



Inflammation and oxidative stress in first degree relatives of type 2 diabetics

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ABSTRACT

Indians are more susceptible to diabetes mellitus (DM) because of genetic reasons & improper life-style habits. Currently, the occurrence of DM has been prevalent in youngsters especially in India, in our present study, we attempted to explore the role of oxidative stress, inflammation in first degree relatives of type 2 diabetes mellitus (FDRDM). Inflammation was assessed by using high sensitive C reactive protein (hsCRP), Interleukin 6 (IL6), Tumor necrosis factor-alpha (TNF alpha), and oxidative stress by using malondialdehyde and total antioxidant status. FDRDM and control groups had similar for age, height, and waist-hip ratio (WHR). Weight and body mass index (BMI) was significantly high in FDRDM. Total antioxidant levels (TAOS) were less, and malondialdehyde (MDA) was significantly more in the FDRDM group. Inflammatory markers were significantly high in FDRDM. We conclude that increased oxidative stress and inflammation may lead to more derangements in glucose homeostasis in first degree relatives of type 2 diabetes (T2DM), it could increase the chances of development of cardiac events and necessitates early lifestyle modifications.



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diabetes in India (Paul *et al.*, 2012). The manifestations of diabetes in Indians are faster than western people (Ramachandran *et al.*, 1988). Indians are more susceptible to DM because of genetic reasons and improper life-style. Currently, the prevalence of DM is very high among youngsters, especially in India, due to the innate nature of DM. In addition to that, FDRDM tends to have a similar cultural, social, and economic background that is reported to increase the risk of development of T2DM in those who already had genetic exposure.

INTRODUCTION

The incidence of diabetes and prediabetes is increasing worldwide. Experts projected that by 2030, the numbers might reach 470 million (Anjana *et al.*, 2011). In 2011, the Indian Medical Association estimated that 62.4 million people are living with

A genetic component has a crucial role in T2DM. The risk of development of T2DM in children with no parents with DM and DM parents was 14% and 29.2 %, respectively (Weijnen *et al.*, 2002). The fundamental trait and primary pathogenesis is insulin resistance (Reaven, 1988). Subsequently, FDRDM shows insulin resistance even before the development of DM. Non-diabetic FDRDM has a

higher incidence of obesity, insulin resistance (IR), and higher cardiac and vascular risk (Martín-Timón *et al.*, 2014). Earlier studies have demonstrated that inflammation plays an essential role in a pathological role in the development of IR and T2DM. However, inflammation has an essential role in the development of IR, or an epiphenomenon of obesity itself is still unclear (Haffner, 2003). Earlier studies had reported the role of family history of DM, which can cause a more significant risk of development of coronary heart disease (CHD), even in the nondiabetic population (Eschwege *et al.*, 1985).

The higher levels of free-radicals may lead to the initiation of stress signaling pathways which in turn drains enzymatic, nonenzymatic antioxidants, causing a deteriorative role on the quality of life (QOL) of the individual, plays a crucial role in several diseased conditions like DM (Figueroa-Romero *et al.*, 2008). Other mechanisms lead to increased levels of oxidative stress because of increased blood glucose levels in diabetic patients. Few of them are “glucose auto-oxidation, high glucose flux through the polyol pathway, non-enzymatic and progressive glycation of proteins and the formation of advanced glycosylation end products” (AGEs) (Bolajoko *et al.*, 2008).

However, the data regarding the importance of oxidative stress and inflammatory markers in FDRDM is less. Hence, we attempted to explore the role of oxidative stress and inflammation in FDRDM.

MATERIALS AND METHODS

Ethics clearance was obtained, and informed written consent was taken from all the participants. The site of conduct of experiments was the Department of Physiology's research laboratory, F.H. Medical College, Agra, India.

Subjects

Individuals of the FDRDM group (n = 37) were recruited in the age group of 18 – 30 years, from the individuals attending F.H. Medical College and Hospital, Agra, India Hospital, along with D.M. patients. We had excluded the individuals if they are on medication for any health-related illness, any condition which prevents participating moderate form of physical activity, subjects if they are doing routine physical activity like exercise, yoga, meditation, and any other biofeedback practices. The control group (n=37) were people without a family history of D.M., and young age and gender-matched individuals.

They were instructed to have adequate rest one day before testing and not to do heavy exercise, not to take coffee, or any other beverages, alcohol, and nicotine products one day before the examination.

After overnight fasting, they have attended the laboratory (Sacks *et al.*, 2011). A blood sample was taken from median cubital vein sodium fluoride containers soon after coming to the laboratory.

Recording of anthropometric and basal parameters

After they emptied the bladder, participants' height, weight was measured, and Body mass index (BMI) was calculated. Waist Hip circumference was measured as an index of abdominal fat proportion.

Blood collection and storage

Blood was collected through vein puncture, and allowed to clot and centrifuge at 3,000 RPM at 4° C for 10 min (Remi - refrigerated centrifuge) from which the serum was separated and stored in a frozen state at – 80 °C for analysis.

Measurement of inflammatory markers and oxidative stress markers

Was carried out by commercially available kits.

RESULTS AND DISCUSSION

Table 1. Shows the comparison between baseline parameters. Controls and FDRDM No significant difference was found between controls and the FDRDM group. FDRDM group showed significantly higher weight & BMI. As shown in Table 2, Total antioxidant levels were less, and malondialdehyde was significantly more in FDRDM. Inflammatory markers like TNF alpha, IL6, and hs CRP were depicted in Table 3. These inflammatory markers were significantly high in FDRDM in comparison to age and gender-matched controls.

The primary objective of our study was to explore the role of inflammation and oxidative stress in FDRDM. While controls and FDRDM, both groups were age, WHR, and eight, FDRDM subjects had significantly higher weight and BMI. In this study, we found, Total antioxidant levels were less, and malondialdehyde was significantly more in FDRDM.

These higher levels of MDA in the FDRDM group could be due to the elevated generation of lipid peroxides, its entry into the circulation, and these results are consistent with earlier reports (Rani and Mythili, 2014; Ganjifrockwala *et al.*, 2017).

A significantly reduced total antioxidant levels in FDRDM in the present study and has also been reported by other authors (Eldin *et al.*, 2014). This reduced TAOS levels could be attributed to increased oxidative stress. This is evidenced by higher levels of lipid peroxidation as well as by the higher utilization of antioxidants against oxidative stress to minimize the damage.

Table 1: Demographic profile of controls and FDRDM

| Sl.No | Parameter | Mean + SD | | P value |
|-------|--------------------------|----------------|----------------|---------|
| | | Controls | Cases (FDRDM) | |
| 1 | Age (years) | 20.64 + 1.96 | 20.67 + 1.78 | 0.951 |
| 2 | Height (cms) | 167.32 + 8.44 | 163.08 + 10.50 | 0.060 |
| 3 | Weight (kg) | 58.91 + 9.98 | 67.51 + 12.45 | 0.002 |
| 4 | BMI (kg/m ²) | 21.0189 + 2.38 | 25.9649 + 4.40 | 0.000 |
| 5 | WHR | 0.8186 + 0.07 | 0.84 + 0.04 | 0.77 |

Table 2: Oxidative stress markers of controls and FDRDM

| Sl.No | Parameter | Mean + SD | | P-value |
|-------|-----------|-------------|-------------|---------|
| | | Controls | Cases | |
| 1 | TAOS (mM) | 1.36 + 0.38 | 0.64 + .43 | 0.000 |
| 2 | MDA (mM) | 6.09 + 1.05 | 9.03 + 8.55 | 0.042 |

Table 3: Inflammatory markers of controls and FDRDM

| Sl.No | Parameter | Mean + SD | | P value |
|-------|-------------------|------------------|-------------------|---------|
| | | Controls | Cases | |
| 1 | TNF alpha (pg/ml) | 138.15 + 56.25 | 254.10 + 65.75 | 0.000 |
| 2 | IL 6 (pg/ml) | 4.80 + 1.05 | 13.0078 + 0.85 | 0.000 |
| 3 | Hs CRP (ng/ml) | 2941.96 + 498.44 | 9634.11 + 6093.20 | 0.000 |

In this study, we have observed that inflammatory markers were significantly high in FDRDM in comparison to age and gender-matched controls.

Increased inflammatory cytokines were shown to interfere with insulin signaling (insulin resistance) or beta-cell destruction, causing hyperglycemia (Dandona *et al.*, 2004), which in turn could raise oxidative stress and lead to the vicious cycle.

CONCLUSIONS

Based on the results of our study, we conclude that higher levels of oxidative stress and inflammation may lead to more derangements in glucose homeostasis in FDRDM, and it increases the risk of development of cardiovascular disease and necessitates early lifestyle modifications.

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