Original Article

Evaluation of the Role of Oxidative Stress and Inflammation in the Causation of Type II Diabetes Mellitus in Human Subjects

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ABSTRACT

OBJECTIVE: To inspect the impact of oxidative stress and inflammation on the causation of type 2 diabetes mellitus in human subjects.

METHODOLOGY: A Case - control study on 200 randomly enrolled subjects (age range 20-40 years), including 100 T2 DM patients (56 males and 44 females) and 100 healthy controls (60 males and 40 females) matched for socioeconomic status were randomly enrolled from and were inhabitants of Hyderabad and Jamshoro districts of Sindh province, this research was conducted at postgraduate research laboratory of Institute of Biochemistry, University of Sindh Jamshoro from January-December 2019. Serum samples of the subjects were analyzed by kit methods for the amounts of creatinine, uric acid, total antioxidants, iron, C-reactive protein, superoxide dismutase, catalase, glutathione peroxidase, xanthine oxidase, lactate dehydrogenase, malondialdehyde and nuclear factor kappa- B. Urine samples collected on spot were investigated for pH and protein content by using urine dip strip automatic reader "Urisys 1100* Roche".

RESULTS: Physical measurements disclosed that obesity was more common in diabetic patients (26%) than in controls (10%). Serum analysis results showed that T2 DM patients as against the controls had significantly raised superoxide dismutase ($p<0.01$) and C-reactive protein ($p<0.005$); and decreased uric acid ($p<0.006$), iron ($p<0.01$) and xanthine oxidase ($p<0.04$) levels. Spot urine analysis results showed that controls compared to T2 DM patients excreted significantly ($p<0.003$) more acidic urine.

CONCLUSION: From the results of this study, we concluded that oxidative stress together with low grade inflammation plays an important role in the causation of T2 DM.

KEYWORDS: Diabetes Mellitus, Antioxidants, Inflammation, Oxidative Stress

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INTRODUCTION

Diabetes mellitus (DM) in adult people is a global chronic health issue that is developed when the pancreas fails to form sufficient insulin or when the insulin produced by the pancreas cannot be effectively used to maintain the normal blood glucose level. This ultimately leads to hyperglycaemia- an important feature of diabetes mellitus[1]. Uncontrolled diabetes mellitus is known to cause various micro vascular and macro vascular complications[2]. Type 2 diabetes mellitus (T2 DM) was cause of about five million deaths in 2015. International Diabetic Federation (IDF) report of 2017, shows that about 451 million people are victim of DM globally and by year 2045, this figure is expected to reach 693 million[3].

The occurrence of DM has increased globally. Previously T2 DM was reported in adults only, but now it is frequently reported in youths and children as well[4]. The overall incidence of DM reported for Pakistan is 11.77%. Diabetes Mellitus type 2 is more common: in males (11.20%) compared to females (9.19%); in urbanized areas than in rural areas (10.34%) [5]. Pakistan is one of the lowest per capita income bearing country in South Asia where the frequency and commonness of diabetes mellitus is continuously rising and will cause major challenges in future if not be reversed. Thus, elucidation of the underlying cause for increase in the prevalence of T2 DM is very much required for the development of new therapeutic options. In this context, it is hypothesized that oxidative stress (developed due to any reason) and inflammation could be the possible factors involved in the causation of T2 DM in human subjects.

MEDHODLOLOGY

A Case - control study on 200 randomly enrolled subjects (age range 20-40 years), including 100 T2 DM patients (56 males and 44 females) and 100 healthy controls (60 males and 40 females) matched for socioeconomic status were randomly enrolled from Hyderabad and Jamshoro districts of Sindh province was conducted, the reported research has been carried out in the postgraduate research laboratory of Institute of Biochemistry, University of Sindh Jamshoro from January-December 2019. Of these subjects, none was on any dietary supplements in addition to being non-smokers and non-alcoholics. They also had no related disorders such as, endocrine disorders, urinary tract infections and inflammatory diseases. Before getting written informed consent

from the participants to voluntarily participate, all of them were explained the nature and purpose of this study and of possible harms and benefits of the study. Bioethical Committee of the University of Sindh Jamshoro provided the ethical approval of the study.

Body mass index (BMI) of each study subject was determined by dividing his/her weight in kg with square of tallness in centimeters.

Serum creatinine, uric acid, CRP, LDH and iron levels were determined by using commercial kits supplied by Roche on Cobas 4000 c311 Analyzer.

Serum MDA, SOD, GPx, XO and total antioxidants were determined by using commercial ELISA Kits supplied by Korean Biotech Company on Elisa Reader DIA Source Belgium Analyzer.

Spot urine specimens were analyzed for acid and protein content by using urine dip strip automatic reader "Urisys 1100* Roche".

Statistical analysis of the data gathered was carried out by using SPSS version 22.0. The results obtained are presented as mean ± S.D. Student's independent samples t-test has been applied to detect any significant differences ($p < 0.05$) in the mean values of the parameters measured between T2 DM patients and control subjects.

RESULTS

BMI results (Table I) revealed that T2 DM patients were more obese (26%) than the control subjects (10%). Serum analysis results (Table II) show that DM patients as against the controls had significantly raised SOD ($p<0.0128$), CRP ($p<0.032$), and decreased uric acid ($p<0.0067$), iron ($p<0.0147$), XO ($p<0.0360$) levels. Comparison of urine parameters between DM patients and controls (Table III) disclosed that the urine of controls was significantly ($p<0.003$) more acidic than the urine of DM patients.

TABLE I:
BODY MASS INDEX OF RECRUITED SUBJECTS

BMI Kg/m^2	Body Status	Controls %	T2 DM patients %
18.5-24.9	Normal weight	65	56
25-29.9	Overweight	25	18
≥30	Obese	10	26

TABLE II: COMPARISON OF SERUM PARAMETERS BETWEEN CONTROLS AND T2 DM PATIENTS

Serum parameter	Controls (n=100)	T2 DM patients (n=100)	p- value
	Mean ± SD	Mean ± SD	DM vs Controls
Creatinine (mg/dL)	0.61±0.15	0.70±0.50	0.2669
Uric acid (mg/dL)	6.13±5.98	4.30±2.04*	0.0067
Total antioxidants (U/ml)	0.52±0.20	0.51±0.21	0.8411
Iron (µg/dL)	87.48±34.00	74.80±27.09*	0.0147
CRP(mg/dL)	0.10±0.05	0.13±0.06*	0.032
MDA (nmol/ml)	0.55±0.20	0.56±0.17	0.8778
NF-KB (ng/ml)	1.24±0.44	1.37±0.40	0.0818
SOD (U/L)	1.19±0.19	1.30±0.26*	0.0128
Catalase (KU/L)	0.79±0.42	0.70±0.52	0.2518
LDH (U/L)	164.8±40.37	171.86±62.28	0.4687
XO (ng/ml)	1.03±0.41	0.86±0.47*	0.0360
GPX (mg/dL)	0.75±0.25	0.72±0.18	0.482

TABLE III: COMPARISON OF URINE PARAMETERS BETWEEN CONTROLS AND T2 DM PATIENTS

Urine parameter	Controls (n=100)	T2 DM patients (n=100)	p- value
	Mean ± SD	Mean ± SD	DM vs Controls
pH	5.82±0.72	6.29±0.72	0.0003
Protein (g/L)	0.25±0.08	0.32±0.18	0.1838

DISCUSSION

Mankind has suffered a lot owing to diabetes mellitus-connected complications. In developing countries, it is considered as a calamity to the patients and burden to their families and the society. Our result that obesity is more common in DM patients than in controls confirms the reports of previous investigators who proposed that obesity is the key culprit involved in the causation of DM[6,7]. Diet[8] and sedentary lifestyles[9] have been associated with an increase in the incidence of obesity among children and youths. Consumption of increased amounts of red meat, sweets and fried food has been implicated with the higher risk of development of insulin resistance and T2 DM, while frequent intake of vegetables and fruits has been shown to reduce the incidence of DM[8].

Physical inactivity has been linked to increased risk of developing T2 DM [9] as it diminishes insulin sensitivity and enhances insulin resistance. This along with disorders in glucose & fatty acid metabolism are now considered as foremost initiators of DM[10]. This has been suggested because abnormal glucose and fatty acids metabolisms could result in generation of reactive oxygen species capable of: damaging cellular organelles and enzymes, increased lipid peroxidation, development of insulin resistance. Significantly raised serum SOD (cause of oxidative stress) and CRP (marker of low- grade inflammation) levels detected in DM patients as against the controls indicates that oxidative stress creates sub-clinical inflammation that leads to insulin resistance and hence to development and advancement of T2 DM[11].

We observed significantly low levels of serum uric acid

($p<0.0067$) in DM patients compared to control subjects. Our finding is in accord with many other investigators[12-14]. The decreased serum uric acid level in DM patients could be because of increased urate excretion[14].

We found significantly reduced serum iron levels in DM patients than in controls. This result is in contrast to recent report[15].

CONCLUSION

From the results of this study, we concluded that oxidative stress together with low grade inflammation plays an important role in the causation of T2 DM.

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AUTHOR CONTRIBUTIONS

Khand TU: Literature search, data collection and statistical analysis of the data.

Chana NA: Study design, write up of the research article.

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