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ORIGINAL ARTICLE

Alteration in Serum MDA levels is an early predictor in Type 2 Diabetes related complications.

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ABSTRACT… Objective: To determine the alterations in serum Malon-Di-Aldehyde (MDA) levels in type 2 diabetes mellitus (T2DM) with and without complications. **Study Design:** Cross Sectional study. **Setting:** Al-Tibri Medical College and Hospital and Jinnah Post Graduate Medical Centre Karachi. **Period:** June 2017 to December 2017. **Material & Methods:** This cross sectional study included 10 healthy controls as group 1, 30 diabetics without complications as group 2 and 30 diabetics with complications as group 3. Quantitative evaluation regarding MDA measurement in serum was done among three groups along with fasting sugar (FBS) as well as glycated hemoglobin (HbA1c). **Results:** MDA measurements in serum were significantly raised in group 2 and group 3 as compare to the controls ($P<0.001$). **Conclusion:** Current study reveals that the MDA is a biomarker induces type 2 diabetic related complications, so it must be valuable by considering as an early predictor in diagnosis of type 2 diabetic complications. Current findings reveals increase in oxidative stress in diabetics patients in comparison with nondiabetic individuals.

Key words: Malon-Di-Aldehyde, Oxidative Stress, Type 2 Diabetes Mellitus.

INTRODUCTION

Globally type 2 Diabetes Mellitus is one of the main health issue as a leading cause of metabolic disturbances.[1] Despite of strict blood sugar controlling regimes and lifestyle modifications the exact pathogenesis behind diabetic complications is still not fully understood.[2] Several studies have shown that T2DM typically takes few years for micro vascular complications in organs like kidney, eyes and nerves to get affected.[3] It is documented that about 20 to 40% of diabetic patients will develop organ dysfunction and complications like diabetic nephropathy, diabetic neuropathy and diabetic retinopathy.[4] Hence it's a crucial step to rule out the T2DM patient who can develop serious complications. No doubt there are several established markers for assessment of diabetic complications but sometimes they are not the only strong predictor of risk for micro vascular complications of T2DM risk due to some limitations.[5] It has been proven that patients with chronic metabolic diseases like T2DM are under enhanced state of oxidative stresses.[6] This oxidative stress is due to production of free radicals or reactive oxygen species (ROS) which are then responsible for cellular organelle damage and thus plays an important role in the development of diabetic vascular disease.[7] In healthy bodies oxidative stress is counteracted by the antioxidants present inside tissue thus forming ROS as short lived and unsuitable markers detecting early stages of cellular stress.[8] However in certain metabolic syndromes sustained and uncontrolled release of ROS cause them to react with various molecules and make them suitable and early markers of onset of cellular stress.[9] In T2DM Chronic oxidative stress is particularly more injurious to pancreatic islet as these cells express lower amount of anti-oxidant enzymes.[10] Therefore early detection of such stress markers in T2DM can reduce the risk of serious complications like retinopathy, nephropathy, neuropathy.[11]

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Certain domineering oxidative stress biological indicators or markers during diabetes are malondialdehyde MDA, Advanced oxidation protein products AOPP, protein carbonyls PCO.[12] The most important oxidative product of lipid peroxidation is MDA which has evidential association of marked increase in plasma levels in T2DM and several microvascular complications.[13] There are several biochemical processes behind elevation of MDA in T2DM such as leakiness of cell membranes, imbalance of membrane bound enzymes and alteration of surface receptor molecules.[10] Despite of documented role of increased levels of serum MDA in T2DM there is paucity of literature on predicting possible future complications in pre T2DM by timely recognition of fluctuations of serum MDA levels.

MATERIAL & METHODS

Current study was performed at Al-Tibri medical college and hospital and Jinnah Post graduate Medical Centre Karachi and start from June 2017 to December 2017. The study design was cross sectional. The size of population was calculated by open epi calculator. A total of 70 subjects were estimated by acquiring 95% confidence interval, prevalence of 12% and margin of error was 5%. The study included 3 groups which were selected by nonprobability convenient sampling method. Group 1 included 10 which were gender & age method, healthy controls, Group 2 included 30 clinically diagnosed & confirmed cases of T2DM without complications and Group 3 included 30 known cases of T2DM with complications. Medical records of Group 2 and 3 subjects were recorded to confirm diabetes associated complications like retinopathy, neuropathy, nephropathy and CVS complications were included. Hyperglycemia induced by pregnancy and other endocrine diseases were excluded from the study.

The ethical approval was taken by the Human Research Ethics Committee of the Isra University Hyderabad (IERC/ATMC/20/012). All eligible volunteers were informed about the aims and procedures of this study. 5 ml of venous blood was collected from each subject and was estimated for Random blood sugar RBS and glycated hemoglobin (HbA1C). RBS was calculated by using Glucose PAP Innoline kit. Merk private limited Pakistan. HbA1c was estimated by using Cobas c 111, Tina-quant hemoglobin A1C Gen. 2- hemolysate application kit. Estimation of MDA was done by thiobarbituric acid reactive substance assay followed by measurement of coloured product. read plate at 532 nm with M 201 micro plate reader ELISA.[14] SPSS version 21.0 was used for the evaluation of data and one way ANOVA was applied to find out the difference among quantitative variables. Significance was taken with P value <0.05.

RESULTS

The study includes normal control and T2DM with complications. Table-I showed age and gender (male and female) were placed into 3 groups. Group 1 is healthy control, group 2 is T2DM without complications and Group 3 is T2DM with complications. Also Table-I showed the characteristics of the study group showing diabetic male were more prevalent as compared to diabetic women. It also showed that most commonly involved age group in diabetics was in 4^{th} and 5^{th} decade.

The fasting blood glucose, their glycated hemoglobin and malondialdehyde (oxidative stress) were estimated and grouped into Group 1 healthy control, Group 2 T2DM without complications and Group 3 T2DM with complications. Further the normal control and T2DM with complications kidney disease patients distribution on Table-II shows the showed significant increase in fasting glucose level and HbA1c and serum MDA levels in diabetic groups compared with healthy group. Our results of current study indicate that these biomarkers can provide help in assessing for rapid diagnosis as well as better treatment options. More research to be needed to compare our findings.

DISCUSSION

T2DM is a multifactorial disease and a major cause of hidden redox reactions causing severe complications.[15] Early prediction of harmful oxidative stress markers such as MDA may prevent the development of morbidities associated with T2DM by timely drug and lifestyle modification.[7]

	Group 1	Group 2	Group 3
Age	47.13+4.99	48.60+9.05	50.43+15.29
Gender Male Female	 5 (50%) 5 (50%)	 20 (67%) 10 (33%)	 25 (83%) 5 (17%)
Group 1: Healthy controls Group 2: T2DM without complications Group 3: T2DM with complications			

Table-I. Frequency distribution of demographic variables among study groups

Variables	Group 1	Group 2	Group 3	P value
FBS (mg/dl)	108.43±7.28	181.47±74.72	228.60±64.94	0.001
HbA1c %	4.30±0.36	7.54±4.34	10.12±6.67	
MDA (mmol/dl)	1.24±1.39	1.77+0.55	2.95±1.86	
Group 1: Healthy control Group 2: T2DM without complications Group 3: T2DM with complications				

Table-II. Comparison of biochemical results of study groups using One Way Anova test

In our study most commonly observed age groups were in 4th to 5th decade which was in similarity with other authors.[16] Similarly most of the T2DM affected subjects were males which are in similarity with study done by previous authors.[16] Whereas Nair A in 2017 observed females as more prevalent group as compared to males.[17,18] According to our study FBS levels for T2DM without complications was 181.74±74.72 mg/dl which was in contrast to previous studies which showed FBS <180 mg/dl in uncomplicated T2DM.[19,20] Our study revealed FBS of complicated T2DM was 228±64.94mg/dl which was in discordance from the results by previous authors. These differences might be due to consciousness and positive attitude of patient towards risk of T2DM and timely approach to clinician was practiced in contrast of to our study subjects where self-management of diseases were practiced causing difficult in control of the condition.[21]

This study showed HbA1c was <8% in diabetic without complications and >8% in T2DM with complications which was in similarity with previous studies.[22,23] This underlines the fact that our study subjects were not under good glycemic control. As we have already discusses the role of ROS in progression of T2DM. This was evident by our study showing significant difference in serum MDA levels of healthy and disease individuals which is in similarity to the previous studies done previous authors.[24,25] We found MDA levels significantly high in diabetic patients with complications as compared to healthy controls which was in in consonance with the reports available in the literature.[26] In contrast to our results Sharma S in 2020 established MDA levels for uncontrolled T2DM as 3.94±1.02. This difference could be due to increase in sample size in their study.[27] Furthermore our results were in accordance with the preceding exploratory studies showing the significant rise in level of MDA in diabetics as compared to control.[16,20]

Our aim was to recognize MDA levels to prevent delayed complications. Current study findings reveals that the patients with diabetes has higher risk to vulnerable with oxidative stress as well as the patients having high blood sugar was associated with free radical induced lipid peroxidation.

CONCLUSION

Present study reveals that the MDA is a biomarker which induces type 2 diabetic related complications, so it may be useful in consideration as an early predictor in diagnosis of type 2 diabetic complications. Present findings reveals increase in oxidative stress in diabetics patients

in comparison with nondiabetic individuals.

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2	Syed Naqeeb Ali	Analysis and interpretation.	
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4	Shahid Zafar	Statistical expertise.	
5	Najia Soomro	Critical Revision.	
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