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### RHEUMATOLOGICAL MANIFESTATIONS OF TYPE 2 DIABETES MELLITUS

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**ABSTRACT: AIM:** To determine the prevalence of rheumatic musculoskeletal manifestations in type 2 diabetic individuals and compare them with non-diabetic individuals. **METHODS:** 100 type 2 diabetic patients and 100 age and sex matched individuals were included in the study. Complete musculoskeletal examination was carried out which included examination of shoulder joints, hands, back and knees. Patients were also asked to mark the sites of pain on a mannequin. Intensity of pain was marked on a visual analogue scale. These variables were then evaluated using Chi square test. **RESULTS:** Prevalence of RMS was found to be much higher in case of diabetic individuals except osteoarthritis. 49 patients out of 100 diabetic patients were found to have some form of rheumatic musculoskeletal manifestations. Diabetic cheiroarthropathy was found in the highest number of cases. A significant relation of these manifestations was found with age, duration of diabetes and glycemic control. A significant relation was also found between these manifestations and chronic microangiopathic complications like retinopathy and nephropathy. **CONCLUSION:** A detailed examination of musculoskeletal system is an important part of care in patients with type 2 diabetes and some of the manifestations could be a simple and reliable marker of microangiopathic complications like retinopathy and nephropathy.

**KEYWORDS:** RMS- rheumatic musculoskeletal manifestations, ADA-American diabetic association, LJM- limited joint mobility, DC- dupuytren's contracture, OA- osteoarthritis, DISH-diffuse idiopathic skeletal hyperostosis.

**INTRODUCTION:** Diabetes mellitus is a global health problem estimated to affect 84 million people by 2030<sup>1</sup>. In contrast to the life threatening macro and microvascular complications of diabetes mellitus, rheumatological disorders cause considerable morbidity<sup>2</sup>. Musculoskeletal complications are the most common endocrine arthropathies. These manifestations which are some of the causes of chronic disability, involve not only the joints, but also bones and soft tissues<sup>3</sup>. The various musculoskeletal manifestations include adhesive capsulitis, diabetic cheiroarthropathy, dupuytren's contracture, flexor tenosynovitis, diffuse idiopathic skeletal hyperostosis, osteoarthritis and neuropathic joint.

The prevalence of rheumatological manifestations in patients with diabetes mellitus has been found to be more than non diabetics<sup>4</sup>. Stiffening of joints in diabetes mellitus is considered to be caused by deposition of abnormal collagen in the connective tissue around the joints, enzymatic and non-enzymatic glycosylation of collagen and abnormal cross linking of collagen<sup>6</sup>. There have been a number of studies in the western world to know the prevalence of rheumatological manifestations whereas in our country there is a paucity of reports that describe rheumatological disabilities in diabetic patients.

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## MATERIALS AND METHODS:

**Patients and study design:** We performed a case control study between Jan 2012 to Sep 2013 to evaluate rheumatological manifestations in 100 patients suffering from type 2 diabetes in the department of Medicine, Sri Guru Ram Dass Institute of Medical Sciences and Research, Amritsar. An equal number of age and sex matched controls were also included in the study. The cases were diagnosed to have type 2 diabetes mellitus as per the ADA criteria i.e. one of the following

- 1) Symptoms of diabetes plus random blood glucose concentration of more than or equal to 200mg/dl.
- 2) Fasting plasma glucose of more than or equal to 126mg/dl.
- 3) HBA1C of more than 6.5%
- 4) Two hour plasma glucose of more than or equal to 200mg/dl during an oral glucose tolerance test.

The prevalence of rheumatological manifestations was compared in both the groups and prevalence of individual manifestation was also noted in cases. The following patients excluded from the study 1. Patients with secondary diabetes e.g. Cushing syndrome 2. Type 1 diabetic patients and MODY 3. Patients with diseases associated with rheumatological manifestations e.g. CVA with frozen shoulder, alcoholism with Dupuytren's contractures. The selected cases and controls were subjected to a series of tests to determine the various musculoskeletal complications... Patients were asked to self-mark the areas of pain on a mannequin and intensity of pain will be marked on a visual analogue scale (VAS). Following this a detailed and systemic examination was performed in the following order; hands followed by shoulders, spine and finally the lower limbs and findings were noted. The study and control group were compared using the data thus obtained. RMS was diagnosed using the standard definitions. Range of movements in shoulder and small joints of hand shall be measured using a goniometer and finger goniometer respectively rounded to the nearest 1 degree. Peripheral neuropathy was diagnosed using 128 Hz tuning fork for perception of the vibration sense.

## STANDARDISED DEFINITION USED IN DIAGNOSIS

1. Adhesive capsulitis (frozen shoulder)-Patients having shoulder pain which occurs on movement of the shoulder joint, with a minimum VAS score of 30mm and limitation of active and passive range of movement, provided the shoulder X-ray is normal.
2. Carpal tunnel syndrome-Diagnosis of carpal tunnel syndrome is based on Durkan carpal compression test, Tinel's test and Phalen's test.
3. Dupuytren's contracture-Patients having pitting and thickening of palmar skin, fixed to skin and deep fascia along with contracture of ring and little finger.
4. Diabetic cheiroarthropathy-The condition can be diagnosed using Prayer's sign.
5. Flexor tenosynovitis-Patients having thickening along the affected flexor tendon sheath on the palmar aspect of the finger and hand. The locking phenomena may be reproduced with active or passive finger flexion.
6. Diffuse idiopathic skeletal hyperostosis-The presence of more than two bridges between contiguous vertebrae on X-ray thoraco-lumbar spine is considered as the selection criteria for the diagnosis of DISH.

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7. Osteoarthritis Knee-Diagnosed using the Altman's criteria of radiographic osteophytosis along with one of the following criteria.
  1. Age>60years      2. Pain      3. Crepitus      4. Morning stiffness<30 min
8. Peripheral neuropathy-Peripheral neuropathy is diagnosed by demonstrating absence of various sensations like light touch, temperature, and vibration sense. Vibration sense is tested by using tuning fork of 128 HZ (dorsum of hand, palm, dorsum of foot, sole and plantar surface of ball of big toe).

After examination, the clinical diagnosis of the rheumatological manifestation was made and recorded. Routine investigations were carried out. These included hemogram, ESR, urea, creatinine, uric acid, lipid profile, urine for microalbuminuria, glycosylated haemoglobin and X-rays of the relevant joints. The cohort was divided into two groups based on the presence of rheumatic musculoskeletal manifestations. Difference in proportion between these groups across age, gender, duration of diabetes, severity (glycosylated hemoglobin) was estimated using the chi square test and student's t test. A P value <0.05 was considered statistically significant.

**RESULTS:** A total of 100 cases (49 males and 51 females) and 100 age and sex matched controls (61 males and 39 females) included in the study were thoroughly examined during the study period. The mean age of the patients was found to be 57.72 $\pm$ 10 years and the mean duration of diabetes was found to be 8 $\pm$ 4 years. The difference in the age groups and sex ratio was statistically insignificant. Rheumatic musculoskeletal manifestations were found in 49 cases and 26 controls. The various rheumatic musculoskeletal manifestation in diabetic patients as compared to non-diabetic individuals are as follows diabetic cheiroarthropathy in 32 cases vs. 17 controls, osteoarthritis in 18 cases vs. 26 controls, carpal tunnel syndrome in 15 cases vs. 3 controls, dupuytren's contracture in 13 cases vs. 3 controls, frozen shoulder 12 cases vs. flexor tenosynovitis in 8 cases vs. 1 control, diffuse idiopathic skeletal hyperostosis in 6 cases vs. 1 control and neuropathic joint in 6 cases vs. 0 control. The difference in both the groups was found to be statistically significant.

Sl. no.	Musculoskeletal manifestation	Prevalence in cases
1	Diabetic cheiroarthropathy	32(32%)
2	Osteoarthritis	18(18%)
3.	Carpal tunnel Syndrome	15(15%)
4.	Dupuytren's contracture	13(13%)
5.	Frozen shoulder	12(12%)
6.	Neuropathic joint	6(6%)
7.	Flexor tenosynovitis	8(8%)
8.	Diffuse idiopathic skeletal hyperostosis	6(6%)

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Sl. no.	Musculoskeletal manifestation	Prevalence in controls
1	Osteoarthritis	26(26%)
2	Diabetic cheiroarthropathy	17(17%)
3	Frozen shoulder	4(4%)
3.	Carpal tunnel Syndrome	3(3%)
4.	Dupuytren's contracture	3(3%)
6.	Diffuse idiopathic skeletal hyperostosis	1(1%)
7.	Flexor tenosynovitis	1(1%)
8.	Neuropathic joint	0(0%)

Pain sites were also marked on VAS by 50 patients in the case group out of which 32 patients were found to have rheumatic musculoskeletal manifestations. In the control group pain sites were marked by 32 patients out of whom 20 patients were found to have rheumatic musculoskeletal manifestations. The most common site of pain was knees. A score of 0 was considered as 'no pain', 1-3 was labeled as 'mild pain' and >6 as 'severe pain'. Moderate to severe pain was reported by 50% of the patients.

The relation of these manifestations with glycemic control was also evaluated. The distribution of the entire cohort based on HbA1C was grouped in to two (<8 good control, >8 poor control). Glycosylated haemoglobin was found to have a significant relation with the manifestations as indicated by table no.

	RMSD	Good glycemic control	Poor glycemic control	P value
1.	carpal tunnel syndrome	1	14	<.001
2.	Diabetic cheiroarthropathy	3	29	<.001
3.	osteoarthritis	5	22	<.001
4.	flexor tenosynovitis	0	8	.003
5.	DISH	0	6	.012
6.	neuropathic joint	0	6	.012
7	frozen shoulder	4	12	.03
8.	Dupuytren's contracture	3	29	.04

Also significant association was noted between certain manifestations and chronic microangiopathic conditions like retinopathy and nephropathy. Diabetic cheiroarthropathy was found to have a statistically significant relationship with retinopathy and nephropathy. Out of 32 patients with diabetic cheiroarthropathy 26 patients and 21 patients ( $p<.001$ ) were found to have retinopathy and nephropathy respectively. Similarly out of 13 type 2 diabetic patients with dupuytren's contracture 10 ( $p=.008$ ) and 9( $p=.002$ ) were found to have retinopathy and nephropathy

**DISCUSSION:** The present study showed three important findings. The frequency of rheumatic musculoskeletal manifestation in type 2 diabetic patients was 49%. Second the most common

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musculoskeletal manifestation was found to be diabetic cheiroarthropathy. Third, there was significant association between the vascular complication and the manifestations.

A higher prevalence of rheumatic musculoskeletal manifestation except osteoarthritis was noted in type 2 diabetes than non-diabetics. The most common rheumatic musculoskeletal manifestation was diabetic cheiroarthropathy which was found to be present in 32 % cases. The results were consistent with the study conducted by Chammas et al<sup>6</sup> where the prevalence of diabetic cheiroarthropathy was found to be present in 33 % of the diabetic individuals. All the changes showed marked correlation with the presence of microangiopathic complications like retinopathy and nephropathy as found in the present study. The study conducted by Chammas et al<sup>6</sup> didn't show any relation of the findings with the glycemic control as seen in the present study. However another study conducted by Mathew et al<sup>2</sup> showed statistically significant relation between diabetic cheiroarthropathy and glycemic control.

The prevalence of Dupuytren's contracture was found to be 13% in diabetic individuals. Similar results were found in a study conducted by Aydeniz et al<sup>7</sup> in which the prevalence of Dupuytren's contracture was found to be 12.7% as the population size was similar. Dupuytren's contracture like diabetic cheiroarthropathy was also found to have a statistically significant correlation with the microangiopathic complications like retinopathy and nephropathy. Similar result was found in a study conducted by Lawson et al<sup>8</sup>. Out of the 29 diabetic patients with Dupuytren's contracture 18 patients (62%) had diabetic retinopathy however not many studies have evaluated a relationship between Dupuytren's contracture and nephropathy. Diabetic cheiroarthropathy and Dupuytren's contracture can be considered as a useful marker for microvascular complications.

In the present study the prevalence of frozen shoulder was found to be 12%. The results were consistent with the studies performed by Aydeniz et al<sup>7</sup>, Mathew AJ et al<sup>2</sup> and Sarkar et al<sup>9</sup> where the prevalence of frozen shoulder was found to be 15%, 16.45% and 20 % respectively. Study conducted by Schulte et al<sup>10</sup> found a significant relation of frozen shoulder with glycemic control as seen in the present study. However no relation was found with microangiopathic complications.

Diffuse Idiopathic skeletal hyperostosis was present in 6% of the patients suffering from type 2 diabetes when compared to that reported by Sarkar et al (28%)<sup>9</sup> and Mathew et al (14.52%)<sup>2</sup>. However similar results were found in a study performed by Douloumpakas et al<sup>11</sup> in which the prevalence of diffuse idiopathic skeletal hyperostosis was found to be 6%.

Flexor tenosynovitis was found to have a prevalence of 8% in patients suffering from type 2 diabetes. Studies carried out by Sarkar et al<sup>9</sup> and Mathew et al<sup>2</sup> showed the prevalence of flexor tenosynovitis to be 5 and 4.4% respectively whereas the study carried out by Chammas et al<sup>6</sup> showed the prevalence to be 20%.

The prevalence of carpal tunnel syndrome in type 2 DM was found to be 15% as compared to 3% in controls. The results were comparable to a study conducted by Chammas et al<sup>6</sup> where the prevalence of carpal tunnel syndrome in type 2 DM patients was found to be 15-25%. Study conducted by Perkins BA, Olaleye D, Bril V<sup>12</sup> also showed the prevalence of carpal tunnel syndrome in type 2 diabetes mellitus patients to be 14-30% which was significantly higher as compared to the control group. In a study by Attar SM<sup>3</sup> the prevalence of carpal tunnel syndrome was found to be 6.7%. Rajendran et al<sup>13</sup>, Sarkar et al<sup>9</sup> and Mathew AJ, Maneshi F, Kohner EM<sup>2</sup> found the prevalence of carpal tunnel to be 5.3%, 4% and 32% respectively. In our study carpal tunnel syndrome was also

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found to have a statistically significant relation ( $p < .001$ ) with glycemic control.

Prevalence of neuropathic joints was also found to be low i.e. 6%. The previous studies as shown in a study by Sarkar et al<sup>9</sup> found the prevalence to be 2%. The difference could be attributed to the difference in the occupation as well as weight of the patients as obesity is regarded as a major factor in the pathogenesis of Charcot's joint.

The prevalence of osteoarthritis knee in diabetic individuals was found to be 18%. The results were comparable to a study conducted by Sarkar et al<sup>9</sup> and Mathew AJ, Maneshi F, Kohner EM<sup>2</sup> which showed the prevalence of osteoarthritis knee to be 22.5% and 20.04%. In our study controls were also found to have a higher prevalence (26%) of osteoarthritis knee. However the difference was found to be statistically insignificant ( $p = .172$ ). This is in line with the study by Sturmer et al<sup>14</sup> and Sarkar et al<sup>9</sup> who didn't find a significant association between type 2 DM and osteoarthritis knee. Based on these studies, we cannot definitely conclude that diabetes is an independent risk factor for osteoarthritis since many potential confounders may interfere with the results such as age and level of activity. The reason for lower prevalence in type 2 diabetics may be attributed to the fact that diabetics may be less ambulatory than non-diabetics due to morbidity associated with the disease.

From this study we conclude that a through musculoskeletal examination could be useful in detection of the rheumatic musculoskeletal manifestations. This could be helpful in preventing chronic disability in patients and improving the quality of life. Glycemic control can also be helpful in prevention of these manifestations These manifestations could also be helpful in predicting microangiopathic complications like retinopathy and nephropathy.

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