Clinical Study of Rheumatological Manifestations in Type 2 Diabetes Mellitus Patients
(Original Article)

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Abstract
Objectives: Type 2 diabetes mellitus is associated with various rheumatological manifestations that are debilitating and affect the quality of life. The present study was conducted to find the prevalence of rheumatological manifestations in type 2 diabetics and to study its correlation with the duration of diabetes.

Methods: 100 type 2 diabetics and 50 age and sex matched non diabetics were examined for rheumatological manifestations during the period August 2014 to August 2015 in Mamata General Hospital, Khammam. Apart from routine investigations renal function tests, fasting and postprandial blood glucose, rheumatoid factor, serum uric acid and x-rays of involved joints wherever required were done.

Results: Rheumatological manifestations were seen in 31% of patients with type 2 diabetes mellitus compared to 16% in non diabetics. Periarthritis of shoulder was seen in 18% diabetics compared to 4% in nondiabetics and was statistically significant. It was the most common manifestation among type 2 diabetics accounting for 55% of the cases. Diffuse idiopathic skeletal hyperostosis was observed in 3% of diabetics and none of the non diabetics. Osteoarthritis of knee was noted in 8% of diabetics compared to 10% of non diabetics. Carpal tunnel syndrome was seen in 3% of diabetics and 2% non diabetics. Dupuytren's contracture, cheiroarthropathy and flexor tenosynovitis was not found in both the groups. The manifestations were more predominant in females 43.6% as compared to males 23%. Majority of the diabetic patients with rheumatological manifestations 32.25% were noted to have 1 to 5 years of duration of the disease which was not statistically significant.

Conclusion: Rheumatological manifestations are more prevalent in type 2 diabetics than non diabetics especially periarthritis of shoulder. They are predominantly seen in females and have no correlation to the duration of diabetes mellitus.

Keywords: Diabetes, Rheumatological manifestations, Periarthritis of shoulder, diffuse idiopathic skeletal hyperostosis, Osteoarthritis of knee, Carpal tunnel syndrome
INTRODUCTION
Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action or both. It is associated with long term damage, dysfunction and failure of various organs, especially the eye, kidneys, nerves, blood vessels and skeletal system. Type 2 diabetes mellitus is the most common form accounting for 85-95% of all cases. Although the other complications of diabetes mellitus are recognized as the major causes of morbidity and mortality, the musculoskeletal or rheumatological manifestations associated with it may be very debilitating. Many of these complications are treatable with resultant improvement in quality of life and more independence in activities of daily living. Some of the manifestations like adhesive capsulitis of shoulder and diffuse idiopathic skeletal hyperostosis have a close association with diabetes mellitus that they often lead to diagnosis of diabetes in otherwise asymptomatic patients. So it is important to recognize the various joint and bone manifestations of diabetes. This study is conducted to identify the prevalence of various rheumatological manifestations in patients with type 2 diabetes mellitus.

AIMS AND OBJECTIVES OF THE STUDY
1. To study the prevalence of various rheumatological manifestations in patients with type 2 diabetes mellitus.
2. To study the correlation between duration of diabetes mellitus and the occurrence of rheumatological manifestations

MATERIALS and METHODS
Source of data:
Inpatients and outpatients with type 2 diabetes mellitus at Mamata Medical College and Hospital.

Sample size:
Hundred patients with type 2 diabetes mellitus and fifty cases of age and sex matched non diabetics are included using random sampling technique.

Design of the study:
Cross-sectional study

Duration of study:
One year.

Inclusion criteria:
Inpatients and outpatients with type 2 diabetes mellitus at Mamata Medical College and hospital. The criteria for diagnosis of diabetes mellitus are according to the criteria laid down by the American Diabetes Association, 2013.

- Fasting blood glucose >126mg/dl
- Postprandial blood glucose >200mg/dl
- Symptoms of diabetes plus random blood glucose >200mg/dl

The control group will comprise of subjects without family history of diabetes mellitus, fasting blood sugar values <126mg/dl and postprandial blood sugar values <200mg/dl.

Exclusion criteria:
- Patients with history of injury or fractures in the joint region.
- Patients with history of end stage renal disease.
- Patients with history of chronic liver disease.
- Patients with rheumatoid arthritis.

Procedure
100 patients with type 2 diabetes mellitus both inpatients and outpatients at Mamata Medical College Hospital and 50 non diabetics were included in the study. Demographic characteristics such as age and sex were recorded. Symptoms suggestive of joint involvement such as pain, stiffness, restriction of joint movement and swelling of the joint with the duration of symptoms were documented. History regarding the duration of diabetes, age of onset of diabetes, mode of treatment, and family history of diabetes was documented. Presence of hypertension, ischemic heart disease was recorded.
On general physical examination vital data such as pulse, blood pressure and temperature were recorded. The anthropometric measurements, weight in kilograms and height in metres was recorded. The body mass index was calculated and measurement of waist and hip circumference was done.

A detailed systemic and musculoskeletal system examination was done. The diagnosis of periarthritis of the shoulder was made if history of shoulder pain was present for atleast 3 months and progressive limitation of shoulder movement, particularly half the range of external rotation. Patients who were previously diagnosed to have periarthritis and recovered were also included.

The diagnosis of diffuse idiopathic skeletal hyperostosis was made if complaints of pain and stiffness in the back was present and X–ray of spine showed presence of more than two bridges between contiguous vertebrae. Joint mobility of the fingers was diagnosed if the patients were not able to approximate palmar surfaces and fingers with fingers splayed. The other joints like hip, knee, ankle, wrist and small joints of the hand were examined for osteoarthritis, Charcot’s joint. The palms were examined for Dupuytren’s contracture and flexor tenosynovitis.

Presence of sensory neuropathy was defined by symptoms of tingling and numbness over the extremities, with or without impaired touch and vibration sense. Presence of motor neuropathy was noted. Dilated fundoscopy was done for all patients to look for diabetic retinopathy.

**Investigations**

Fasting and postprandial blood sugars were done. Renal function tests included blood urea, serum creatinine and urine analysis. Urine was analysed for sugars, ketone bodies and protein. Complete blood count, erythrocyte sedimentation rate, rheumatoid factor, serum uric acid were done. The rheumatoid factor upto 20IU/dl and serum uric acid upto 7 mg/dl was taken as normal. 2X-rays of hand, shoulder, knee, spine and other involved joints wherever necessary were done.

**Statistical analysis**

The prevalence rates were calculated in percent of total cases in each group and wherever applicable, prevalence amongst two groups was subjected to statistical analysis using Fisher’s exact test and Chi-square test. The p value of less than 0.05 was considered significant.

**RESULTS**

During the period of one year hundred patients with type 2 diabetes mellitus and 50 non diabetics were included in the study.

The following observations were made:
Figure No. 1: Age Distribution

Majority of the study cohort, 32% (32 patients) among diabetics belonged to the age group of 61 to 70 years and in non-diabetics 32%(16 patients) belonged to age group of 41 to 50 years. Mean age of the diabetics was 57.59 ± 10.44 years and non-diabetics was 52.40 ± 10.36 years.

Figure 2: Sex Distribution

In the 100 diabetics included in the study, 61% were males and 39% were females. Out of 50 non-diabetics, 50% were males and 50% were females.
Figure 3: Duration of diabetes

Majority of the diabetic population (37%) had 1-5 years of duration of the disease.

Mean duration of disease was 7± 6.99 years.

Figure 4: Prevalence of rheumatological manifestations

Yes = Patients with rheumatological manifestations
No = Patients without rheumatological manifestations

Rheumatological manifestations were seen in 31 patients (31 %) with type 2 diabetes mellitus and 8 patients (16 %) without diabetes. It is statistically significant with p value of 0.048 calculated using Pearson’s chi square test.
Table 1: Associated medical illness and family history of diabetes in patients with rheumatological manifestations.

<table>
<thead>
<tr>
<th>Group</th>
<th>Manifestations</th>
<th>Hypertension</th>
<th>Family history of diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Diabetics</td>
<td></td>
<td>10</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>17</td>
<td>52</td>
</tr>
<tr>
<td>Non-diabetics</td>
<td>Present</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>7</td>
<td>35</td>
</tr>
</tbody>
</table>

In the 31 type 2 diabetic patients with rheumatological manifestations, 10 patients had hypertension and 12 patients had family history of diabetes.

Figure 5: Modes of treatment

Yes = Patients with rheumatological manifestations
No = Patients without rheumatological manifestations

In the 31 type 2 diabetic patients with rheumatological manifestations, 80.64% were on oral hypoglycaemic agents and 19.36% were on insulin.
**Figure 6:** Rheumatological manifestations in patients with type 2 diabetes mellitus

![Pie chart showing rheumatological manifestations]

FZ - Frozen shoulder  
DISH - Diffuse idiopathic skeletal hyperostosis  
CTS - Carpal tunnel syndrome  
OA - Osteoarthritis  
CJ - Charcot’s joint

Among the 31 type 2 diabetics with rheumatological manifestations, the commonest is periarthritis of shoulder accounting for 55% of the cases.

**Figure 7:** Comparison of prevalence of various rheumatological manifestations among diabetics and non diabetics

![Bar chart showing prevalence of rheumatological manifestations]

FZ - Frozen shoulder  
DISH - Diffuse idiopathic skeletal hyperostosis  
CTS - Carpal tunnel syndrome  
OA - Osteoarthritis  
CJ - Charcot’s joint  
CA - Cheiroarthropathy  
DC - Dupuytren’s contracture

CJ - Charcot’s joint  
CA - Cheiroarthropathy  
DC - Dupuytren’s contracture

Among the 31 diabetic patients with manifestations, 16 had frozen shoulder, 6 had osteoarthritis of the knee, 3 had DISH, 3 had carpal tunnel syndrome and 1 had Charcot joint of the ankle. Both osteoarthritis of knee and periarthritis of shoulder were seen in 2 diabetics. Among 8 non diabetic patients with rheumatological manifestations, 2 had frozen shoulder, 5 had osteoarthritis of the knee, and 1 had carpal tunnel syndrome. None of them were found to have cheiroarthropathy, flexor tenosynovitis and Dupuytren’s contracture. A
A statistically significant association was found for the prevalence of periarthritis among type 2 diabetics and non diabetics (p value=0.033).

**Table 2: Sex distribution of rheumatological manifestations**

<table>
<thead>
<tr>
<th>Group</th>
<th>Manifestations</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetics</td>
<td>Present</td>
<td>14 (23%)</td>
<td>17 (43.6%)</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>47 (77%)</td>
<td>22 (56.4%)</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>61 (100%)</td>
<td>39 (100%)</td>
</tr>
<tr>
<td>Non-diabetics</td>
<td>Present</td>
<td>2 (8%)</td>
<td>6 (24%)</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>23 (92%)</td>
<td>19 (76%)</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>25 (100%)</td>
<td>25 (100%)</td>
</tr>
</tbody>
</table>

The prevalence of rheumatological manifestations in the diabetic population is greater in females (43.6%) as compared to males (23%) which is statistically significant (p = 0.03). In case of non-diabetics it is more common in females but is statistically insignificant (p = 0.123).

**Figure 8: Age wise distribution of rheumatological manifestations among diabetics and non diabetics**

The rheumatological manifestations were more prevalent in 51-60 year age group followed by 61 to 70 year age group among diabetics. In the non-diabetics it was commonly found in age group of 51 to 60 years.
Majority of the diabetic patients with rheumatological manifestations, 10 patients (32.25%) were noted to have 1 to 5 years of duration of the disease. It is not statistically significant.

Figure 9: Correlation of rheumatological manifestations with the duration of diabetes mellitus

Figure 10: Association of body mass index with the prevalence of rheumatological manifestations.

The majority of the type 2 diabetics with rheumatological manifestations, 14 patients (14%) and 5 (10%) non diabetic patients with rheumatological manifestations are found to have BMI of 18-24.9 kg/m². It is statistically insignificant.
Figure 11: Association of waist hip ratio with rheumatological manifestations

The mean waist to hip ratio was 0.939 and 0.932 in diabetics, 0.954 and 0.918 in non diabetics with and without rheumatological manifestations respectively. It is statistically non significant (p=0.325).

Figure 12: Correlation of rheumatological manifestations with microvascular complications of diabetes.

Yes = Patients with rheumatological manifestations No = Patients without rheumatological manifestations

The above figure shows that none of the type 2 diabetics with rheumatological manifestations had associated microvascular complications like nephropathy and retinopathy.
Figure 13: Correlation of fasting blood sugar levels with rheumatological manifestations in type 2 diabetics

Yes = Patients with rheumatological manifestations
No = Patients without rheumatological manifestations

The mean FBS among patients with and without rheumatological manifestations was 165.96±68.34 mg/dl and 165.39±74.58 mg/dl. No statistically significant correlation (p=0.971) was noted between mean fasting blood sugar levels and the prevalence of rheumatological manifestation in diabetics.

Figure 14: Correlation of post prandial blood sugars with rheumatological manifestations in type 2 diabetics.

Yes = Patients with rheumatological manifestations
No = Patients without rheumatological manifestations

The mean PPBS among type 2 diabetics with and without rheumatological manifestations was 228.32±109.88 mg/dl and 252.493 ±80.81mg/dl. No statistically significant correlation (p=0.275) was noted between mean post prandial blood sugar levels and the prevalence of rheumatological manifestations in diabetics. In the non diabetics also no correlation was found.
**Figure 15**: Correlation of rheumatological manifestations with rheumatoid factor.

The mean value of RA factor was 11.51IU/ml in diabetics with manifestations, as compared to 22.41IU/ml in case of non-diabetics. No significant difference is noted in RA factor in diabetics with and without rheumatological manifestations.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA Factor</td>
<td>11.51</td>
<td>11.45</td>
</tr>
<tr>
<td>Diabetics</td>
<td>22.41</td>
<td>14.59</td>
</tr>
<tr>
<td>Non-diabetics</td>
<td>14.59</td>
<td>14.59</td>
</tr>
</tbody>
</table>

Yes = Patients with rheumatological manifestations
No = Patients without rheumatological manifestations
DISCUSSION
The current study is a cross sectional study which was conducted for a period of one year from August 2014 to August 2015. It included 100 patients with type 2 diabetes mellitus and 50 non diabetics at Mamata Medical College Hospital. A detailed medical history, general physical and systemic examination was carried out to identify the prevalence of the rheumatological manifestations. Investigations such as complete blood count, fasting and postprandial blood sugars, renal function tests, serum uric acid, erythrocyte sedimentation rate, rheumatoid factor, urine analysis and X-rays of hand, shoulder, knee, spine and involved joints wherever necessary were done.

In the present study, prevalence of rheumatological manifestations was greater in patients with type 2 diabetes mellitus (31%) compared to the non diabetics (16%). It is consistent with the study done by Caglerio E in which 36% of the diabetics had rheumatological manifestations as compared to 9% of non diabetics and study done by Douloumpakas which showed 82.6% of type 2 diabetics had rheumatological manifestations.

Periarthritis of the shoulder was found in 18% of the type 2 diabetics as compared to 6% in non diabetics in the present study. Comparison of the present study with other studies for the prevalence of periarthritis in type 2 diabetics and non diabetics:

<table>
<thead>
<tr>
<th>STUDY</th>
<th>DIABETICS</th>
<th>NONDIABETICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sarkar RN^5</td>
<td>17.9%</td>
<td>7%</td>
</tr>
<tr>
<td>Bridgman^12</td>
<td>11%</td>
<td>2.5%</td>
</tr>
<tr>
<td>Mavrikakis^13</td>
<td>31.8%</td>
<td>10.3%</td>
</tr>
<tr>
<td>Pal^14</td>
<td>19%</td>
<td>5%</td>
</tr>
<tr>
<td>Caglerio E^9</td>
<td>12%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Among the 18 diabetic patients with periarthritis of shoulder it was found unilaterally in 83.4% and bilaterally in 16.6% of the patients. This is comparable to the study done by Mavrikakis in which 71.4% had unilateral and 28.6% had bilateral involvement of the shoulder joint. The bilateral involvement was more frequent in diabetics (16.6%) than in non diabetics (0%). It is comparable to the study done by Spanheimer RJ in which bilateral shoulder involvement was reported in 33 to 42% of diabetics and 5 to 20% in non diabetics.

In our study there is no difference in the duration of diabetes among patients with and without adhesive capsulitis i.e. the mean duration of diabetes of patients with or without periarthritis of shoulder was 6.66 years and 7 years respectively which was inconsistent with the study done by Pal and Balci N.

The mean age of type 2 diabetics with periarthritis of shoulder was 55.6 years. It is comparable to the study done by Arkkila PE and Balci N which showed increased prevalence of periarthritis after the age of 50 years.

In the present study periarthritis of shoulder was not associated with increased prevalence of other hand syndromes like limited joint mobility, carpal tunnel syndrome and Dupuytren’s disease. No association was found with the microvascular complications of diabetes such as diabetic retinopathy and nephropathy. This was inconsistent with the studies done by Arkkila PE and Balci N.

In studies done by Bridgman and Mavrikakis adhesive capsulitis of shoulder was seen in patients with poor glycemic control. However in the present study no significant difference in the fasting blood sugar (156.77 and 165.39mg/dl) and post prandial blood sugar levels (235.83 and 252.49mg/dl) is found.
The study by Renard reported that 15% of diabetics and 5% of non diabetics had carpal tunnel syndrome. In our study carpal tunnel syndrome was found in 3% of the type 2 diabetics and 2% of the non diabetics.

In our study 8% of the diabetics and 10% of the non diabetics had osteoarthritis and mainly knee joint was involved. It is inconsistent with the study done by Sarkar RN in which osteoarthritis was found in 31% of the diabetics out of which 85% were type 2 diabetics and usually found to involve the non weight bearing joints. Increased prevalence was seen in females than males which was consistent with the study done by Sarkar RN.

Diffuse idiopathic skeletal hyperostosis is seen only in 3% of the type 2 diabetics as compared to 2% of the non diabetics which was not consistent with the various studies which reported increased prevalence of diffuse idiopathic skeletal hyperostosis in diabetics as compared to non diabetics.

In this study all 3 diabetics with DISH are above 50 years of age with mean of BMI of 25.6kg/m² which was consistent with the study done by Sarkar RN that reported all type 2 diabetics with DISH were above the age of 45 years and had BMI of more than 25kg /m². A study done in Hungary showed that DISH is more frequent in males whereas in the present study all the three patients with DISH were females.

Study done by Sarkar RN showed that the neuroarthropathy of knee and foot was seen in 3.2% diabetics as compared to 0.6% of the non diabetics, however in our study it was seen in 1% of the diabetics and 0% of non diabetics.

Various studies showed increased prevalence of limited joint mobility, Dupuytren’s disease and flexor tenosynovitis in diabetics compared to nondiabetics. However these manifestations were not noted in both the groups in the present study.

In the present study no difference is seen in the mean FBS (165.96mg/dl and 165.39mg/dl) and PPBS (228.32mg/dl and 252.49mg/dl) among patients with and without rheumatological manifestations. It was comparable to the study done by Cagliero E which showed that the mean blood sugar levels were slightly higher in patients with hand and shoulder syndromes than those without, but was not statistically significant.

In the present study no significant association is found between the BMI and waist hip ratio to the prevalence of rheumatological manifestations. No correlation is seen with respect to the rheumatoid factor.

In the present study, rheumatological manifestations had greater prevalence among the type 2 diabetics as compared to the non diabetics and the most common rheumatological manifestation was periarthritis of shoulder followed by osteoarthritis of the knee. There was no association found between the level of glycemic control and the increased prevalence of rheumatological manifestations.

CONCLUSION

The study has found that the prevalence of rheumatological manifestations is greater in patients with type 2 diabetes mellitus than in the non diabetic population and is statistically significant. They are more commonly seen in females as compared to the males. Periarthritis of shoulder is the commonest rheumatological manifestation in type 2 diabetics. There is no correlation seen with the duration of diabetes and the prevalence of rheumatological manifestations. This study included a small group of type 2 diabetics and hence would be beneficial to undertake the study by including a larger group.

REFERENCES

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