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ORIGINAL ARTICLE

Musculoskeletal manifestations in diabetic versus prediabetic patients

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Abstract

Aim: This study was carried out to evaluate the prevalence of musculoskeletal manifestations in a sample of patients with diabetes mellitus (DM) and those with prediabetes and compare the findings between the two groups.

Methods: One hundred and eighty-eight patients with DM and 125 prediabetic subjects were randomly enrolled in this cross-sectional study. Demographic data and past history were recorded. Musculoskeletal physical examinations were done by a single rheumatologist. Regression analyses were employed to assess the crude and adjusted effects of determinants on DM musculoskeletal manifestations (DMMMs).

Results: Female/male ratio was not significantly different between diabetic and prediabetic patients (4.4 *vs*. 4.7, respectively, $P = 0.9$). However, diabetic patients were significantly older than the prediabetic ones (56.6 *vs*. 52 years, respectively, $P = 0.0001$); 83.5% of diabetic patients and 52.8% of prediabetic ones had at least one musculoskeletal manifestation ($P = 0.0001$). The prevalence of knee osteoarthritis and shoulder involvement were almost two times more common ($P = 0.0001$ and $P = 0.015$) in diabetic patients than in prediabetic ones (73.4% *vs*. 38% and 21.2% *vs*. 9.5%, respectively). Prevalence of carpal tunnel syndrome (CTS) was 48% and 36.5% in patients with diabetes and prediabetes, respectively ($P = 0.053$). Multivariate backward regression analysis showed age, sex, BMI (body mass index) and DM as the significant determinants in development of musculoskeletal manifestations in all subjects. Age and BMI were the only significant factors associated with musculoskeletal manifestations in both diabetic and prediabetic patients.

Conclusion: Diabetic and prediabetic patients may show high prevalence of musculoskeletal manifestations. In non-diabetic patients diagnosed with CTS, prediabetes might be ruled out.

Key words: diabetes mellitus, musculoskeletal manifestations, prediabetes.

INTRODUCTION

Diabetes mellitus (DM) is among the first seven leading causes of death worldwide.[1] It involves multiple organs such as nervous system, kidneys and eyes. In other words, DM brings along many recognized complications that grab the immediate attention of both clinicians and patients. Musculoskeletal system involves 60–70% of body mass and includes muscles, bones, joints and the surrounding connective tissues.[2] However, involvement of the musculoskeletal system is usually unrecognized or under-recognized.[3,4] Many diabetic patients suffer from musculoskeletal manifestations which cause substantial morbidities in their lives.[5] Poor

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diagnosis and management of musculoskeletal complications leads to more inactive life style, poorer control of blood sugar, earlier appearance of DM complications and consequently, worsened quality of life.[5] Early diagnosis of musculoskeletal complications in diabetic patients can prevent early onset of long-term morbidities. A few investigators demonstrated age and DM duration as risk factors for musculoskeletal manifestations.[6–10] For instance, Hoff *et al.*[8] demonstrated an odds ratio (OR) of 1.6 for patients aged < 60 with DM versus subjects aged < 60 with no DM, whereas for those aged ≥ 60 years, the OR was only 1.1. Similarly, Mathew *et al.*[6] showed an OR of about 1.5 for DM duration as a significant risk factor for musculoskeletal manifestations. Two studies also revealed musculoskeletal-associated co-morbidities such as retinopathy in patients with DM.[3,11] For example, Attar *et al.*[3] showed an OR of 3.21 for retinopathy. The prevalence of prediabetic state is increasing worldwide and will include close to half a billion world population by 2030.[12] Rough estimates show that for every diabetic patient, there are three prediabetic patients aged ≥ 20 years in the US.[13] Although the relationship of other co-morbidities such as neuropathy and retinopathy in prediabetic state has been vastly studied,[14–19] the picture of musculoskeletal involvement in this phase has been less clearly drawn. The nature, prevalence and the determinant factors of musculoskeletal manifestations in diabetic and prediabetic patients have not yet been studied in detail in Iran. The current study was conducted to assess the prevalence of musculoskeletal manifestations in a sample of patients with DM and those with prediabetes and compare the findings between the two groups.

METHODS

Study design and population

This was a cross-sectional study carried out in Isfahan Endocrine and Metabolic Research Center (IEMRC) affiliated with Isfahan University of Medical Sciences (MUI) during the time period of September 2011 to March 2012. Isfahan, the second largest city in Iran, is located in the central part of country. The city has around two million people in a province of over five million. Approval of the MUI Ethics Committee was obtained before the start of study. Given the $Z_{1-\alpha/2} = 1.96$, $P1$ and $P2 = 0.5$ and $d = 0.1$ (P and d denote expected prevalence and precision, respectively), the calculated sample size was 98 in each group. We increased the total sample size to over 300, in order to have an 80% power to detect the appropriate OR at two different prevalence levels of the musculoskeletal manifestations.

The patients were diagnosed according to American Diabetes Association (ADA) criteria[20] as follows: fasting blood sugar (FBS) ≥ 126 mg/dL or a 2-h postprandial plasma blood sugar ≥ 200 mg/dL for diabetic patients and impaired FBS (100–125 mg/dL) or impaired glucose tolerance test (GTT, 2-h postprandial plasma blood sugar of 140–199 mg/dL) for prediabetic subjects. All diabetic and prediabetic patients were randomly selected from the population covered by IEMRC. IEMRC has registry profiles of prediabetic and diabetic patients of the city of Isfahan. Two hundred and twenty patients with DM and 250 with prediabetes were called. All prediabetic patients were relatives of diabetic patients. They were followed up regularly every year by checking their FBS or GTT. When their FBS fulfilled the ADA criteria for prediabetes, they were diagnosed with 'prediabetes'. The first time that FBS test fulfilled the criteria of prediabetes was considered as the beginning of prediabetes.

Exclusion criteria included past history of autoimmune rheumatic diseases and trauma-associated musculoskeletal involvements. Demographic data (age and sex) and full past history were recorded. A thorough musculoskeletal physical examination was conducted in all patients by a single rheumatologist, who assessed shoulders, elbows, hands, knees and feet, evaluating the most common musculoskeletal manifestations presented in patients with DM. These manifestations were defined as follows.

1. Rotator cuff tendinitis: tenderness was present on the lateral side of the head of the humerus below the acromion. Active abduction of arm induced severe pain, especially in the arc between 60 and 120°.[21]
2. Frozen shoulder: it is known as adhesive capsulitis. Total movement limitations on passive and active movements were present, principally on abduction and external rotations.[21]
3. Tennis elbow: It is also known as lateral epicondylitis. Tenderness of the soft tissue over the lateral epicondyle was present. Wrist extension and supination against resistance reproduced the pain.[21]
4. Golf elbow (medial epicondylitis): tenderness on distal side of medial epicondyle was present. Wrist flexion and pronation against resistance while the elbow was extended reproduced the pain.[21]
5. De Quervain's tenosynovitis: pain and tenderness on styloid process of radius confirmed by Finkelstein's test.[21]

6 Trigger finger: it was diagnosed by finger locking in extension and/or flexion.[22]
7 Carpal tunnel syndrome (CTS): it was diagnosed by positive Tinel sign or positive Phallen sign.[23]
8 Dupuytren's contracture: it was defined by palmar and digit nodules, palmar thickening, band formation and digital flex contractures.[24]
9 Limited joint mobility syndrome: it is also known as diabetic cheiroarthropathy, and was diagnosed by positive Prayer sign.[25]
10 Knee osteoarthritis: presence of knee pain and at least three of the followings confirmed the diagnosis of knee osteoarthritis: aged older than 50 years, stiffness less than 30 min, crepitus, bony tenderness, bony enlargement and no palpable warmth.[26]
11 Charcot joint: typical neuropathic arthropathy characterized by acute/subacute monoarthritis along with swelling, erythema, significant sensory deficit and a degree of pain that was less than expected in weight-bearing joints (foot joints). The sensation was evaluated by monofilament test.[27]

Statistical analysis

SPSS program (SPSS Inc., Chicago, IL, USA) was used to analyze the data. Student's *t*-test was applied to compare continuous variables between diabetic and prediabetic patients. Chi-square test was used to compare categorical variables between the two groups. Univariate logistic regression analysis was employed to evaluate the crude effects of determinants on DM musculoskeletal manifestations (DMMMs). All factors were used in multivariate backward stepwise logistic regression analysis to estimate their adjusted effects on DMMMs. *P*-value = 0.05 was considered to remove variables from the models. The OR and the 95% confidence intervals (CIs) were computed in the regression analyses.

RESULTS

Baseline features

One hundred and eighty-eight consenting patients with type 2 DM and 125 prediabetic subjects who consented to participate in the study were enrolled. Female/male ratio in prediabetic and diabetic patients was 4.7 (103/22) and 4.4 (154/35), respectively ($P = 0.9$). The mean (SD) age of diabetic patients was 56.6 (9) years whereas the mean age of prediabetics was 52 (8.8) years ($P = 0.0001$). The mean (SD) duration of diabetes was 11.3 (6.7) years, whereas the mean duration of prediabetes was 2.85 (1.5) years ($P = 0.0001$). Comparison of different baseline features between the two groups is presented in Table 1.

Musculoskeletal manifestations

One hundred and fifty-seven diabetic patients (83.5%) and 66 prediabetics (52.8%) had at least one of the musculoskeletal manifestations ($P = 0.0001$). Knee osteoarthritis, CTS and rotator cuff tendinitis were the most common musculoskeletal manifestations in decreasing order. However, the prevalence of musculoskeletal manifestations in shoulder ($P = 0.015$) and knee ($P = 0.0001$) joints was significantly more common in diabetic patients than in prediabetics (Table 1).

According to the quality of control of blood sugar, the patients were divided in three groups of poor control (HbA1C $\geq$ 8%), moderate control (HbA1C 6.5–8%) and good control (HbA1C < 6.5%). The prevalence of musculoskeletal manifestations in the three groups is summarized in Table 2.

Determinants of presence of musculoskeletal manifestations in all patients

Univariate logistic regression analysis was applied to assess the correlation of each variable (independent factor) with the presence of musculoskeletal manifestations (dependent factor) in all subjects. The results of significant correlations and the related ORs are revealed in Table 3. All factors were included in multivariate backward stepwise logistic regression analysis. Implementation of backward multivariate logistic regression analysis eliminated nine factors and demonstrated age, sex, BMI and presence of DM as the significant determinants in the presence of any musculoskeletal manifestations in all subjects (Table 3).

Determinants of presence of musculoskeletal manifestations in prediabetics

The results of univariate logistic regression analysis, the significant correlations and their ORs are shown in Table 4. Multivariate backward logistic regression analysis showed that age and BMI of patients may significantly determine the presence of musculoskeletal manifestations in prediabetic patients (Table 4).

Determinants of presence of musculoskeletal manifestations in diabetics

The significant results of univariate logistic regression analysis and the associated ORs are demonstrated in Table 5. After execution of multivariate backward logistic regression analysis, BMI and age of the

Table 1 Comparison of different patients' characteristics between the two groups

		Pre-diabetics, n = 125	Diabetics, n = 188	
Patients characteristics				P†
Age, years	Range	30–75	30–79	
	Median	51	57	
	Mean (SD)	52 (8.8)	56.6 (9)	0.0001
Duration, years	Range	1–13	1–35	
	Median	3	10	
	Mean (SD)	2.85 (1.5)	11.3 (6.7)	0.0001
Systolic BP, mmHg	Range	90–170	85–170	
	Median	120	120	
	Mean (SD)	118 (15.1)	120.8 (15.8)	0.1
Diastolic BP, mmHg	Range	30–90	50–111	
	Median	80	80	
	Mean (SD)	75.9 (9.3)	76 (9.3)	0.9
LDL, mg/dL	Range	37–251	34–184	
	Median	117.5	91	
	Mean (SD)	117.8 (35.4)	95.8 (26.2)	0.0001
HDL, mg/dL	Range	20–80	13–92	
	Median	44	42	
	Mean (SD)	44.8 (10.3)	42.8 (11.7)	0.1
TG, mg/dL	Range	27–382	42–740	
	Median	143	137	
	Mean (SD)	152.3 (64.3)	160.1 (86.3)	0.4
Waist circumference, cm	Range	70–127	70–136	
	Median	97	102	
	Mean (SD)	96 (10)	102.5 (12.7)	0.0001
BMI, kg/m^2	Range	19.2–39.4	17–68.4	
	Median	28	29.9	
	Mean (SD)	28.4 (4.1)	30.3 (5.9)	0.001
HbA1C, %	Range	4.1–9.9	4.9–13	
	Median	5.6	7.3	
	Mean (SD)	5.6 (1.1)	7.6 (1.8)	0.0001
Musculoskeletal manifestations				P‡
Shoulder	Normal	113 (90.5%)	148 (78.7%)	0.015
	Rotator cuff tendinitis	12 (9.5%)	36 (19.1%)	
	Frozen shoulder	0	4 (2.1%)	
Elbow	Normal	120 (96%)	170 (90.4%)	0.064
	Tennis elbow	5 (4%)	18 (9.6%)	
	Golf elbow	0	0	
Wrist	Normal	79 (63.5%)	98 (52.1%)	0.053
	De Quervain's tenosynovitis	0	0	
	Carpal tunnel syndrome	46 (36.5%)	90 (47.9%)	
Hand	Normal	125 (100%)	184 (97.9%)	0.26
	Trigger finger	0	2 (1.1%)	
	Dupuytren's contracture	0	2 (1.1%)	
	Limited joint mobility syndrome	0	0	
Knee	Normal	77 (62%)	50 (26.6%)	0.0001
	Osteoarthritis	48 (38%)	138 (73.4%)	
Foot	Normal	125 (100%)	188 (100%)	NA
	Charcot joint	0	0	
Any musculoskeletal manifestations	No	59 (47.2%)	31 (16.5%)	0.0001
	Yes	66 (52.8%)	157 (83.5%)	

†Student's t-test was applied to compare means between the two groups. ‡Chi-square test was applied to compare distributions of findings between the two groups. BP, blood pressure; HbA1C, glycated hemoglobin; HDL, high density lipoprotein; LDL, low density lipoprotein; NA, not applicable; SD, standard deviation; TG, triglyceride.

Table 2 Distribution of musculoskeletal manifestations in diabetic patients according to different levels of HbA1C

	HbA1C			*P*-value
	< 6.5%	6.5–8%	≥ 8%	
Any musculoskeletal manifestations				
No	9 (5%)	11 (6%)	9 (5%)	0.6
Yes	56 (31%)	44 (24%)	53 (29%)	

HbA1C, glycosylated hemoglobin.

patients remained as the only significant factors in determining the presence of DMMMs in diabetic patients (Table 5).

DISCUSSION

The current study showed the high rates of DMMMs in patients with type 2 DM and the high rates of musculoskeletal manifestations in prediabetic patients. The attribution of type 2 DM in development of DMMMs has also been shown by other studies. For instance, Mathew *et al.*[6] demonstrated high prevalence of DMMMs in Indian diabetic patients compared to a healthy population. However, this is one of the few studies showing the high prevalence of musculoskeletal manifestations in prediabetes. Arup *et al.*[28] conducted a study on patients with rheumatologic manifestations in a tertiary care center and observed impaired glucose tolerance test in 20.4% of patients with frozen shoulder, 25.2% of cases with osteoarthritis and 25% of those with Dupuytren's contracture. Origuchi *et al.* reported an interesting retrospective study which examined the levels of hemoglobin A1C in a total of 498 patients with rheumatic diseases over a 1-year period. They observed HbA1C > 5.6% in 82% of patients and concluded that the incidence of prediabetes might be high in patients with rheumatic disease.[29] The most common DMMM in our study was knee osteoarthritis followed by CTS and rotator cuff tendinitis. The same pattern was observed in prediabetic patients.

Gulliford *et al.*[30] showed the higher incidence of CTS in prediabetic patients compared with healthy controls (relative risk = 1.36). Only knee osteoarthritis and rotator cuff tendinitis were significantly more common in diabetic patients than in prediabetic ones. In other words, both musculoskeletal manifestations were almost two times more prevalent in diabetic patients. On the other hand, the prevalence of the most common musculoskeletal manifestations in the general population of Iran found by the Community Oriented Program for Control of Rheumatic Diseases (COPCORD) study were knee osteoarthritis, rotator cuff tendinitis and CTS (Table 6).[31–33] The selected COPCORD studies represented almost all ethnic groups of urban populations in Iran. The comparison of our findings with those of COPCORD studies showed that these three musculoskeletal manifestations were much more preva-

Table 3 Univariate and multivariate backward stepwise logistic analyses in all subjects

Characteristics	Prediabetic and diabetic patients					
	Crude effect			Adjusted effect		
	β	*P*	OR (95% CI)	β	*P*	OR (95% CI)
Sex (female *vs*. male)	−0.62	0.013	0.54 (0.33–0.88)	−0.97	0.014	0.38 (0.17–0.82)
Age	0.07	0.0001	1.07 (1.05–1.1)	0.07	0.0001	1.07 (1.03–1.10)
DM (no *vs*. yes)	−1.51	0.0001	0.22 (0.13–0.37)	−1.17	0.0001	0.31 (0.16–0.57)
BMI	0.144	0.0001	1.15 (1.08–1.23)	0.11	0.002	1.10 (1.04–1.20)
Waist	0.052	0.0001	1.05 (1.03–1.08)	Deleted by backward elimination		
Duration of DM	0.133	0.0001	1.14 (1.08–1.21)	Deleted by backward elimination		
SBP	0.004	0.60	1.004 (0.99–1.020)	Deleted by backward elimination		
DBP	0.13	0.33	1.01 (0.990–1.040)	Deleted by backward elimination		
Neuropathy (yes *vs*. no)	−0.93	0.06	0.39 (0.150–1.050)	Deleted by backward elimination		
HbA1C	0.313	0.0001	1.37 (1.160–1.620)	Deleted by backward elimination		
LDL	−0.013	0.002	0.99 (0.098–0.995)	Deleted by backward elimination		
HDL	−0.014	0.21	0.99 (0.960–1.008)	Deleted by backward elimination		
TG	0.001	0.40	1.001 (0.99–1.005)	Deleted by backward elimination		

BMI; body mass index; DBP, diastolic blood pressure; DM, diabetes mellitus; HbA1C, glycosylated hemoglobin; HDL; high density lipoprotein; LDL, low density lipoprotein; OR, odds ratio; SBP, systolic blood pressure; TG, triglyceride.

Table 4 Univariate and multivariate backward stepwise logistic regression analyses in prediabetic patients

Characteristics	Pre-diabetic patients, n = 125					
	Crude effect			Adjusted effect		
	β	*P*	OR (95% CI)	β	*P*	OR (95% CI)
Sex (female *vs*. male)	−0.813	0.10	0.44 (0.17–1.150)	Deleted by backward elimination		
Age	0.060	0.008	1.06 (1.016–1.11)	0.054	0.035	1.05 (1.004–1.1)
BMI	0.142	0.004	1.15 (1.05–1.270)	0.14	0.01	1.15 (1.03–1.27)
Waist	0.030	0.10	1.03 (0.99–1.070)	Deleted by backward elimination		
SBP	0.001	0.95	1.001 (0.98–1.02)	Deleted by backward elimination		
DBP	−0.004	0.84	0.99 (0.96–1.030)	Deleted by backward elimination		
HbA1C	0.160	0.39	1.17 (0.81–1.680)	Deleted by backward elimination		
LDL	−0.002	0.68	0.998 (0.98–1.008)	Deleted by backward elimination		
HDL	−0.018	0.31	0.98 (0.95–1.020)	Deleted by backward elimination		
TG	0.001	0.81	1.001 (0.99–1.006)	Deleted by backward elimination		

BMI; body mass index; DBP, diastolic blood pressure; DM, diabetes mellitus; HbA1C, glycosylated hemoglobin; HDL; high density lipoprotein; LDL, low density lipoprotein; OR, odds ratio; SBP, systolic blood pressure; TG, triglyceride.

Table 5 Univariate and multivariate backward stepwise logistic regression analyses in patients with type 2 diabetes mellitus

Characteristics	Patients with type 2 diabetes mellitus, n = 188					
	Crude effect			Adjusted effect		
	β	*P*	OR (95% CI)	β	*P*	OR (95% CI)
Sex (female *vs*. male)	0.723	0.1	2.06 (0.85–5)	Deleted by backward elimination		
Age	0.087	0.0001	1.1 (1.04–1.14)	0.071	0.013	1.07 (1.015–1.13)
BMI	0.124	0.009	1.13 (1.03–1.24)	0.109	0.025	1.11 (1.014–1.226)
Waist	0.052	0.002	1.05 (1.02–1.09)	Deleted by backward elimination		
Duration of DM	0.075	0.035	1.08 (1.005–1.16)	Deleted by backward elimination		
SBP	−0.001	0.95	0.99 (0.97–1.02)	Deleted by backward elimination		
DBP	0.034	0.11	1.03 (0.99–1.08)	Deleted by backward elimination		
Neuropathy (yes *vs*. no)	−0.164	0.75	0.85 (0.30–2.40)	Deleted by backward elimination		
HbA1C	0.110	0.35	1.11 (0.89–1.40)	Deleted by backward elimination		
LDL	−0.013	0.07	0.98 (0.97–1.001)	Deleted by backward elimination		
HDL	−0.002	0.91	0.99 (0.96–1.03)	Deleted by backward elimination		
TG	0.002	0.55	1.002 (0.99–1.007)	Deleted by backward elimination		

BMI; body mass index; DBP, diastolic blood pressure; DM, diabetes mellitus; HbA1C, glycosylated hemoglobin; HDL; high density lipoprotein; LDL, low density lipoprotein; OR, odds ratio; SBP, systolic blood pressure; TG, triglyceride.

lent in diabetic and prediabetic patients than in the general population. Given the similarity of our population with that of COPCORD studies, our findings point out clearly that DM and prediabetes are both determinants of these three musculoskeletal manifestations, especially CTS. Although the association between DM and CTS has been ascribed before,[34,35] our finding highlighted the importance of paying special attention to prediabetes in non-diabetic patients diagnosed with CTS. In order to properly manage musculoskeletal manifestations in non-diabetic patients, prediabetes might be ruled out. Mistreatment of DMMMs by medical doctors or careless attention to DMMMs by patients with type 2 DM is very common.[5] The direct consequence of mismanagement of DMMMs will be decreased quality of life. Because of the high prevalence of DM and prediabetes, the burden on the health system could be enormous.

Age and BMI of the patients were the only significant factors to determine the presence of musculoskeletal manifestations in both diabetic and prediabetic patients. In other words, the older and the more obese patients with DM or prediabetes might have the higher probability of having musculoskeletal manifestations. The correlations of the above-mentioned determinants and musculoskeletal manifestations in diabetic and pre-

Table 6 Comparison of different musculoskeletal manifestations between our diabetic/prediabtic patients and normal population of urban COPCORD studies in Iran

Musculoskeletal manifestations	Prevalence, %				
	Our study		Iran COPCORD (Tehran)†	Iran COPCORD (Sanandaj)‡	Iran COPCORD (Zahedan)§
	Prediabetes	Diabetes			
Rotator cuff tendinitis	9.5	19.1	2.5	Not reported	Not reported
Frozen shoulder	0	2.1	0.54	1	0.47
Tennis elbow	4	9.6	1.21	0.7	1
Golf elbow	0	0	0.51	0.4	0.1
De Quervain's tenosynovitis	0	0	0.23	0.14	0.42
Carpal tunnel syndrome	36.5	47.9	1.3	1.5	1.9
Trigger finger	0	1.1	0.21	0.4	0.04
Dupuytren's contracture	0	1.1	Not reported	Not reported	Not reported
Limited joint mobility syndrome	0	0	Not reported	Not reported	Not reported
Knee osteoarthritis	38	73.4	15.3	18.8	17
Charcot joint	0	0	Not reported	Not reported	Not reported

†Reference 31; ‡Reference 32; §Reference 33. COPCORD, Community Oriented Program in the Rheumatic Diseases.

diabetic patients have not been vastly investigated.[36–39] A few studies revealed significant associations of age and DM duration with DMMMs.[6,36]

The pathogenesis of musculoskeletal manifestations in prediabetes and DM is not well defined. Different studies have shown that in patients with metabolic syndrome, musculoskeletal pain, neck pain, shoulder pain and tendinopathies are more common than in people with no metabolic syndrome.[40–42] Furthermore, the role of excess of advanced glycation end-products (AGEs) has been previously noticed.[43,44] Uncontrolled DM and/or long duration DM were associated with higher AGEs and consequently, higher deposition in different organs such as connective tissues.[45] The resultant thicker fibrous tissue limited the normal functionality of the joints.[46] Then, the higher the duration of DM results in the higher production of AGEs, and consequently the higher the detrimental effects on the musculoskeletal systems. That is why musculoskeletal manifestations are more common in DM than in prediabetes. This pathogenic effect of AGEs has been implicated in the development of different DMMMs, such as rotator cuff tendinitis, frozen shoulder and trigger finger.[46] Similarly, the association between osteoarthritis and DM has been investigated. Articular degeneration of cartilage in diabetic osteoarthritis has been probably the result of adipokine/cytokines secreted from adipose tissues and extracellular accumulation of AGEs.[47,48] One of the limitations of the current study was lack of healthy subjects. However, the study population in our research included urban people living in the second largest city of Iran, Isfahan. Likewise, the populations investigated by COPCORD studies were urban people living in large cities in Iran. Then, it seems prudent to compare our findings with those of the COPCORD studies. A few musculoskeletal manifestations such as diffuse idiopathic skeletal hyperostosis were not evaluated in the current study because X-ray was necessary for this diagnosis and the Ethics Committee did not approve taking X-rays of all subjects. Although physical examination was not 100% sensitive or specific in diagnosing many cases, sticking to the diagnostic guidelines and definitions presented in the references[21–27] promoted the accuracy of diagnoses. Application of other diagnostic methods could have increased the sensitivity and the specificity of diagnosis but, some of them, such as X-ray had ethical barriers to be used for all subjects. On the other hand, inclusion of musculoskeletal manifestations due to autoimmune rheumatic diseases and trauma could have been more illuminative. This was one of the first and few studies carried out to evaluate the prevalence of musculoskeletal manifestations in prediabetes. Another strength of our study was inclusion of patients with prediabetes from a well-established registry and having approximate duration of prediabetes.

In conclusion, this study showed high prevalence of musculoskeletal manifestations in diabetic and prediabetic patients. Special attention should be made to knee, shoulder and wrist in these patients.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTION

Study design: Alimohammad Fatemi, Bijan Iraj, Jafar Barzanian, Mohammadreza Maracy. Data gathering: Alimohammad Fatemi, Jafar Barzanian. Data analysis: Abbas Smiley, Mohammadreza Maracy. Primary draft of article: Abbas Smiley, Alimohammad Fatemi, Bijan Iraj. Final draft of article: all authors.

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