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ALTERATIONS IN PLASMA ANTIOXIDANT ENZYME LEVELS AND SERUM LIPID PROFILE PARAMETERS IN RELATION TO LIPID PEROXIDATION IN INDIVIDUALS WITH MATERNALLY INHERITED TYPE 2 DIABETES MELLITUS

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ABSTRACT: Aim: The present study aimed to evaluate the antioxidant potential and lipid profile parameters, in relation to lipid peroxidation in patients with maternally inherited type 2 diabetes mellitus and in healthy normal individuals. **Methods:** All standard methods were used to estimate enzymatic antioxidants [Catalase, Copper containing Superoxide Dismutase (CuSOD), Manganese containing Superoxide Dismutase (MnSOD) and Glutathione Peroxidase (GPX)], non enzymatic antioxidant [Reduced Glutathione (GSH)], lipid peroxidation [Malondialdehyde (MDA)]; and lipid profile parameters [High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL), Triglyceride (TG) and Cholesterol]. Correlations between MDA and all parameters were sought using Spearman's rank correlation coefficient. **Results:** Significantly lower mean activities of catalase, CuSOD, MnSOD and GSH and significantly higher mean activity of GPX and higher mean concentration of MDA were reported in plasma samples from patients with type 2 diabetes mellitus as compared to healthy individuals. A significantly lower mean level of HDL and significantly higher mean levels of LDL, TG and Cholesterol were noted in patients with type 2 diabetes mellitus than healthy control individuals. Further, weak to moderate correlations were observed between MDA and CuSOD, MnSOD and GPX. No significant correlation was observed between MDA with GSH and with lipid profiles. **Conclusion**: In conclusion, lipid peroxidation may be a useful marker for early diagnosis and prognosis of secondary complications in patients with maternally inherited type 2 diabetes mellitus.

INTRODUCTION: Diabetes mellitus is pervasive around the globe [1]. In the year 2000 the widespread of the diabetes mellitus in the world was 171 million, which is expected to raise up to 366 million by the year 2030 [2]. In India, diabetes mellitus is an alarming disease. At present more than 40 million people are diagnosed with diabetes, showing that India leads the world in diabetes mellitus [3].

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Diabetes mellitus is a metabolic disorder characterized by hyperglycemia often accompanied by glycosurea, polydipsia and polyurea [4]. Oxidative stress and dyslipidemia have been involved in the pathogenesis of diabetes mellitus and associated complications like cardiovascular disease and atherosclerosis [5]. In the last few decades, extensive body of literature regarding mitochondria has shown its pivotal role in the pathogenesis of type 2 diabetes mellitus via insulin resistance [6-10].

Mitochondria are the main site for oxidative phosphorylation and prevalent almost in every living cell [11]. Mitochondria contain its own genetic material and inherited maternally [12, 13]. The mitochondrial DNA (Deoxyribonucleic acid) in

association with the nuclear DNA codes the polypeptides of the electron transport chain (ETC). Mitochondrial DNA lacks in histone proteins and DNA repair enzymes, making it more susceptible to oxidative damage. Aberrant mitochondrial DNA can code, defective polypeptides of the ETC, resulted in less ATP (Adenosine Triphosphate) production. Lower concentration of ATP opens the ATP sensitive potassium channel and prevented cellular depolarization, which results in halting the influx of calcium ions.

Thereby resisting the insulin release from insulin stored vesicles. Moreover, defective complexes of the ETC sometime leak an electron flowing through it and can generate reactive oxygen species like superoxide anion, which may lead to other free radicals like, hydrogen peroxides, peroxinitrates and hydroxyl radicals [14]. Diabetes mellitus has been associated with redox alterations, which are due to the impaired action of antioxidant enzymes and increased production of free radicals [15, 16]. Hence, patients with maternal inheritance of type 2 diabetes mellitus are more prone to oxidative stress result in early secondary complications than type 1 and juvenile diabetes mellitus.

Free radicals are highly reactive in nature and can attack on carbon-carbon double bonds of the membrane phospholipid and initiate the process of lipid peroxidation [17, 18]. Malondialdehyde, the end product of the lipid peroxidation is widely used in monitoring the status of oxidative stress [19, 20, 21]. Altered oxidative stress can increase the production of malondialdehyde [22]. Therefore, monitoring the level of malondialdehyde in these patients may provide a hint for early diagnosis of the secondary complications.

MATERIALS AND METHODS:

Family history and sample collection:

Type 2 diabetes patients having a history of maternal inheritance of it, have been selected for this study. Blood samples were drawn from 150 patients (from 18 families, ages ranging from 18 to 72 years), who came for routine blood glucose monitoring at "Swami Vivekanand Medical Mission Hospital" Nagpur, Maharashtra, India, over a one year period (May 2014 to May 2015), to compare, blood samples were drawn from 150 healthy normal individuals (ages ranging from 18 to 72 years). Proper informed consents were taken from the patients and healthy individuals.

Ethics in the study:

This study is approved by the Institutional Ethical Committee of "Swami Vivekanand Medical Mission" Nagpur, Maharashtra, India.

Inclusion Criteria and Exclusion criteria:

Inclusion Criteria:

Patients having a history of maternally inherited type 2 diabetes mellitus.

Exclusion criteria:

Any kind of history of paternal inheritance of type 2 diabetes mellitus, type 1 diabetes mellitus and juvenile diabetes mellitus.

Sample preparation:

2 ml blood sample was withdrawn from each patient and healthy individual. From this, 1 ml was collected in a non anticoagulant tube to obtain serum for the analysis of lipid parameters and remaining 1 ml blood sample was collected in EDTA (Ethelene Diamine Tera Acetic acid) containing vacutainer tubes to obtain plasma. Both the tubes were centrifuged at 1500 RPM for 15 minutes. Blood cells carry over were removed by recentrifugation. The separated serum and plasma samples were immediately processed for the lipid profile and antioxidant potential examination.

Quantitative analysis of antioxidant enzymes

All standard methods were used to quantify the levels of antioxidant enzymes in collected plasma samples. The activity of Catalase (µmoles of hydrogen peroxide consumed / mg protein/ ml/ minute) was estimated by using the method given by Aebi et al. (1983) [23]. In plasma samples, the addition of 2 mM of cyanide inactivated CuSOD (Copper containing Superoxide Dismutase); MnSOD (Manganese containing Superoxide Dismutase) remain unaffected by it. Similarly, addition of 25 microliters of ice cold chloroform/ ethanol solution inhibited the activity of MnSOD and CuSOD remains unaffected by it [24, 25]. The activities of CuSOD (units / mg protein/ ml / minute) and MnSOD (units / mg protein/ ml / minute) were estimated as per the protocol given by

Marklund and Marklund (1974) [26], in which inhibition of pyrogallol autooxidation defines one unit of enzyme activity. Glutathione peroxidase activity (µg of reduced glutathione consumed/ mg protein/ ml / minute) was estimated by the method of Rotruck et al. (1973) [27].

Quantitative analysis of non enzymatic antioxidant:
Concentration of GSH (µmoles/ mg protein/ ml / minute) was estimated as per the method of Beutler et al. (1963) [28], in which glutathione reacts with 5,5'- dithio bis-2, nitro benzoic acid (DTNB) to produce stable yellow colored complex.

Determination of lipid peroxidation:
The formation of MDA (nmole/ mg protein/ ml /hour), determines the level of lipid peroxidation. MDA was assayed in the form of thiobarbituric acid reactive substances (TBARS) as per the method of J stocks et al. (1978) [29].

Determination of lipid profile parameters:
Lipid profile parameters were analyzed using Micros 60 autoanalyser by Horiba, using all standard kits. Protocols were run according to the instructions provided by manufacturers. Results were reported in mg/dL.

Statistical analysis:
Statistical analysis was performed with Med Calc statistical software (version10.1.2.0). All results were expressed in Mean ± SEM. Significant differences in enzymatic (Catalase, MnSOD, CuSOD and GPX), non enzymatic (GSH) and lipid peroxidation (MDA) between control and individuals with type 2 diabetes were observed using a "t" test. The correlation between MDA and other parameters (enzymatic, non enzymatic and lipid profile) were sought by using Spearman's rank correlation coefficient and data represented in "r_s" and "p" values. The correlation coefficients with "r_s" values; ≤0.35, 0.36 to 0.67 and 0.68 to 1.0 were considered to represent weak, moderate and strong correlations respectively [30, 31]. $p<0.05$ was considered as a standard for significant differences.

RESULTS:
Levels of blood fasting glucose and activities of antioxidant enzymes in plasma samples: The mean level of fasting blood glucose and the mean activities of antioxidant enzymes were examined in samples from control and individuals with type 2 diabetes mellitus (**Table 1).**

Fasting glucose:
The mean level of fasting glucose (mg /dL) for control samples and individuals with type 2 diabetes mellitus was 76.293±1.078 and 211.706±3.538 respectively. This result showed that the level of fasting glucose was significantly higher in individuals with type 2 diabetes mellitus as compared to control samples ($p<0.0001$).

The non significant correlation was observed between MDA and fasting glucose (r_s = 0.086, $p>0.05$) (**Table 4**).

Catalase:
The mean activity of catalase (units/mg protein/ml/minute) for control samples and individuals with type 2 diabetes mellitus was 0.5127±0.0172 and 0.4454± 0.0156 respectively. This result corroborated that the activity of catalase was significantly decreased in individuals with type 2 diabetes mellitus as compared to control samples ($p<0.01$).

When the activity of catalase was plotted against the level of MDA in individual samples (**Fig. 1a**), a positive correlation was noted (r_s=0.368, $p<0.0001$) (**Table 4**); that is, an increase in the activity of catalase correlated with an increase in the concentration of MDA in the samples.

CuSOD:
The mean activity of CuSOD (units / mg protein / ml / minute) for control samples and individuals with type 2 diabetes mellitus was 2.2717±0.199 and 1.5162±0.0452 respectively. This result showed that the activity of CuSOD was significantly lower in individuals with type 2 diabetes mellitus as compared to control samples ($p<0.001$). When the activity of CuSOD was plotted against the level of MDA in individual samples (Fig. 1b), a positive correlation was noted (r_s = 0.363, $p<0.0001$) (**Table 4**); that is, an increase in the activity of CuSOD correlated with an increase in the concentration of MDA in the samples.

MnSOD:
The mean activity of MnSOD (units/ mg protein/ ml / minute) for control samples and individuals with type 2 diabetes mellitus was 1.9879±0.1284 and 1.5899±0.0617 respectively. This result showed that the activity of MnSOD was significantly lower in individuals with type 2 diabetes mellitus as compared to control samples ($p<0.01$). When the activity of MnSOD was plotted against the level of MDA in individual samples (Fig. 1c), a positive correlation was noted (r_s = 0.370, $p<0.0001$) (**Table 4**); that is, an increase in the activity of MnSOD correlated with an increase in the concentration of MDA in the samples.

GPX:
The mean activity of GPX (units/ mg protein/ ml / minute) for control samples and individuals with type 2 diabetes mellitus was 0.000733±0.000026 and 0.000953±0.000038 respectively. This result showed that the activity of GPX was significantly higher in individuals with type 2 diabetes mellitus as compared to control samples ($p<0.0001$). When the activity of GPX was plotted against the level of MDA in individual samples (Fig. 1d), a positive correlation was noted (r_s = 0.306, $p<0.001$) (Table 4); that is, an increase in the activity of GPX correlated with an increase in the concentration of MDA in the samples.

TABLE 1: MEAN LEVEL OF BLOOD GLUCOSE AND MEAN ACTIVITIES OF ANTIOXIDANT ENZYMES IN SAMPLES FROM CONTROL AND INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS

Parameters tested	Control n=150	Diabetes Mellitus n=150
Fasting Glucose(mg/dL)	76.293±1.078	211.706±3.538*
Catalase(Units/ mg protein/ ml / minute)	0.5127±0.0172	0.4454±0.0156***
CuSOD(Units/ mg protein/ ml / minute)	2.2717±0.199	1.5162±0.0452**
MnSOD(Units/ mg protein/ ml / minute)	1.9879±0.1284	1.5899±0.0617***
GPX(Units/ mg protein/ ml / minute)	0.000733±0.000026	0.000953±0.000038*

Values represent the Mean ± SEM. *P<0.0001,**p<0.001,***p<0.01

CuSOD (Copper containing Superoxide Dismutase), MnSOD (Manganese containing Superoxide Dismutase), GPX (Glutathione Peroxidase)

Concentration of MDA:
The mean level of MDA (nmole / mg protein / ml / minute) for control samples and individuals with type 2 diabetes mellitus was 7.547±0.3075 and 8.971±0.3921 respectively. This result showed that the level of MDA was significantly higher in individuals with type 2 diabetes mellitus as compared to control samples ($p<0.01$) (**Table 2**).

Concentration of non enzymatic antioxidant (GSH) The mean level of GSH (µmole/ mg protein/ ml / minute) for control samples and individuals with type 2 diabetes mellitus was 0.0192±0.00169 and 0.0155±0.00062 respectively. This result showed that the level of GSH was significantly lower in individuals with type 2 diabetes mellitus as compared to control samples ($p<0.05$) (**Table 2**)

No correlation was observed between MDA and GSH (r_s = -0.108, $p> 0.05$) (**Table 4**)

TABLE 2: MEAN LEVELS OF MALONDIALDEHYDE AND REDUCED GLUTATHIONE IN PLASMA SAMPLES FROM CONTROL AND INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS.

Parameters tested	Control n=150	Diabetes Mellitus n=150
MDA (nmoles / mg protein / ml / minute/)	7.547±0.3075	8.971±0.3921*
GSH (µmole/ mg protein/ ml / minute)	0.0192±0.00169	0.0155±0.00062**

The data represent the Mean ± SEM. *p<0.01, **p<0.05
MDA (Malondialdehyde), GSH (Reduced Glutathione)

HDL:
The mean level of HDL (mg /dL) for control samples and individuals with type 2 diabetes mellitus was 41.28±0.79 and 38.60±0.77 respectively. This result showed that the level of HDL was significantly lower in individuals with type 2 diabetes mellitus as compared to control samples ($p<0.05$).

No correlation was observed between MDA and HDL (r_s = -0.0136, $p>0.05$) (**Table 5**).

LDL:

The mean level of LDL (mg /dL) for control samples and individuals with type 2 diabetes mellitus was 136.94±2.48 and 144.14±2.61 respectively. This result showed that the level of LDL was significantly higher in individuals with type 2 diabetes mellitus as compared to control samples ($p<0.05$). No correlation was observed between MDA and LDL ($r_s = 0.0463$, $p>0.05$) (**Table 5**).

TG:

The mean level of TG (mg /dL) for control samples and individuals with type 2 diabetes mellitus was 169.78±1.733 and 174.64±1.084 respectively. This result showed that the level of TG was significantly higher in individuals with type 2 diabetes mellitus as compared to control samples ($p<0.05$). No correlation was observed between MDA and TG ($r_s = -0.0723$, $p>0.05$) (Table 5).

Cholesterol:

The mean level of Cholesterol (mg /dL) for control samples and individuals with type 2 diabetes mellitus was 205.35±2.39 and 213.52±2.33 respectively. This result showed that the level of cholesterol was significantly higher in individuals with type 2 diabetes mellitus as compared to control samples ($p<0.05$). No correlation was observed between MDA and TG ($r_s = 0.0982$, $p>0.05$) (**Table 5**).

TABLE 3: MEAN SERUM LEVELS OF LIPID PROFILE PARAMETERS IN CONTROL AND INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS.

Parameters tested	Control	Diabetes Mellitus
	n=150	n=150
HD (mg/dL)	41.28±0.79	38.60±0.77*
LDL (mg/dL)	136.94±2.48	144.14±2.61*
TG (mg/dL)	169.78±1.733	174.64±1.084*
Cholesterol (mg/dL)	205.35±2.39	213.52±2.33*

The data represent the Mean ± SEM. *p<0.05

HDL (High Density Lipoprotein), LDL (Low Density Lipoprotein), TG (Triglyceride)

TABLE 4: THE CORRELATION COEFFICIENTS BETWEEN THE LEVEL OF MDA AND FASTING GLUCOSE, ENZYMATIC AND NON ENZYMATIC ANTIOXIDANTS IN SAMPLES OF CONTROL AND INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS

Parameters Tested (In diabetes group)	r_s Value (Spearman's rank correlation coefficient)
MDA and Fasting glucose	0.086***
MDA and Catalase	0.368*
MDA and CuSOD	0.363*
MDA and MnSOD	0.370*
MDA and GPX	0.306**
MDA and GSH	-0.108***

The r_s values represent the level of correlations between MDA and different enzymatic and non enzymatic antioxidants. MDA (Malondialdehyde), CuSOD (Copper containing Superoxide Dismutase), MnSOD (Manganese containing Superoxide Dismutase), GPX (Glutathione Peroxidase), GSH (Reduced Glutathione)

*p<0.0001, **p<0.001, ***p>0.05.

TABLE 5: THE CORRELATION COEFFICIENTS BETWEEN MDA AND SERUM LIPID PROFILE PARAMETERS IN CONTROL AND INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS

Parameters Tested (In diabetes group)	r_s Value (Spearman's rank correlation coefficient)
MDA and HDL	-0.0136*
MDA and LDL	0.0463*
MDA and TG	-0.0723*
MDA and Cholesterol	0.0982*

The r_s values represent the level of correlation between MDA and serum lipid profile parameters.

MDA (Malondialdehyde), HDL (High Density Lipoprotein), LDL (Low Density Lipoprotein), TG (Triglyceride). *p>0.05.

DISCUSSION: Mitochondrial abnormalities increase the production of free radicals and reported as a potent culprit for the pathogenesis of maternally inherited type 2 diabetes mellitus [14]. Hitherto, prodigious work on mitochondrial DNA mutations suggested that, mutated mitochondria inherited in the families via mother, meaning, patients with a history of maternal inheritance of type 2 diabetes mellitus are more prone to free radical attack [9, 32, 33]. Furthermore, hyperglycemia in diabetes mellitus could increase free radical concentration, which exerts deleterious effect on cells and organs and result in other serious complications like, cardiovascular diseases, atherosclerosis and aging [34, 35]. In the past few decades, research on diabetes mellitus was strictly focused on insulin related consequences and tended to look at the alterations in the concentration of free radicals and its scavenging system along with the levels of lipid profile parameters [9]. Recently, much prominence has been placed on the correlation studies between enzymatic antioxidants, HbA1c, lipid peroxidation and lipid profile parameters [30]. The present study was undertaken to evaluate the status of oxidative stress and lipid profile parameters including their correlation studies with lipid peroxidation in patients with maternally inherited type 2 diabetes mellitus.

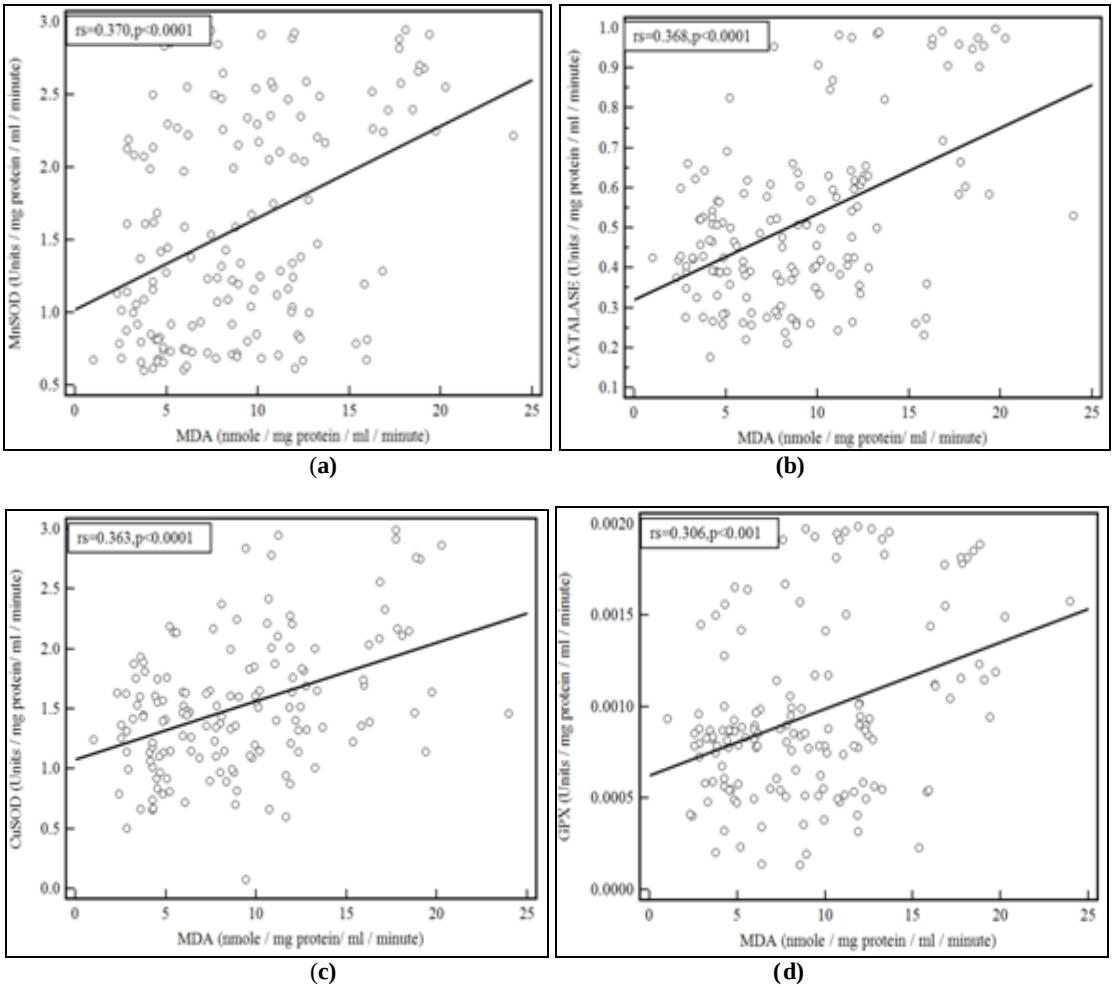

FIG. 1: (a) CORRELATION BETWEEN THE LEVEL OF MDA AND CATALASE IN PLASMA SAMPLES FROM CONTROL AND INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS. (b) CORRELATION BETWEEN THE LEVEL OF MDA AND CuSOD (COPPER CONTAINING SUPEROXIDE DISMUTASE) IN PLASMA SAMPLES FROM CONTROL AND INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS. (c) CORRELATION BETWEEN THE LEVEL OF MDA AND MnSOD (MANGANESE CONTAINING SUPEROXIDE DISMUTASE) IN PLASMA SAMPLES FROM CONTROL AND INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS. (d) CORRELATION BETWEEN THE LEVEL OF MDA AND GPX (GLUTATHIONE PEROXIDASE) IN PLASMA SAMPLES FROM CONTROL AND INDIVIDUALS WITH TYPE 2 DIABETES MELLITUS.

r_s = Correlation Coefficient; p-value represents the significance level.

Catalase is a common enzyme found almost in every living cell and a tetramer of four polypeptide chains; each made from 500 amino acids. The antioxidant action of catalase strictly relies on the four heme groups, which react with hydrogen peroxide; a substrate for catalase [36]. Catalase degraded two molecules of hydrogen peroxide to water and oxygen. However, catalase has been reported with one of the highest turnover number among all antioxidant enzymes [37, 38]. The present study reported, the lower mean activity of catalase in individuals with type 2 diabetes mellitus than control individuals (**Table 1**). In addition to this a significant positive correlation was observed between MDA and catalase (r_s= 0.368, p< 0.0001) (**Table 4, Fig 1a**). Similar results were reported by Manjulata kumawat et al. [39]. The deficient activity of catalase increases the concentration of hydrogen peroxide [40]. Hydrogen peroxide if not removed from the system, is converted to hydroxyl radicals via superoxide catalyzed Haber Weiss reaction [41, 42] and metal catalyzed Fenton reaction [43, 44]. Hydroxyl radicals are potent free radicals to cause oxidative damage at the cellular levels [45]. The decrease activity of catalase is possibly due to high oxidative stress [40, 45].

The Superoxide Dismutase (SOD) is a potent antioxidant enzyme predominantly found in cytosol (SOD1), in the mitochondria (SOD2) and extracellular (SOD3) in humans [46]. As this study strictly cogitated on the maternal inheritance of type 2 diabetes mellitus through mitochondria; it is important to study the activities of SOD in cytosol and mitochondria separately. When, electrons flow through the electron transport chain in mitochondria, some electrons may get leaked through their path in the electron transport chain and generates the superoxide radicals [9, 14]. If superoxide radicals are not removed from the biological system, it can react with the plasma membrane of the cells and initiate the process of lipid peroxidation or can react with nitric oxide to generate peroxinitrate, which is again a potent oxidant [47, 48]. Hence, monitoring the activity of SOD is crucial in patients with maternal history of type 2 diabetes mellitus.

The cytosol of virtually all eukaryotes contain copper containing superoxide dismutase enzyme (SOD1). The present study reported a significant decrease in the mean activity of CuSOD (**Table 1**). A significant positive correlation was also noted between MDA and CuSOD activity (r_s= 0.363, p<0.0001) (**Table 4, Fig. 1b**). The manganese containing superoxide dismutase is predominant in mitochondria and peroxisomes (SOD2). The present study showed a significant decrease in the mean activity of MnSOD (**Table 1**). In addition, a significant positive correlation was noted between MDA and MnSOD (r_s=0.370, p<0.0001) (**Table 4, Fig. 1c**). No prior studies have been cited for the separate estimations of CuSOD and MnSOD in patients with maternal inheritance of type 2 diabetes mellitus. The decrease in the activities of CuSOD and MnSOD possibly due to the high accumulation of hydrogen peroxide and glycation of these enzymes [49, 50].

Glutathione peroxidase is a selenium based antioxidant enzyme; marked for the elimination of hydrogen peroxide via conversion of reduced glutathione to oxidized glutathione [51]. This study showed a significant increase activity of glutathione peroxidase in individuals with type 2 diabetes mellitus than control individuals (**Table 1**). A significant positive correlation was noted between the level of MDA and the mean activity of glutathione peroxidase (r_s=0.306, p<0.001) **(Table 4, Fig 1d**). The present study observed a significant high activity of glutathione peroxidase in individuals with type 2 diabetes mellitus, which is possibly due to the high concentration of hydrogen peroxide [52, 53].

Glutathione is a thiol group containing non enzymatic antioxidant, playing a pivotal role in free radical scavenging mechanism [54]. It could be a marker for diabetes mellitus [55]. Glutathione occurred in both reduced (GSH) and oxidized form (GSSG). The reduction and oxidation of glutathione depend on the disulphide bonds of cysteine amino acids [56, 57]. This study showed a significantly lower concentration of reduced glutathione (**Table 2**). In addition to this, insignificant correlation was observed between the level of MDA and GSH (r_s = -0.108, p>0.05) (**Table 4).** The depleted concentration of GSH is possibly due to the high activity of glutathione peroxidase required to remove accumulated hydrogen peroxide. Moreover, NADPH

(Nicotinamide Adenine Dinucleotide Phosphate), required for the resynthesis of reduced glutathione from oxidized glutathione using glutathione reductase enzyme. NADPH utilization in the polyol pathway during hyperglycemia may lead to a GSH reduction [30, 58].

As quoted earlier, the formation of malondialdehyde by free radicals attacks on polyunsaturated fatty acid of the plasma membrane, represents the status of redox alterations within individuals [17, 18]. Many studies have revealed that lipid peroxidation is responsible for the progression of diabetes mellitus [59, 60]. It could be a marker of DNA damage, protein dysfunction and default cell to cell communication, which originates many serious complications in the patients [59]. In the present study a significant increase in the concentration of malondialdehyde was reported (**Table 2**). Similar findings were reported by Bhatia et.al. [21] and Griesmacher et al. [61] on diabetes mellitus with and without complications.

Alterations in lipid profile parameters accompanied with the pathogenesis of diabetes mellitus [62, 63]. Dyslipidemia associated with insulin resistance in type 2 diabetes mellitus is characterized by the elevated level of triglyceride and the decreased level of high density lipoprotein [63]. Dyslipidemia has been reported for the lipid peroxidation in patients of diabetes mellitus [64]. The present study demonstrated a significantly increased concentration of LDL, cholesterol and TG (**Table 3**) in individuals with type 2 diabetes mellitus than control individuals. Unlike this result, a significant decrease in the concentrations of HDL was reported in individuals with type 2 diabetes mellitus than control individuals (**Table 3**). Furthermore, no correlations were sought between the level of MDA and high density lipoprotein (r_s = -0.0136, p>0.05), low density lipoprotein (0.0463, p>0.05), triglyceride (r_s = -0.0723, p>0.05) and cholesterol (r_s = 0.0982, p>0.05) (**Table 5**).

HDL is known to be good cholesterol and essential for certain biochemical functions in the body. While, hyperglycemia leads to the glycation of LDL and make it more susceptible to oxidation, which increases its atherogenicity; hence LDL is called as bad cholesterol [65]. An imbalance between the levels of HDL and LDL ratio enhances the risk of cardiovascular disease in patients [66]. In diabetes mellitus, the decrease level of HDL is possibly due to impaired function of lipoprotein A1 [67].

CONCLUSION: The present study demonstrates oxidative stress and dyslipidemia in the patients having a history of maternal inheritance of type 2 diabetes mellitus. Lipid peroxidation shows significant correlation with enzymatic antioxidants and non significant correlations with lipid profile parameters. This is possibly because of the defective mitochondria. High oxidative stress due to defects in mitochondria may increase the level of lipid peroxidation in families. Hence, lipid peroxidation may be a useful marker for oxidative stress, which may help in early diagnosis and prognosis of secondary complications in maternally inherited type 2 diabetes mellitus. Further, new drug discoveries are essential to halt the insulin resistance, created via mitochondrial abnormalities. However, large cohort and meta-analysis studies on different populations are required to know more about the pathogenesis of maternal inheritance of type 2 diabetes mellitus.

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