Study of Rheumatological Musculo-Skeletal Manifestations among Patients with Controlled and Uncontrolled Type II Diabetes Mellitus at a Tertiary Care Centre of North Karnataka, India

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ABSTRACT

Introduction: Several musculoskeletal manifestations and rheumatological complications are associated with Diabetes Mellitus (DM) which are poorly understood and often clinically over looked. So the Study was done to see prevalence of Rheumatological Musculoskeletal Manifestations (RMSM) in Type 2 Diabetic Mellitus (T2DM) patients and to examine their relationship with duration of diabetes and glycemic control.

Material and Methods: A cross sectional study conducted among 400 T2DM patients over a period of one year to assess the prevalence of various rheumatological manifestations and complications. The relationship between these complications with duration of diabetes, long-term glycemic control and other risk factors was determined.

Results: Out of 400 Type 2 Diabeteic Patients RMSM were found in 63% (126 patients) cases in uncontrolled T2DM and 38% (76 patients) in controlled T2DM cases. The various rheumatic musculoskeletal manifestation in uncontrolled vs. controlled diabetic patients respectively were as follows diabetic cheiroarthropathy in 23% vs. 11% , osteoarthritis in 19% vs. 14% , diffuse idiopathic skeletal hyperostosis in 18% vs. 8%, frozen shoulder 17% vs. 6% cases, carpal tunnel syndrome in 12.5% vs. 5% cases, dupuytren's contracture in 9% vs. 3.5% cases, flexor tenosynovitis in 7% vs. 3% cases, and neuropathic joint in 4% vs.0.5% cases. A significant relation of most of these manifestations was found with age, duration of diabetes, glycemic control, and vascular complications. Prevalence of osteoarthritis and flexor tenosynovitis did not show any significant difference between the two groups.

Conclusion: Rheumatologic manifestations are quite common in diabetes and are found with proportionately higher prevalence in patients with poor glycemic control. Its early detection and management may significantly reduce morbidity in T2DM patients.

Keywords: T2DM, RMSM, Diabetic Cheiroarthropathy, DISH, Neuropathic Joint

INTRODUCTION

Diabetes Mellitus is one of the four priority Non-Communicable Diseases (NCDs) targeted for action by world leaders. If not controlled optimally, it may lead to several complications.[1] With major focus targeted towards various micro and macro vascular complications among diabetes patients, several complications occuring due to other patho-physiological mechanisms are often neglected, such as rheumatological musculoskeletal manifestations which are often associated with significant morbidity.

In 2004, the National Health Interview Survey determined that 58% of diabetes patients would have functional disability.[2] The exact etiology of diabetes-associated musculoskeletal disorders remains obscure, however, there is evidence that hyperglycemia may accelerate non-enzymatic glycosylation and abnormal collagen deposition in periarticular connective tissues leading to diffuse arthrofibrosis.[3,4] These manifestations are closely linked to age[5], poor glycemic control[6], prolonged disease duration[7,8], and vascular complications of diabetes.[9] In contrast to the life threatening macro and microvascular complications of diabetes mellitus, rheumatological disorders cause considerable morbidity[10] but are often missed and under treated. Hence, this study was taken up with the objective to study the prevalence of rheumatological musculoskeletal manifestations (RMSM) in type 2 diabetic mellitus (T2DM) patients and to examine their relationship with duration of diabetes and glycemic control.

MATERIAL AND METHODS

The present cross-sectional study was conducted from June 2015 to May 2016 in Karnataka Institute of Medical Sciences, Hubli after getting approval by the Institutional Ethics Committee. A total of 400 T2DM patients were included in the study after obtaining written informed consent. Among these, 200 controlled and 200 uncontrolled T2DM patients were taken after determining their mean HbA_{1C} level by by Particle Enhanced Immuno-turbidimetric Assay Method. Mean HbA_{1C} level was calculated from the results obtained during the last three visits, as a single reading doesn't correlate with tissue levels of advanced glycosylation end products.[11] HBA_{1C} of >8 is the level where American Diabetes Association suggests action to be taken[12] and has been taken as poor glycemic control in our study. Musculoskeletal complications were determined by clinical examinations, x-ray and if needed CT scan/MRI.

Inclusion criteria: T2DM patients over and above 30 years of age, attending KIMS OPD and/or admitted at KIMS Hospital, Hubli, who consented to be a part of the study were included.

Exclusion Criteria Following patients were excluded from the study.

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1. Patients with Renal Osteodystrophy (Diabetic End Stage Renal Disease).
2. RheumatoidArthritis patients associated with deformities of hand and secondary osteoarthritis.
3. Patients with collagen vascular disorder such as SLE.
4. Patients having diseases associated with rheumatological manifestations e.g. CVA with frozen shoulder, alcoholism with dupuytren's contracture etc.
5. Patients with history of trauma associated musculoskeletal morbidities.
6. Patients with secondary diabetes e.g. Cushing syndrome, Type 1 diabetic patients and MODY3.

Defining various Musculoskeletal complications

1. **Cheiroarthropathy** was evaluated by the "prayer sign", in which the patient was asked to touch the palmar surfaces of the interphalangeal joints together with the fingers fanned and the wrist maximally extended. If they were unable to do so, the test was considered to be positive.[13]
2. **Periarthritis (Frozen Shoulder):** The diagnosis of Periarthritis (Frozen Shoulder) was made in patients with pain in the shoulder for at least 1 month, an inability to lie on the affected shoulder, and restricted active and passive shoulder joint movements in at least three planes.[14,15]
3. **Carpal Tunnel Syndrome-** Diagnosis of Carpal Tunnel Syndrome was based on Durkan carpal compression test, Tinel's test and Phalen's test.
4. **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.
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 contagious vertebrae on X-ray thoraco-lumbar spine is considered as the selection criteria for the diagnosis of **DISH.**
7. **Osteoarthritis** Knee-Diagnosed using the Altman's criteria[16] of radiographic osteophytosis along with one of the following criteria.
   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).

STATISTICAL ANALYSIS

Frequency tables, percentages, means, standard deviation were

S. No	Demographic Parameter		Uncontrolled t2dm pts (Hba_{1c} ≥8) n=200	Controlled t2dm pts (Hba_{1c} <8) n=200	Total	% Of patients
1	Age	31-40 Yrs	58	73	131	32.75
		41-50 Yrs	70	62	132	33.00
		>50 Yrs	72	65	137	34.25
2	Gender	Male	88	123	211	52.75
		Female	112	77	189	47.25
3	Bmi	≤25	72	116	188	47.00
		>25	128	84	212	53.00
4	Duration of dm	0-5 Yrs	47	58	105	26.25
		6-10 Yrs	50	51	101	25.25
		11-15 Yrs	55	47	102	25.50
		>15 Yrs	48	44	92	23.00
5	Fbs	<126	94	112	206	51.50
		≥126	106	88	194	48.50

T2dm = type two diabetes mellitus; hba_{1c} = glycosylated haemoglobin; % = percentage; yrs = years; bmi = body mass index; dm = diabetes mellitus; fbs = fasting blood sugar.

Table-1: Demographic profile of the study population

Sl No	RMSM	Uncontrolled T2DM (n=200)	Controlled T2DM (n=200)	P value	Odds Ratio	95% CI
1	Diabetic cheiroarthropathy	46(23%)	22(11%)	<0.01*	2.41	1.39-4.20
2	Osteoarthrits	38(19%)	28(14%)	0.178	1.44	0.85-1.50
3	Dish	36(18%)	16(8%)	<0.01*	2.52	1.35-4.72
4	Frozen shoulder	34(17%)	12(6%)	<0.01*	3.21	1.61-6.40
5	Carpel tunnel syndrome	25(12.5%)	10(5%)	<0.01*	2.71	1.27-5.81
6	Dupuytren's contracture	18(9%)	07(3.5%)	0.02*	2.73	1.11-6.68
7	Flexor tenosynovitis	12(6%)	06(3%)	0.148	2.06	0.76-5.61
8	Neuropathic joint	08(4%)	01(0.5%)	0.04*	8.29	1.02-66.92
9	None	74(37%)	124(62%)	<0.01*	0.36	0.24-0.54

* Significant; RMSM = Rheumatological Musculo-Skeletal Manifestations; T2DM = Type Two Diabetes Mellitus; DISH = Diffuse Idiopathic Skeletal Hyperostosis; CI = Confidence Interval

Table-2: Prevalence of RMSM in uncontrolled and controlled T2DM Patients

used as descriptive statistics. Existence and strength of association was found out by using chi-square test and odds ratio at 95% confidence intervals. The results with p value <0.05 were taken as statistically significant.

RESULTS

A total of 400 cases (211 males and 189 females), 200 controlled and 200 uncontrolled type 2 diabetes mellitus patients were included in the study. The mean age of the patients was found to be 49.32 ± 6 years. In uncontrolled group 28 (48.2%), 40 (57.1%) and 58 (80.5%) patients and 14 (19.1%), 22 (35.4%) and 40 (61.5%) in controlled T2DM group showed RMSM in the age groups 30-40 years, 40-50 years and >50 years respectively. The p value in both groups was <0.01 showing a significant association of age with RMSM. The mean duration of diabetes was found to be 8.16 ± 3.83 years.

Other demographic parameters included in the study are listed in Table 1. Overall 50.5% of type 2 diabetes mellitus patients showed at least one RMSM. They were found in 63% (126 patients) cases in uncontrolled T2DM and 38% (76 patients) cases in controlled T2DM cases. There was no significant difference in occurrence of musculoskeletal complications among different gender.

The various rheumatic musculoskeletal manifestation in uncontrolled vs. controlled diabetic patients respectively are as follows diabetic cheiroarthropathy in 23% vs. 11%, osteoarthritis in 19% vs. 14%, diffuse idiopathic skeletal hyperostosis in 18% vs. 8%, frozen shoulder 17% vs. 6% cases, carpal tunnel syndrome in 12.5% vs. 5% cases, dupuytren's contracture in 9% vs. 3.5% cases, flexor tenosynovitis in 6% vs. 3% cases, and neuropathic joint in 4% vs.0.5% cases. The difference in both the groups for most of the RMSM was found to be statistically significant (Table 2).

The relationship of duration of diabetes with various rheumatological complications in uncontrolled and

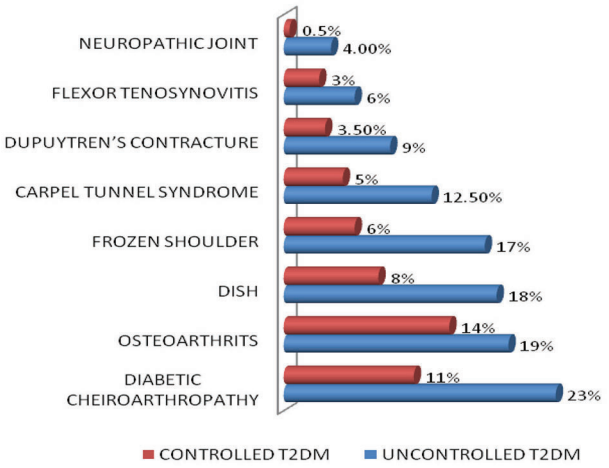

Figure-1: Bar diagram showing Prevalence of RMSM in uncontrolled and controlled T2DM Patients

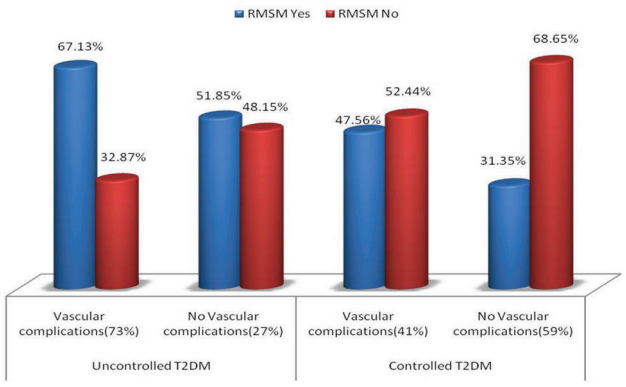

Figure-2: Column diagram showing RMSM and Vascular complications in Uncontrolled and Controlled T2DM Patients

RMSM	Uncontrolled T2DM				Controlled T2DM				
	0-5 Yrs n (%)	6-10 Yrs n (%)	11-15 Yrs n (%)	>15 Yrs n (%)	Chi sq. Test	0-5 Yrs n (%)	6-10 Yrs n (%)	11-15 Yrs n (%)	>15 Yrs n (%)	Chi sq. Test
DC	4 (8.51)	8 (16)	14 (25.45)	20 (41.67)	P=0.001*	2 (3.45)	4 (7.8)	7 (14.9)	10 (22.7)	P=0.01*
OA	5(10.6)	8 (16)	11(20)	14(29.1)	P=0.127	4(6.9)	6 (11.76)	8 (17.02)	10 (22.7)	P=0.08
DISH	3 (6.38)	6 (12)	10 (18.18)	17 (35.42)	P<0.005*	1(1.72)	2(3.92)	5 (10.64)	8(18.18)	P=0.01*
FS	2 (4.26)	4 (8)	10 (18.18)	18 (37.5)	P<0.005*	0 (0)	2 (3.92)	4 (8.51)	6 (13.64)	P = 0.02*
CTS	1 (2.13)	4 (8)	6 (10.91)	14 (29.17)	P<0.005*	0 (0)	1 (1.96)	3 (6.38)	6 (13.64)	P= 0.01*
DuC	1 (2.13)	2 (4)	5 (9.09)	10 (20.83)	P=0.001*	0 (0)	1 (1.96)	2 (4.26)	4 (9.09)	P=0.01*
FT	2 (4.26)	2 (4)	4 (7.27)	4 (8.33)	P=0.507	0 (0)	1 (1.96)	2 (4.26)	3 (6.81)	P= 0.217
NJ	0 (0)	1(2)	2 (3.63)	5 (10.4)	P=0.053	0 (0)	0 (0)	0 (0)	1 (2.27)	P=0.312
Total in each age group	47 (100)	50 (100)	55 (100)	48 (100)		58 (100)	51 (100)	47 (100)	44 (100)	

* Significant; DC= Diabetic Cheiroarthropathy, OA= Osteoarthritis, DISH= Diffuse Idiopathic Skeletal Hyperostosis, FS= Frozen Shoulder, CTS= Carpal Tunnel Syndrome, DuC= Dupuytren's Contracture, FT= Flexor Tenosynovitis, NJ= Neuropathic Joint. Yrs= years, grp= group

Table-3: Duration of type 2 DM and various RMSM in uncontrolled and controlled T2DM patients

controlled type 2 diabetis mellitus patients is shown in Table 3 below. There was a significant association between most of the RMSM with duration of T2DM.

In patients with BMI >25, out of 212 patients, 55.6% showed RMSM. While in patients with BMI ≤25, out of 188 patients, 44.4% showed RMSM. The difference was statistically significant highlighting that BMI is an important risk factor for RMSM. There was no statistically significant association observed between FBS and RMSM in type 2 diabetes mellitus patients (Table 4).

Various vascular complications observed in study population in controlled and uncontrolled T2DM patients are listed in Table 5. Vascular complications were observed in 146 (73%) patients in uncontrolled T2DM and in 82 (41%) patients in controlled T2DM group. There was a statistically significant association between the two groups for neuropathy, retinopathy and PVD.

There was a significant association seen between vascular complications of T2DM and RMSM in both uncontrolled and controlled diabetes patients (Table 6). Out of 146 patients who showed vascular complications in uncontrolled T2DM, 67.13% showed RMSM while in controlled T2DM, out of 82 patients who showed vascular complications, 47.56% had RMSM.

DISCUSSION

Diabetes mellitus is associated with various rheumatological manifestations which have been generally ignored and poorly treated as compared to other complications such as neuropathy, retinopathy and nephropathy. We also observed a positive correlation between rheumatological complications with disease duration and glycemic control. Overall prevalence of RMSM in type 2 diabetes mellitus patients was found to be 50.5%. They were found in 63% (126 patients) cases in uncontrolled T2DM and 38% (76 patients) cases in controlled T2DM cases respectively. Diabetic chieroarthropathy was the most common musculoskeletal manifestation followed by DISH and frozen shoulder respectively.

Diabetic chieroarthropathy was found in 34% of the patients in our study which is consistent with the study conducted by Chammas et al[17] where the prevalence was found to be 33% in diabetic individuals. The prevalence of Diabetic chieroarthropathy was significantly higher in uncontrolled type 2 diabetes mellitus group than in controlled type 2 diabetes mellitus patients.

The prevalence of osteoarthritis in diabetic individuals was found to be 33%. The results were similar to studies conducted by Sarkar et al[18] and Mathew AJ et al[10] where the prevalence of osteoarthritis was 31% and 32.64% respectively. The difference between uncontrolled and controlled diabetes group was not statistically significant (p=.258). This is in line with the study by Sturmer et al[19] and Sarkar et al[18] who didn't find a significant association between type 2 DM and osteoarthritis knee. Based on these studies, we cannot definitely conclude that diabetes

Risk Factor		RMSM		Total	P Value	Odds ratio	95% CI
		Yes (%)	No (%)				
BMI	>25	118(55.6)	94(44.4)	212	0.02*	1.55	1.05-2.31
	≤25	84(44.7)	104(55.3)	188			
FBS	>126	103(53.1)	91(46.9)	194	0.314	1.22	0.83-1.81
	≤126	99(48)	107(52)	206			
T2DM	Uncontrolled	126(63)	74(37)	200	<0.01*	2.78	1.85-4.17
	Controlled	76(38)	124(62)	200			
Total		202	198	400			
* Significant							

Table-4: Relationship of BMI and FBS with RMSM in TYPE 2 DM patients

Vascular Complications	Uncontrolled T2DM (%)	Controlled T2DM (%)	P Value	Odds ratio	95% CI
Neuropathy	64 (32%)	42 (21%)	0.01*	1.72	1.10-2.72
Retinopathy	36 (18%)	20 (10%)	0.02*	1.97	1.09-3.55
Nephropathy	30 (15%)	18 (9%)	0.06	1.78	0.95-3.31
CAD	22 (11%)	16 (8%)	0.30	1.42	0.72-2.79
CVA	16 (8%)	10 (5%)	0.22	1.65	0.73-3.73
PVD	11 (6%)	03 (2%)	0.04*	3.82	1.04-13.91
*Significant, CVA= Cerebrovascular accident, CAD= Coronary artery disease, PVD= Peripheral vascular disease					

Table-5: Vascular Complications in Uncontrolled and Controlled T2DM Patients

T2DM	Vascular complications	RMSM			P value	Odds ratio	95% CI
		Yes (%)	No (%)	Total (%)			
Uncontrolled T2DM	Yes (%)	98(67.13)	48(32.87)	146(100)	0.04	1.89	1.003-3.58
	No (%)	28 (51.85)	26(48.15)	54(100)			
	Total	126 (63)	74(37)	200(100)			
Controlled T2DM	Yes (%)	39 (47.56)	43(52.44)	82(100)	0.02	1.98	1.10-3.55
	No (%)	37 (31.35)	81 68.65)	118(100)			
	Total	76 (38)	124 (62)	200(100)			

Table-6: RMSM and Vascular complications in Uncontrolled and Controlled T2DM Patients ble 6: RMSM and Vascular complications in Uncontrolled and Controlled T2DM Patients

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 associated morbidity.

DISH was found in 26% of the cases in our study which is consistent with the study by Holt[20] who reported a 25% prevalence of DISH, especially of the spine, and pelvic ligaments among patients with type 2 DM. Sarkar et al[18] and Mathew et al[10] reported a prevalence of 28% and 14.52% respectively for DISH. The difference in uncontrolled and controlled diabetes mellitus group was statistically significant.

In the present study the prevalence of frozen shoulder was found to be 23% which is consistent with the study by Ramchurn et al.[6] with a prevalence of 25%. Aydeniz et al[7], Mathew AJ et al[10] and Sarkar et al[18] found the prevalence of frozen shoulder as 15%, 16.45% and 20 % respectively. The prevalence of frozen shoulder was statistically significantly between uncontrolled and controlled type 2 diabetes mellitus patients.

The prevalence of carpal tunnel syndrome was found to be 17.5%, the difference being statistically significant in uncontrolled and controlled type 2 diabetes mellitus patients. The results were comparable to a study conducted by Chammas et al[17] where the prevalence of carpal tunnel syndrome in type 2 DM patients was found to be 15-25%.

The prevalence of dupuytren's contracture was found to be 12.5% in diabetic individuals. The difference in uncontrolled and controlled diabetes mellitus group was statistically significant. Similar results were found in a study conducted by Aydeniz et al[7] in which the prevalence of dupuytren's contracture was found to be 12.7% Ramchurn et al[6] reported 13% prevalence of Dupuytren's contracture in their study.

In our study, Flexor tenosynovitis had a prevalence of 9% in patients suffering from type 2 diabetes. Studies carried out by Sarkar et al[18] and Mathew et al[10] showed the prevalence of flexor tenosynovitis to be 5 and 4.4% respectively whereas the study carried out by Chammas et al[17] showed the prevalence to be 20%. The respective prevalence in uncontrolled and controlled type 2 diabetes mellitus patients was 7% vs. 3% which was not statistically significant.

Prevalence of neuropathic joints was also found to be 4.5%. Sarkar et al[18] reported a prevalence of neuroarthropathy of knee and foot as 3.1%.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 difference in uncontrolled and controlled diabetes mellitus group was statistically significant.

Thus, there was a statistically significant increased prevalence of most of the rheumatological complications between patients of uncontrolled and controlled type 2 diabetes mellitus with the exception of osteoarthritis and flexor tenosynovitis.

Also there was a significant association seen between vascular complications of T2DM and RMSM in both uncontrolled and controlled type 2 diabetes patients. Study by Gurinder Mohan et al[21] noted significant association between certain manifestations and chronic microangiopathic conditions like retinopathy and nephropathy. Diabetic cheiroarthropathy and dupuytren's contracture were found to have a statistically significant relationship with retinopathy and nephropathy.[21]

CONCLUSION

In our study proportionately higher prevalence of rheumatological complications was observed in uncontrolled type 2 diabetes mellitus patients than among patients with good glycemic control. We recommend thorough evaluation for rheumatological complication along with micro and macrovascular complications, as they are often missed or clinically overlooked, especially among those with poorly controlled diabetes and those with vascular complications. This study also highlights the importance of various other risk factors for RMSM such as duration of diabetes and obesity (BMI). Early detection, diagnosis, good glycemic control and treatment may reduce the morbidity associated with RMSM and thereby helps in improving the quality of life in patients with Type 2 Diabetes mellitus.

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