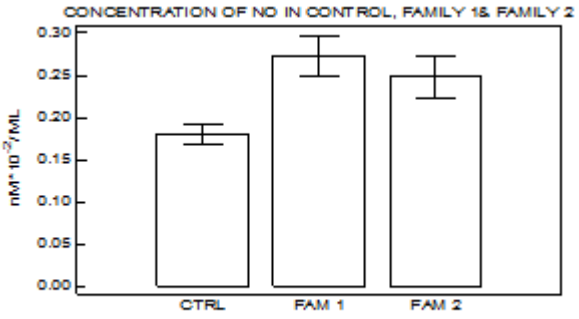

(E)

Figure 2: The activity of various antioxidant enzymes, including catalase represented by a graph (A), the Mn/FeSOD and Cu/Zn SOD represented by (B) and (C) respectively; similarly the concentration TBARS shown by (D) and the concentration of Nitric Oxide shown by (E) in normal control subjects and in patients with diabetes of family 1 and family 2.

We evaluated the levels of antioxidant enzymes in maternally inherited type 2 diabetes mellitus and in a healthy control subjects. The results of this study, clearly corroborates the oxidative stress in both family 1 and family 2. Catalase is the important antioxidant enzyme found nearly in all cells [40] which converts hydrogen peroxide into water molecule and oxygen [41]. Hydrogen peroxide if not removed from the biological samples it may convert into hydroxyl radicals, which may impart more oxidative stress. Hydroxyl radicals are the potent free radical, which is reported as the deadliest free radical which has ever been found. Hence catalase plays an important role in free radical scavenging [42]. Statistical analysis affirms that not only in family 1 but also in family 2 there is a significant decrease in the activity of catalase enzyme in both the diabetic families. This is in accordance with various other studies [43,44]

Like the catalase enzyme, Manganese/ Iron Superoxide Dismutase and Copper/ Zinc containing Superoxide Dismutase also plays a central role in the defence mechanism against the free radicals damage [45]. The main function of the Superoxide Dismutase enzyme is to eradicate superoxide anion which can cause damage to cells, cellular membranes, DNA and other biological organelles. Superoxide Dismutase converts superoxide anion radical into the hydrogen peroxide molecule [46,47]. Many studies showed that there is decreased activity of Mn/Fe SOD and Cu/Zn SOD in type 2 diabetes mellitus than normal control samples [48]. This study also shows a significant decrease in the activity of Mn/Fe SOD and Cu/Zn SOD in patients with type 2 diabetes.

Malonaldehyde formation is an indication of increased lipid peroxidation in diabetes mellitus [49]. It is used to determine the oxidative stress through determining the balance between free radicals and antioxidant enzymes [50]. We analysed the significant increase in the concentration of malonaldehyde in both diabetic families. The increased concentration of malonaldehyde indicates an oxidative stress in patients with diabetes. Various other studies showed an increase in oxidative stress in diabetes mellitus [43,51,52].

Statistics showed somewhat similar results for the concentration of nitric oxide to those of malonaldehyde. Nitric oxide may react with superoxide anion and can form peroxinitrite molecules, which can harm cellular mechanism. Hence, it is very essential to maintain the concentrations of free radicals like nitric oxide and superoxide radicals [53]. Although, the life span of nitric oxide is very less, increased concentration can induce an oxidative stress and may play a pivotal role in diabetes mellitus [54]. The present study, exhibited significant increase in the concentration of nitric oxide in both the families of diabetic patients. Certain other studies have also demonstrated an increase concentration of nitric oxide in patients with diabetes than control [55,56].

Table 2 : A Statistical analysis of various antioxidant enzymes, lipid peroxidation and nitric oxide.

ENZYMES	*GROUPS*	*MEAN±SD*	*P-VALUE*
CATALASE	CONTROL	0.3659±0.0931	
(Units/Mg protein/ML)	FAMILY1	0.1805±0.0752	<0.01
	FAMILY2	0.2160±0.0400	<0.01
Mn/Fe SOD	CONTROL	0.0376±0.0074	
(Units/Mg protein/ML)	FAMILY1	0.0244±0.0064	<0.01
	FAMILY2	0.0215±0.0115	<0.05
Cu/Zn SOD	CONTROL	0.1325±0.0308	
(Units/Mg protein/ML)	FAMILY1	0.0379±0.0203	<0.001
	FAMILY2	0.0532±0.0305	<0.01
MDA	CONTROL	0.2048±0.1247	
($nM \times 10^{-3}$ / ML)	FAMILY1	0.4487±0.1656	<0.05
	FAMILY2	0.3767±0.1022	<0.05
NO	CONTROL	0.1800±0.0303	
($nM \times 10^{-2}$ / ML)	FAMILY1	0.2483±0.0611	<0.05
	FAMILY2	0.2733±0.0592	<0.05

Mitochondrial DNA lacks histone proteins and DNA repair mechanisms, which increases the chances of its damage by free radicals [57]. Colossal work on mitochondrial DNA exhibited its role in maternally inherited type 2 diabetes mellitus [21,22,23]. For last few decades, researchers have been working on mitochondrial DNA to identify the various mitochondrial DNA mutations, which can play a pivotal role in the pathogenesis of type 2 diabetes mellitus. Over more than 40 different mitochondrial DNA mutations associated with type 2 Diabetes Mellitus have been identified yet [58]. In this study, the absence of 3243 A/G mutation has been observed in the selected families (Fig: 2), this was according to the study of Naveed AK et.al. [59].

5. Conclusion

This study cogitated on oxidative stress and 3243 A/G mitochondrial DNA mutation in two families with a history of maternally inherited type 2 diabetes mellitus. Decrease activities of various antioxidant enzymes like catalase, Mn/Fe SOD, Cu/Zn SOD with increase concentration of nitric oxide and lipid peroxidation providing a straight forward evidence of oxidative stress in both diabetic families. Increased oxidative stress can cause other complications like DNA and cellular damage in the patients. Therefore, monitoring oxidative stress in patients with maternally inherited type 2 diabetes mellitus could be of utmost importance to prevent these complications. The undertaken study did not observe a 3243A/G mutation in patients with a history of maternally inherited type 2 diabetes mellitus, other mutations meight be present in selected families.

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