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ORIGINAL ARTICLE

Rheumatoid Factor in Type 2 Male Diabetes Mellitus Patients in a Tertiary Care Hospital of Bangladesh

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Abstract

Background: Type 2 diabetes mellitus is a chronic disease characterized by relative or absolute deficiency of insulin, resulting in glucose intolerance. O**bjectives**: The present study was planned to see the associations of serum uric acid with positive Rheumatoid factor in type 2 male diabetes mellitus patients**. Methodology**: This case control study was carried out at the department of Biochemistry at Ibrahim Medical College, Dhaka, Bangladesh. The duration of the study was from June 2015 to June 2016 for a period of one year. In this present study, male patients with type 2 diabetes mellitus were taken as case group and age and sex matched healthy male were taken as control group. Rheumatoid factor was measured from the blood of all case and control group respondents. Others blood para meters were also measured for the correlation with the diabetes mellitus patients. R**esults**: In this present study, 110 male patients presented with type 2 diabetes mellitus were recruited as case and age and sex matched healthy male were recruited as control. More rheumatoid factor positive in type 2 DM male patients with the uric acid range between 6.5 to 9.5 mg/dL. The number of patients was 5 out of total 9 rheumatoid factor positive cases. In this study serum uric acid was significantly correlated with rheumatoid factor in type 2 male diabetic patients**.** Rheumatoid factor positive cases were taking insulin among 9 and it was statistically significantly associated ($p<0.001$)**. Conclusion**: In this study serum uric acid is significantly associated with positive rheumatoid factor in type 2 male diabetic patients. [*Journal of Current and Advance Medical Research 2017;4(2):58-62*]

Keywords: Rheumatoid factor; type 2; male; diabetes mellitus

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Introduction

Rheumatoid arthritis (RA) is a systemic, autoimmune disorder that primarily manifests as chronic synovial inflammation of multiple joints. Over the last few decades it has become increasingly apparent that chronic activation of the immune system, as observed in the pathogenesis of RA, is associated with corollary changes in intermediary metabolism, potentially leading to increased risk of cardiovascular disease (CVD)[1-2]. Several reports have discussed the association between chronic inflammatory disease states and disorders in intermediary metabolism[3–7], particularly peripheral insulin resistance (IR). In addition, numerous independent studies have implicated the association of multiple immune regulatory components (including tumor necrosis factor [TNF] and interleukin-6 [IL-6]) in RA, IR, and type 2 diabetes mellitus (DM)[6,8-11].

Disease-associated reduction in lean muscle mass and sedentary lifestyle likely further contributes to IR in patients with RA[12]. Although the prevalence of type 2 DM might be expected to be increased among patients with RA, large cross-sectional studies have not definitively established an association between these two conditions. As because type 2 DM and IR are important risk factors for CVD, common co-morbidity in patients with RA[1-2], a review of the literature to examine factors associated with glucose regulation and type 2 DM in RA patients is warranted. Diabetic individuals maintained on insulin therapy are perforce subjected to repeated immunization by a foreign protein. Production of anti-insulin-antibodies by many such individuals appears likely[5].

In view of the findings cited above, as well as the possibility that circulating antigen-antibody complexes may also stimulate RF production, it has been considered that individuals receiving injections of exogenous insulin might exhibit an increased frequency of RF activity as compared to control groups. Formation of RF-like antibodies has been noted in rabbits after hyper-immunization with bacterial antigen[1] or ovalbumin[2]. Therefore, the present study was undertaken to see the associations of serum uric acid with positive rheumatoid factor in type 2 male diabetes mellitus patients**.**

Methodology

The present study was carried out at the department of Biochemistry, Ibrahim Medical College (IMC), Dhaka, Bangladesh. The duration of the study was from June 2015 to June 2016. Type 2 male diabetes mellitus patients were taken as cases and healthy male were included as control. The patients were selected from OPD of Bangladesh Institute of Research and Rehabilitation for Diabetes, Endocrine and Metabolic Disorders, (BIRDEM), Dhaka, Bangladesh. The controls were selected from the healthy male workers of BIRDEM and IMC. Subjects who had not willing to participate and patients associated with infections, arthritis, cardiac and renal failures were excluded from the present study. Subjects with a current or previous history of rheumatoid arthritis or other diseases known to be associated with a significant frequency of RF activity were excluded. A detailed patient information was filled in proforma contains patients name, age, sex, diet (fast food habit), clinical history and family history of diabetes. All the patients of case and control groups were asked to attend in the OPD of BIRDEM with overnight fasting. Blood pressure and height, weight, body mass index, waist and hip circumference were measured.

Two ml blood sample was collected in fluoride vaccutainer for estimation of fasting blood sugar and 4 ml blood was collected in plain vaccutainer for estimation of serum uric acid and serum lipid profile. Two hours after breakfast blood was collected for estimation of blood sugar from all type 2 male diabetes mellitus patients and healthy male control. Estimation was done by Tulip corolyzer fully autoanalyzer (ACON- USA) for uric acid and lipid profile estimation. Positive sera were taken as those exhibiting a 1+ or higher degree of agglutination in the SLT and a titre of 1:20 or more in the TSC test. Sera examined with the TSC test were first adsorbed overnight with an equal volume of packed washed tanned un-sensitized sheep cells to remove heterophil activity.

Serological results were grouped in two categories like those from patients who had received multiple injections of insulin; those from patients who had neverreceived insulin and who were instead maintained on dietary or oral hypoglycemic drugs.

Student ‘t’ test has been used to find the significance of study parameters on continuous scale between two groups and Chi-square test has been used to analyze the data having ordinal variables. Significant figures were analyzed. The statistical software namely EPI Info 7.0 and Vassar stats (www.vassarstats.net) were used for the analysis of the data. A p value of <0.05 was considered as significant.

Results

Total one hundred ten (110) of type 2 male diabetes mellitus patients as cases and one hundred (100) healthy male controls were included in this study. Table 1 showed the distributions of study population according to age. The 41 to 50 years of study subjects were more in case group (39) whereas in control it was 30 to 40 years of study subjects (40).

Table 1: Distributions of Study Population According to Age

Age Group	Group		Total
	Case	Control	
30 to 40 Years	16	40	56
41 to 50 Years	39	33	72
51 to 60 Years	36	21	57
61 to 70 Years	19	6	25
Total	**110**	**100**	**210**

Table 2: Comparison of Different Characteristics and Biochemical Parameters of Study Subjects

Variables	Case	Control	P value
Age(years)	51.83 ±9.911	44.81 ±9.66	0.0001
Duration of diabetes (years)	6.87 ±5.54	00	0.0001
Body mass index (kg/m2)	25.43 ±3.19	24.96 ±3.02	0.274
Exercise time (hours)	1.94 ± .831	1.12 ±.327	0.0001
Waist circumference(cm)	94 ±7.06	90.95 ±9.51	0.010
Hip circumference (cm)	102 ±6.19	98.48 ±8.24	0.104
Waist: Hip	0.92 ±.03	0.91±.03	0.035
Systolic BP (mm of Hg)	128 ±16.75	122 ±11.28	0.002
Diastolic BP (mm of Hg)	85 ±8.41	81 ±6.18	0.000
Fasting blood sugar (mmol/L)	8.19 ±2.48	7.31 ±3.13	0.025
2hours ABF (mmol/L)	11.29 ±3.47	10.19 ±3.95	0.033
HBA_1C (mg%)	7.96 ±6.04	7.93 ±2.01	0.026
TG (mg%)	189.72±111.36	200 ±104.49	0.468
Cholesterol (mg%)	179 ±43	183 ±42.25	0.495
HDL-C (mg%)	38.38 ±13.77	38.14 ±5.52	0.870
LDL-C (mg%)	102.10 ±35.79	110 ±33.23	0.088
Uric acid (mg%)	8.39 ±2.61	5.14 ±.84	0.0001

P value <0.05 is statistically significant

Table 2 showed comparison of base line characteristics of study subjects. There were significant differences in mean of age, duration of DM, exercise time, waist hip ratio, systolic blood pressure and diastolic blood pressure within case and control but no significant differences of mean BMI was found between case and control. The mean age, duration of DM, exercise time, waist hip ratio, systolic blood pressure and diastolic blood pressure and BMI were 51.83 ±9.911 years, 6.87 ±5.54 years, 1.94 ± .831 hours, .92 ±.03, 128 ±16.75mm of Hg, 85 ±8.41 mm of Hg and 25.43 ±3.19 Kg/m^2 respectively whereas in controls these were (44.81 ±9.66 yrs, 00 years, 1.12 ±.327 hours, 0.91±.03, 122 ±11.28 mm of Hg, 81±6.18 mm of Hg and 24.96±3.02 Kg/m^2 respectively. Significant differences were found in mean of FBS, ABF, HbA1C and S. Uric acid between case and control, but there were no significant differences of mean TG, Cholesterol, HDL and LDL. The mean of FBS, ABF, HbA1C and S. Uric acid among the cases were 8.19 ±2.48 mmol/L, 11.29 ±3.47 mmol/L, 7.96 ±6.04 mg%, 189.72 ±111.36 mg/dl, 179 ±43 mg/dl, 38.38 ±13.77 mg/dl, 102.10 ±35.79 mg/dl and 8.39 ±2.61 mg/dl respectively, on the other hand among the control these were 5.91 ±1.13 mmol/L, 9.19 ±1.95 mmol/L, 5.93 ± 1.01mg%, 200 ±104.49 mg/dl, 183 ±42.25 mg/dl, 38.14 ±5.52 mg/dl, 110 ±33.23 mg/dl and 5.14 ±.84 mg/dl respectively. Rheumatoid factor was positive in 9 study subjects among the case group and in control group it was 0 (Table 3).

Table 3: Distribution of Rheumatoid factor in the study population

Rheumatoid Factor	Case	Control	Total
Positive	9	0	9
Negative	101	100	201
Total	110	100	210

This table 4 showed the distribution of uric acid category and rheumatoid factor in overall study population.This table also showed that more Rheumatoid factor positive in type 2 male DM with

the uric acid range between 6.5 to 9.5 mg/dL and that number of patients was 5 out of total 9 Rheumatoid factor positive cases. The Chi-Square tests between uric category and rheumatoid factor cross-tabulation (overall) study population and showed the significant correlation between uric category and positive rheumatoid factor.

Table 4: Distribution of Uric Acid Category and Rheumatoid Factor in Overall Study Population

Uric Acid (mg/dL)	Rheumatoid Factor		Total
	Positive	Negative	
3.5 to 6.4	1	121	122
6.5 to 9.4	5	49	54
9.5 to 12.4	2	24	26
>12.5	1	7	8
Total	**9**	**201**	**210**

P value=0.031

Table 6 shows the distribution of rheumatoid factor and drugs of diabetes and their association and it shows that 5 rheumatoid factor positive cases are taking insulin among 9 of that positive cases and shows the association between them it was statistically significantly associated.

Table 5: Distribution of Rheumatoid Factor and Drugs of Diabetes and their Association

Drugs of Diabetes	Rheumatoid Factor		Total
	Positive	Negative	
Diet Control	0	104	104
Oral hypoglycemic	4	60	64
Insulin	5	26	31
Insulin & Tablet	0	11	11
Total	**9**	**201**	210

P value <0.05 is statistically significant; p value=0.001

Discussion

Previous studies based on healthcare utilization data have reported an increased risk of type 2 diabetes in patients with RA[1-2]. In contrast, this study showed that male patients with type 2 diabetes were associated with a significantly increased risk for incident RA. The increased risk of type 2 diabetes in patients with RA was proposed to be due to the long-term use of steroids during RA treatment[3]. Nevertheless, a Canadian study was using a population-based health insurance database and have been demonstrated a similar risk of incident type 2 diabetes in patients with RA with or without adjusting for the use of oral or topical glucocorticoids[4]. Conversely, decreased insulin sensitivity was reported in patients with RA upon long-term exposure to steroids[5]. Thus, the role of long-term steroid use among patients with RA in the development of type 2 diabetes still requires further investigation. Furthermore, lifestyle changes after diagnosis of rheumatoid arthritis[6] might also contribute to an increase in the risk of developing type 2 diabetes.

One health insurance database study performed in the United Kingdom concluded that the observed association between patients with RA (rheumatoid arthritis) and incident type 2 diabetes could substantially explained by obesity and lifestyle factors[7-8].

The findings of the present study also showed that between uric category and rheumatoid factor category and cross tabulation study population was done and showed the significant correlation between uric category and rheumatoid factor positive cases. This result is inconsistent with the preceding study. Furthermore, in patients with inflammatory polyarthritis, insulin resistance was closely associated with the presence of rheumatoid factor (RF) and anti-citrullinated protein (Anti-CCP) antibody[9-10]. These findings suggest an important role for chronic systemic inflammation in the pathogenesis of both RA and type 2 diabetes.

This study showed that distribution of rheumatoid factor and drugs of diabetes and their association and it shows that 5 rheumatoid factor positive cases are taking insulin among 9 of that positive case and shows the association between them it was statistically significantly associated.

It is possible that the association between RA (rheumatoid arthritis) and type 2 diabetes might be partially explained by the confounding effect of obesity. Nevertheless, although obesity is a well-established risk factor for type 2 diabetes[11], previous research on the association between body mass index and RA generated inconsistent results. Early studies had indicated a moderate increase in the risk of RA with obesitybut newer studies generally reported that obesity was not a predisposing factor for RA[12-13].

Conclusion

In this study uric acid is significantly associated with positive Rheumatoid factor in type- 2 male diabetic patients. This present study also concludes that insulin taking male diabetics are more prone to develop Rheumatoid arthritis.

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