Original Research Article

A study on role of lipid peroxidation in diabetic patients in Thiruvarur District

S. Sumathi[1], M. Ramadevi[1*]

[1]Associate Professor, Department of Biochemistry, Government Thiruvarur Medical College, Thiruvarur, India
[*]Corresponding author email: **mathivanan.ramadevi @gmail.com**

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Abstract

Introduction: Insulin affects many sites of mammalian lipid metabolism. It stimulates synthesis of fatty acid in liver adipose tissue and in the intestine. The insulin has also been reported to increase the cholesterol synthesis. The activity of lipoprotein lipase in white adipose is also increased. From this point of view, the assessment of various lipid fractions and lipid peroxide in the cases of Diabetes Mellitus may be of some help in the prognosis of patients and in preventing the possibilities of complications or secondary disorders.

Aim of the study: To study the level of lipid peroxide in IDDM and NIDDM. To find out the correlation between Lipid peroxide and Lipid profile in both types of diabetes mellitus

Materials and methods: Participants of the study group were selected from the outpatient's population of the Department of Medicine, Government Thiruvarur Medical College, Thiruvarur. 100 patients were selected for this study. Out of which 50 patients belong to NIDDM and 50 to IDDM group. 50 persons served as a healthy control.

Results: There was a very good positive correlation between MDA and Cholesterol, TGL, LDL, VLDL in both NIDDM and IDDM cases. There was a negative correlation between MDA and HDL in NIDDM and IDDM cases.

Conclusion: In the diabetes mellitus abnormally increased levels of lipid, lipoprotein and lipid peroxides in plasma may be due to the abnormal lipid metabolism. The maximum increase in lipid peroxide was found in a group of diabetes mellitus with complication. Elevated levels of lipid peroxide in diabetes mellitus may be due to the alteration of function of erythrocytes membrane. This inhibits the activity of superoxide dismutase enzyme leading to accumulation of superoxide radicals which cause the maximum lipid peroxidation and tissue damage in diabetes.

Key words

Diabetes mellitus, Lipid peroxidation, Free radicals, Triglyceride level, MDA.

Introduction

Diabetes Mellitus is of three types Type I (IDDM) and Type II (NIDDM), and Gestational Diabetes. By 2025, 300 million people are expected to be diabetic. This will be greatly increased by 19 to 57 million people [1]. Due to the metabolic derangements several metabolisms are severely affected , like lipid metabolism, lipid peroxidation leading to free radical generation (ROS) which triggers the complications like cardiac (atherosclerosis), neurological (Diabetic Foot Ulcer), Nephrological (Nephropathy), Vascular (Micro and Macro) etc., Chronic Diabetes Mellitus leads to the impairment of microcirculation [2] and there is an alteration in structures of glycosaminoglycans, advanced glycation end products (AGEs), Glycoproteins, collagen, polyol pathways which ultimately brings the change in the blood vessels leads to the hardening of vessels [3]. Alteration in the carbohydrate and lipid metabolism leads to the decreased antioxidants and increased generation of free radicals and oxidative stress. Finally, increased coagulability of the endothelial surface leads to microthrombus formation and luminal occlusion with atherosclerotic plaques [4]. There are multiple causes for diabetic neuropathies, including metabolic, vascular, autoimmune, oxidative stress and neurohormonal growth factor deficiency. Free radicals are constantly being generated in the body, as a result of the normal metabolic process [5]. Under physiological conditions, damage due to free radicals is countered by antioxidants. Sometimes excessive free radical formation occurs in the body, and the antioxidant system in the body cannot cope with the situations [6], the pro-oxidants overwhelm the antioxidants. This situation is known as oxidative stress. MDA is the product formed from free radicals as a marker for oxidative stress [7]. In Diabetics, antioxidant systems like GSH, vitamin- C, Magnesium, Vitamin- E are lowered which aggravates the lipid peroxidation. Lipid peroxidation is elevated in Diabetes. Diabetes is usually accompanied by increased production of free radicals or reactive oxygen species which produces oxidative stress [8]. The occurrence of free radical-induced lipid peroxidation causes considerable change in the cell membrane. Peroxidation of Lipid membrane has been related to the pathogenesis of many degenerative diseases such as Atherosclerosis. Atherosclerosis is the most common complication of diabetes [9]. Free radicals damage lipids by initiating a process called Lipid Peroxidation. Decomposition of lipid peroxides forms many cytotoxic compounds like malondialdehyde (MDA). So oxidative stress can be measured by monitoring the changes in malondialdehyde Degree of lipid peroxidation was measured in terms of MDA [10].

Materials and methods

Participants of the study group were selected from the outpatient's population of the Department of Medicine, Government Thiruvarur Medical College, Thiruvarur. 100 patients were selected for this study. Out of which 50 patients belong to NIDDM and 50 to IDDM group. 50 persons served as a healthy control.

Inclusion criteria: All ambulatory NIDDM and IDDM patient without any complications.
Exclusion criteria: Smokers Alcoholics, Renal failure, Bronchial Asthma, History Suggestive of Complications of DM- Angiopathy, Cardiopathy, Retinopathy, Nephropathy.

Detailed history and complete clinical examination were done in all cases. For all the patients, fasting and postprandial blood samples and fasting urine samples were collected. For blood sugar estimation, blood collected in the fluorinated tube. For other investigations in plain tube, samples were collected.

Procedure: To 0.5 ml of plasma, 4 ml of 0.083N sulphuric acid was added. To this mixture 0.5 ml of 10%, phosphor tungstic acid was added and mixed, allowed to stand at room temperature for 5 minutes. The mixture was centrifuged at 3000 rpm for 10 minutes. The supernatant was discarded. To the remaining, 1 ml of TBA was added. The reaction mixture was heated at boiling water bath for 60 mts. After cooling, the mixture was centrifuged at 3000 rpm for 15 mts. The supernatant was transferred to a cuvette. Standard MDA solutions were 2 µmol/L, 4 µmol/L, 6 µmol/L, 8µmol/L and 10 µmol/L and a blank were processed along with the test sample. The absorbance at 530 nm was measured and subtracted from the blank. A calibration graph was prepared using MDA standard.

Statistical analysis

100 patients were selected for each group at a 95% level of significance and power of the study was 90%. p-value of <0.05 considered statistically significant. Data were expressed as mean and standard deviation. Mann-Whitney test, Chi-square test, and Student t-test were used to analyze the data.

Results

Table - 1 shows that the mean value of MDA was high in diabetic patients (Mean 4.63 µmol/L) when compared to control group (Mean 3.61 µmol/L) and the increase was statistically significant (P = 0.0001).

Table - 2 shows a significant increase in MDA levels of NIDDM group (Mean 4.8 µmol/L) as compared to IDDM group (Mean 4.46µmol/L).

Table – 1: MDA levels in control and diabetics.

MDA	**CONTROL GROUP**	**DM GROUP**
Mean	3.61	4.63
S.D.	0.11	0.35
'P'	**0.0001 Significant**	

Table - 2: MDA level in control, NIDDM and IDDM cases.

	Control	**IDDM**	**NIDDM**
MDA level	3.61±0.11	4.46 ± 0.23	4.8 ± 0.37

Table - 3: MDA and HBAIC.

Type of DM Cases	**Average MDA values for cases with**		'p-value '
	Good control (HbAIC <7) Mean ± S.D	**Poor control (HbAIC >7) Mean ± S.D**	
NIDDM	4.37 ±0.08	4.92±0.33	0.0001 Significant
IDDM	4.14 ± 0.1	4.54±0.17	0.0001 Significant
Total DM Cases	4.26 ±0.15	4.73±0.32	0.0001 Significant

Table - 4: Correlation between MDA and lipid profile.

Correlation coefficient with	**The correlation coefficient of MDA with lipids in**		
	NIDDM Cases	**IDDM Cases**	**Total DM Cases**
Total Cholesterol	0.8105	0.6698	0.8248
TGL	0.7096	0.5897	0.7453
HDL	-0.7129	-0.5471	-0.7348
LDL	0.7574	0.5374	0.7566
VLDL	0.6966	0.5824	0.7359

Table - 3 shows a significant elevation in MDA values along with an increase in HbAIC values.

Table - 4 shows there was a very good positive correlation between MDA and Cholesterol, TGL, LDL, VLDL in both NIDDM and IDDM cases. There was a negative correlation between MDA and HDL in NIDDM and IDDM cases.

Discussion

In the present study, an attempt is made to study the influence of dyslipidemia in the complications of diabetes mellitus and how the lipid peroxidation will induce the damage to various organs in the Diabetic Patients. The cause of Diabetic complications is not clearly known and may be Multifactorial [11]. The major emphasis has been placed on the polyol pathway, wherein glucose is reduced to sorbitol by enzyme aldolase reductase. Sorbitol, which appears to function as a toxin, has been implicated in the pathogenesis of retinopathy neuropathic cataract, nephropathy and vascular diseases sorbitol accumulation are associated with a decrease in the myoinositol content, Abnormal phosphoinositide metabolism and a decrease in Na+, K+, ATP use activity. Hyperglycemia is a widely known cause of enhanced plasma Free Radical concentrations [12]. There are many ways by which hyperglycemia may increase the generation of free radicals. Development of atherosclerosis based on metabolic disorders is accompanied by a smoothened response of morphologically unaltered blood vessels to endothelium-dependent vasodilators such as acetylcholine and Bradykinin [13]. If endothelial dysfunction promotes atherosclerosis, it may be a link between hyperglycemia and alterations of large blood vessels. In the present study HDL, cholesterol levels were normal, no change was observed in nephrological cases. The mean value of plasma MDA is high in diabetic patients when compared to control group. Increased lipid peroxidation in diabetes mellitus is due to the excess formation of free radicals. Hyperglycaemia in diabetics causes increased glycation of protein which itself act as a source of free radicals [14]. Metabolic derangements in diabetes lead to an increase in the concentration of oxidizable substrates and compromised detoxification pathways. The study shows that cases on insulin as therapeutic regime (IDDM) had lower mean MDA level (4.46 µmol/L) as compared to those on oral hypoglycaemics (NIDDM) (4.8 µmol/L) indicating the lesser level of oxidative stress in diabetics on insulin. Considering MDA levels among cases on the basis of their glycaemic status, a significant correlation is seen between well-controlled and poorly controlled diabetics (both in IDDM and NIDDM). MDA is higher in individuals with poor glycaemic control compared to good glycaemic control. For every 1% reduction in HbAIC, one can expect a 35% reduction in microvascular complications [15] which can be attributed to a decrease in oxidative stress on treatment. The oxidative stress in IDDM and NIDDM is evidenced by increased levels of plasma MDA, so intensive glycaemic control is well established as a standard of care for patients with diabetes achieving and sustaining glucose control can substantially reduce the risk of microvascular complications in diabetes mellitus [16]. Oxidative stress in terms of MDA is increased in NIDDM when compared to that in IDDM. So insulin therapy has a beneficial effect on oxidative stress [17].

Conclusion

It is evidenced that the level of MDA is increased in both types of DM. To conclude in the era of modern medicine diabetic complications demand prevention and management. The estimation of lipid peroxide in diabetes mellitus is very useful as it may serve as a useful monitor to judge the prognosis of the patient. The detection of the risk factor in the early stages of the disease will help the patient to improve and reduce the morbidity rate. It is with this background that the ray of hope provided by the considerable evidence suggesting the role of prevention of increased

lipid peroxidation could offer a feasible and cost-effective way to reduce the prevalence of diabetic complications.

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