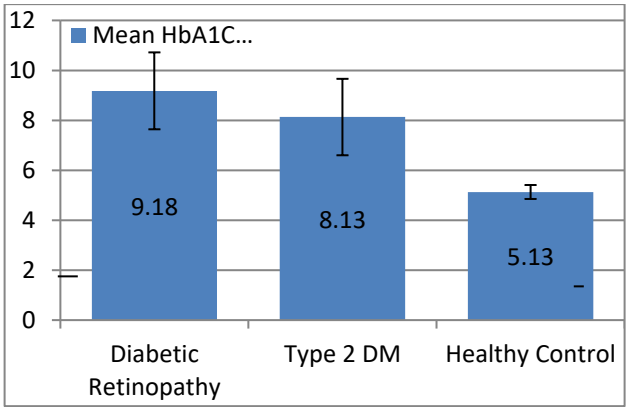

Figure (2): Mean value of HbA1c in every studied group.

The mean value of serum malondialdehyde in diabetic patients with and without retinopathy was significantly higher than the controls (p=0.0001). The mean value of serum malondialdehydein diabetic patients with retinopathy significantly higher than those without retinopathy (p=0.0001 to those without retinopathy (p=0.0001), in table(1).

Table(1): Mean value of serum Malondialdehyde level in thestudied groups.

	T2DM Retinopathy	T2DM	Control	P value
Malondialdehyde (MDA) (nmol/ml) **Mean±SD (Range)**	27.94±4.45 (20.2 - 35.7)	15.84±2.48 (10.34-18.9)	5.2±1.04 (2.76-6.91)	
	ANOVA	DR x C	DM x C	DR x DM
	0.0001^	0.0001#	0.0001#	0.0001#

Asignifican Positive correlation was found between serum MDAand HbA1C in diabetic patient with retinopathy group (r=0.931,p=0.0001) , in Figerue3.

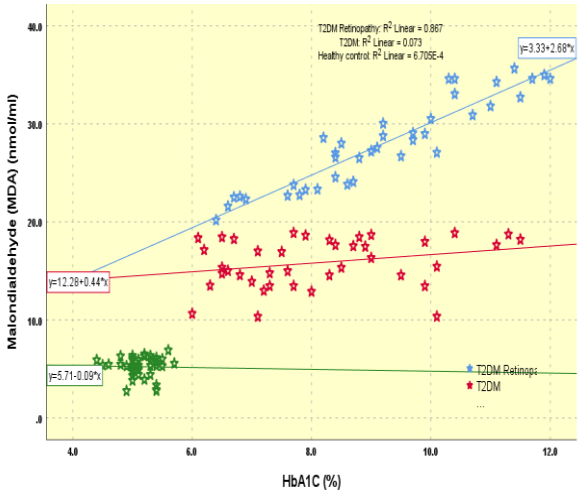

Figure (3) The correlation betweenMDAand HbA1C (r=0.931, p=0.001) in the diabetics retinopathy group

Discussion:

Hyperglycemia causes oxidative stress that is related to diabetes pathophysiology. Strong oxidative stress may reason harm to cells leading tomicrovascular issues that involve diabetes retinopathy **(14).**

MDA is a three-carbon dialdehyde with a high reactivity that is created as a by product of lipid peroxidation **(9).** Itis a marker system thatcan be utilized to detect complications associated with diabetes **(15).**

The result of this study revealeda a higher of serum MDA levels indiabetic both with and without retinopathy. This finding in agreement with Dave *et al*. who showed the MDA levels higher level in patients with DM than in controls. A higher level of oxidants is found in DM, as a result **(16).**Moreover, a recent study revealed higher level of MDA in DR in comparison to both DM without retinal damage and control lsuggesting that the the high level of MDA in diabetic groups result from oxidative stress-induced lipid peroxidation **(9).**

Oxidative stress is important forthe development of diabetes' pathology **(20).** Oxidative stress negatively affects the insulin's functions via numerous pathways interacting and producing ROS. These might weaken the pancreaticislet-cells, which would cause them to release less insulin. Moreover, free radical production via non-enzymatic protein glycation , enhanced lipid peroxidation and glucose oxidation results in cellular injury machinery, alterations to the cell membrane, enzyme damage increased insulin resistance and diabetes risk **(17,18**). The current study found possative correlation betweenMDA and HbA1c which is in line with recent research that found a connection between MDA and HbA1c. **(9, 19).** Uncontrolled diabetes is related to a greater MDA as a lipid peroxidation, indicator perhaps as a result of chronically elevated blood sugar followed by increased oxidative stress., Shawki etal found that MDA is a lipid peroxidation marker that interacts with the phospholipids in cell membranes **(9).**

Conclusions:

Higher serum levels of malondialdehyde is an indicator of increased lipid peroxidation that may be involved in the pathogeneses of retinopathy in uncontrolled type 2 diabetic patients.

Authors' Contributions:

Idea, design, and critical revision of the study: Zena Mohammed Hassan, dr Rana Ali Hamdi. Data gathering, analysis, and interpretation are all steps in the writing of a manuscript. : Zena Mohammed Hassan, dr Rana Ali Hamdi and diagnosis and Samples were provided by: dr Ebtehal Nouri Al Bassam

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Malondialdehyde في بدء وتطور اعتلال الشبكية السكري تقدير دور

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الخلاصة

الخلفية: النتيجة الأكثر شيوعًا لمرض السكري هي اعتلال الشبكية السكري. يلعب الإجهاد التأكسدي جزءًا مهمًا من مسببات مرض السكري واعتلال الشبكية السكري. مالونديالديهيد هو ديالديهيد ذو سمية معتدلة وكثيرا ما يستخدم كمؤشر حيوي للإجهاد التأكسدي وبيروكسيد الدهون.

الأهداف: كان الهدف من هذه الدراسة هو تقييم مستويات مصل الدم للمالونديالديهايد في المرضى الذين يعانون من اعتلال الشبكيةالسكري والذين يعانون من مرض السكري النوع الثاني. ومقارنةا مستواه بالاصحاء. بالإضافة إلى ذلك ، التحقق من العلاقة بين مستوى مالونديالديهيد و وفحص السكر التراكمي في الدم .

الموضوعات والطرق: شملت دراسة الحالات والشواهد هذه (120) فردًا تتراوح أعمارهم بين 40 و 70 عامًا. تم إنشاء ما مجموعه 3 مجموعات من الأشخاص: 40من مرضى السكري من النوع 2 المصابين باعتلال الشبكية كانوا جزءًا من المجموعة 1 ، 40 كان مرضى السكري من النوع 2 غير المصابين باعتلال الشبكية جزءًا من المجموعة 2 ، وكان 40 شخصًا من المجموعة الضابطة .

النتائج: كانت مستويات مصل الدم المالونديهايد اعلى بشكل ملحوظ في مرضى السكري الذين يعانون من اعتلال الشبكية وبدونه مقارنةً بالضوابط (p = 0.0001) ، وكذلك في مرضى السكري الذين يعانون من اعتلال الشبكية عند مقارنتهم بمرضى السكري غير المصابين باعتلال الشبكية (p = 0.0001). بالإضافة إلى ذلك ، في مجموعة مرضى السكري الذين يعانون من اعتلال الشبكية ، تم اكتشاف علاقة إيجابية ذات دلالة إحصائية بين مستوى مصلال دم للمالونديهايد الدم و HbA1C. (r=0.931 ، p=0.0001).

الخلاصة: ا ارتفاع مستويات مصل الدم المالونديهايد هو مؤشر على زيادة بيروكسيد الدهون التي قد تكون متورطة في مسببات أمراض اعتلال الشبكية في مرضى السكري من النوع 2 غير المنضبط.

الكلمات المفتاحية: الإجهاد التأكسدي ، اعتلال الشبكية السكري ، ا لمالونديهايد