Prevalence and Prevention of Rheumatologic Manifestations and their Relationship with Blood Glucose Control in Patients with Type II Diabetes

Abstract

Background: Musculoskeletal disorders in diabetic patients are associated with pain and disability, and thus, a significant reduction in quality of life. The current study was conducted with the aim of evaluating the frequency and prevention of rheumatologic manifestations and their association with blood glucose levels in diabetic patients. **Methods:** In this cross-sectional study, a total of 273 patients with type II diabetes, referred to the diabetes clinic, were selected by using the census method. Using a checklist, demographic, and clinical data, including duration of diabetes, blood glucose level, HbA1c, type of diabetes, BMI, history of smoking, blood pressure, serum cholesterol level, triglyceride, HDL, LDL, and musculoskeletal disorder type were analyzed using SPSS20 software application using independent *t*-test. Modeling was performed to obtain the best fit using logistic regression. The significance level was considered less than 0.05. **Results:** 62.6% of patients had at least one of the rheumatologic complications. The most common complication was related to carpal tunnel syndrome (26.4%), followed by muscle contraction (23.8%). By moderating the effects of other variables, the odds ratio for rheumatoid complications was obtained as 1.74 with one unit of increase in HbA1c, which was statistically significant. In examining the influential variables, high age, gender, smoking, and BMI showed statistically significant effects (). **Conclusions:** Given the high prevalence of musculoskeletal disorders in diabetic patients, early diagnosis and timely treatment of the complications are crucial. It is recommended that musculoskeletal examinations be included as an important part of regular care for these patients.

Keywords: *Glycemic control, HbA1c, musculoskeletal disorder, Rafsanjan, type II diabetes*

Zahra Kamiab,
Negar Shafaee[1],
Poya Saied Askar[2],
Mitra Abbasifard[3]

Department of Family Medicine, School of Medicine, Clinical Research Development Unit, Ali-Ibn Abi-Talib Hospital, Rafsanjan University of Medical Sciences, [1]General Physician, Clinical Research Development Unit, Ali-Ibn Abi-Talib Hospital, Rafsanjan University of Medical Sciences, [2]Medical Student, Rafsanjan University of Medical Sciences, [3]Department of Internal Medicine, School of Medicine; Clinical Research Development Unit, Ali-Ibn Abi-Talib Hospital, Rafsanjan University of Medical Sciences, Rafsanjan, Iran

Introduction

There is no doubt that diabetes is one of the most challenging health problems in the 21st century. In 2013, approximately 382 million cases of diabetes were reported around the world, which is estimated to increase to about 592 million by 2035.[1] In Iran, based on the national reports, the prevalence of the disease was reported as 11.5% (about 4.5 million adult people) in 2011, which shows a growth of 35% compared to 2005[2]; and it is estimated that the number of diabetic patients will reach 9.2 million by the year 2030.[3] This significant growth of the disease will result in an increase in mortality and a decline in quality of life, as well as significant direct and indirect costs imposed on the health care system of the country.[4]

Diabetes is associated with the development of microvascular and macrovascular complications, along with impairment in the function of other organs. One of the most well-known of these complications involves musculoskeletal disorders.[5,6] Although musculoskeletal disorders do not lead to mortality, they are associated with pain and disability and a significant decline in quality of life.[7] In addition, these are among the forgotten complications of diabetes, and patients and health care staff do not pay enough attention to them. The results of various studies have reported different frequencies for the occurrence of such complications. However, the most common musculoskeletal disorders in these patients include shoulder capsulitis, limited joint mobility, Dupuytren's contracture, carpal tunnel syndrome, and trigger finger. Other disorders are less commonly seen, and some disorders, such as myonecrosis, are seen merely in diabetic patients.[8] Among naturally occurring reducing sugars, glucose exhibits the slowest glycation rate, unlike fructose, glucose-6-phosphate or glyceraldehyde-3-phosphate, which

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are intracellularly present at small levels but can form AGEs at a faster rate, especially under high temperatures, i.e., *ex vivo*.[9] Recent studies have suggested that advanced glycation end-products (AGEs) may be a key factor in the development of metabolic memory in diabetic complications, because AGEs are produced and accumulated irreversibly in the body, depending on the degree of blood sugar regulation and duration.[10]

Due to disability and reducing the function of diabetic patients These manifestations are of great importance. According to the costs associated with reducing and destroying patient performance on the community, investigating these rheumatologic manifestations is important.[11] The importance of accurately estimating the prevalence of these disorders and the risk factors associated with them is clear in prevention, early diagnosis, and control of pain and disability caused by them. The objective of this study was to evaluate the prevalence and prevention of rheumatologic manifestations and their association with blood glucose levels in diabetic patients. Moreover, the study aimed to investigate some relevant risk factors in patients visiting a diabetes clinic in an educational hospital.

Methods

In this cross-sectional study, all patients referred to the diabetes clinic of an educational hospital were evaluated in the second half of 2016 based on the study's inclusion and exclusion criteria. The inclusion criteria included having diabetes, and a lack of rheumatoid autoimmune diseases, vascular collagen diseases, chronic kidney disease, and stroke, and lack of musculoskeletal disorders caused by ulcer or injury, which were determined based on clinical examination by a rheumatology specialist using laboratory tests, if necessary. These patients were diagnosed based on the American Diabetes Association criteria. The inclusion criterion included fasting blood glucose equal to or greater than 126 mg/dL in two measurements. The exclusion criteria included a lack of cooperation from patients for any reason and migration from the area of the study. A total of 273 people were selected using the census method. After obtaining a code from the Ethics Committee *(IR.RUMS. REC.1395.88),* a written informed consent form was obtained from diabetic patients before entering the study. A checklist was used to collect the data.

The checklist included two sections. The first section included demographic data (level of education, race, and living place), and the second section included clinical data (duration of diabetes in a month, blood glucose, HbA1c, type of diabetes, BMI, history of smoking, blood pressure, serum level of cholesterol, triglyceride, HDL, LDL, and the type of musculoskeletal disorder found in the patient). types of musculoskeletal disorder included adhesive capsulitis, carpal tunnel syndrome, shoulder-hand syndrome, neuropathic arthritis, Golfer's elbow, arthriticular neuropathy. All of the musculoskeletal

diseases are diagnosed by a rheumatologic specialist Some of them by history and physical examination (clinical manifestations) for example trigger finger and adhesive capsulitis but some of them are diagnosed by clinical manifestation and paraclinical finding such as nerve condition velocity (NCV) (carpal tunnel syndrome). Some parts of the data were collected from the patient's medical records, and the information on the type of musculoskeletal disorder was obtained through clinical examination by a rheumatologic specialist. BMI in these patients was calculated by measuring the height and weight of the patients based on the conventional formula. Laboratory data and the data on the complete physical evaluation of each patient's organs were collected from the checklist of the patient and stored in specific folders on the computer.

Data analysis and statistical methods

The obtained data were entered into SPSS 20 software applications. Descriptive statistics (frequency, mean, and standard deviation) were used to achieve the objectives of the study. Kolmogorov-Smirnov test was also used to examine the distribution of the obtained data. An independent *t*-test was also utilized. Modeling was performed to obtain the best fit using logistic regression. The significance level was considered less than 0.05.

Results

In the present study, a total of 273 patients diagnosed with type II diabetes were investigated. In this study, 52.4% (*n* = 143) of the participants were male and 47.6% (*n* = 130) were female. The number of smokers among the participants in the study was 83 (30.4%). The demographic data and the underlying variables for the participants are presented in Table 1.

Figure 1 shows the frequency of the types of rheumatologic manifestations in diabetic patients. The incidence of at least one of the rheumatologic complications was 62.6%. The highest frequency was seen for carpal tunnel syndrome (72 patients or 26.4%), while the lowest frequency was seen for arthriticular neuropathy (7 patients or 2.6%) and hand-shoulder pain (7 patients or 2.6%).

Table 2 also shows the frequency of age variables, duration of diabetes, serum level of fasting blood glucose, and HbA1c level during examination (quantitative variables).
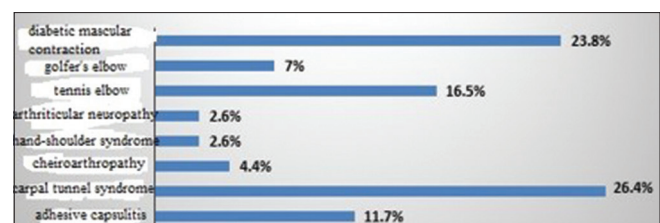

Figure 1: Frequency distribution of types of rheumatologic manifestations in terms of prevalence in research subjects

An independent *t*-test was used to examine the distribution of quantitative variables (FBS, HbA1c) in various rheumatologic manifestations [Table 3].

In the patients, the rheumatologic manifestations of adhesive capsulitis, carpal tunnel syndrome, shoulder-hand syndrome, neuropathic arthritis, Golfer's elbow, and the mean level of FBS were significantly higher than those in people without these manifestations ($P < 0.05$).

To evaluate the risk factors for rheumatologic manifestations, logistic regression model was used, and the relationships between the variables associated with these complications were examined. The individuals with any of the rheumatologic complications were included in the affected group, and individuals without any of these complications were included in the non- affected group. Among different regression models, by adding the effective variables for rheumatologic complications (age, gender, smoking, BMI, HDL, LDL, Chol, TG, systolic blood pressure, FBS, HBA1C, and duration of diabetes), the model with the variables of age, gender, smoking, HBA1C, and BMI was the best model from

a statistical point of view [Table 4]. The results can be interpreted as follows:

With regards to the age variable, the likelihood of rheumatologic complications in people aged 60–80 years was 14.2 times higher than that for people with 60 years of age (baseline group), while it was 19.2 times higher in people aged 80 years and higher compared to people aged less than 60 years ($P < 0.001$). With regard to gender, the likelihood of rheumatologic complications in female patients was 30.47 times higher than that of male patients. And with regards to the smoking variable, the likelihood of rheumatologic complications in smokers was 6.98 times higher than that of non-smokers ($P < 0.001$). With regards to the BMI, the likelihood of rheumatologic complications in the patients with BMI of 18.5-25 was 28.91 times higher than that of the patients in the baseline group with BMI less than 18.5, which was statistically significant ($P < 0.001$). The patients with BMI of 25-30 had a rheumatologic complication rate of 1.16 times more than that of the baseline group (value = 0.83). For patients with $BMI > 30$, compared to the baseline group, these complications were 11.67 times more likely, which was statistically significant ($P = 0.009$). With regards to HbA1c, by moderating the effects of other variables, for one unit of increase in the rate of HbA1c, the likelihood of rheumatoid complications was 1.74, which was statistically significant ($P = 0.01$).

Discussion

Based on the results of this study, 62.6% of diabetic patients suffered from at least one of the rheumatologic complications. The most common complication was carpal tunnel syndrome (26.4%). The mean FBS level in the patients with adhesive capsulitis, carpal tunnel syndrome, shoulder-hand syndrome, neuropathic arthritis, and Golfer's elbow was significantly higher than that of people who did not have these manifestations. Moreover, the mean HBA1C level in the patients with adhesive capsulitis, diabetic cheiroarthropathy, hand-shoulder syndrome, neuropathic arthritis, and tennis elbow was significantly higher than that of people without these manifestations ($P < 0.05$). With regards to the HbA1c variable, after moderating the effects of other variables, for one unit of increase in the rate of HbA1c, the likelihood of rheumatoid complications became 1.74, which was statistically significant. The variables of age, gender, smoking, and BMI had a statistically significant effect on the baseline group. Various studies have reported different rates for musculoskeletal disorders. For instance, its rate has been reported by about 50% in the study conducted by Egede,[12] and 48.4% in the study conducted by Zabihi *et al*.[13] Fatemi *et al*.[14] evaluated the prevalence of musculoskeletal disorders in diabetic and prediabetic patients, and compared the results between the two groups. In this study, 83% of diabetic patients and 53% of pre-diabetic subjects had at

Table 1: Frequency distribution of underlying variables (qualitative variables) related to research samples

Variable		f	%
Gender	Male	143	52.4
	Female	130	47.6
BMI	Lower than 18.5	14	5.1
	18.5-25	159	58.2
	20-30	86	31.5
	More than 30	14	5.1
Level of education	Illiterate	149	54.6
	Diploma and lower	124	45.4
Ethnic group	Iranian	267	97.8
	Afghani	6	2.2
Living place	City	105	38.5
	Village	168	61.5
Smoking	Yes	83	30.4
	No	190	69.6
Blood pressure	Normal	33	12.1
	Abnormal	240	87.9
Cholesterol	Less than 200	75	27.5
	200 to 240	107	39.2
	More than 240	91	33.3
Triglyceride	Less than 150	81	29.7
	150 and more	192	70.3
HDL	Less than 35	76	27.8
	35 and more	197	72.2
LDL	Less than 100	20	7.3
	100-130	140	51.3
	130-160	70	25.6
	160-190	36	13.2
	190 high	7	2.6
Total		273	100

Table 2: Frequency distribution of underlying variables (quantitative variables) related to research subjects

Variable	Minimum	Maximum	SD	Mean	Median
FBS	115	546	81.52	244.24	237
HbA1c	5.2	9.8	0.92	7.8209	8
Duration of diabetes (month)	8	360	99.74	136.9744	120
Age	40	82	111.47	64.5385	65

Table 3: Distribution of variable FBS and HBA1C based on the types of rheumatologic manifestations in research subjects

Rheumatologic complication/ independent *t*-test		FBS			HBA1C		
		Mean	SD	P	Mean	SD	P
Adhesive capsulitis	yes	278.46	70.27	0.002	8.06	0.36	0.012
	no	239.69	81.95		7.78	0.97	
Carpal tunnel syndrome	yes	211.01	59.73	0.001	7.56	1.19	0.068
	no	256.14	85.04		7.91	0.79	
Diabetic cheiroarthropathy	yes	253	26.11	0.164	7.50	1.04	0.006
	no	243.83	83.18		7.83	0.92	
Hand-shoulder syndrome	yes	261	0.000	0.014	9.30	0.000	0.005
	no	243.80	82.54		7.78	0.90	
Neuropathic arthritis	yes	400.00	0.000	0.001>	8.30	0.000	0.000
	no	240.14	78.51		7.80	0.93	
Tennis elbow	yes	230.08	24.61	0.420	8.13	1.13	0.001>
	no	247.03	88.30		7.75	0.86	
Golfer's elbow	yes	345.15	157.73	0.046	8.40	0.54	0.817
	no	236.69	67.47		7.77	0.93	
Diabetic muscle contraction	yes	264.26	122.59	0.908	7.96	1.10	0.121
	no	237.98	62.61		7.77	0.86	

Table 4: Descriptive characteristics of regression of variables affecting rheumatologic complications in patients studied

Variable	Categories	Odds ratio (OR)	df	P	SE	Model coefficient
gender	Male (base)	30.47	1	0.001>	0.533	3.417
	female					
BMI	Less than 18.5 (base)		3	0.001>		
	18.5-20	28.91	1	0.001>	0.753	3.364
	25-30	1.16	1	0.834	0.744	0.156
	Greater or equal to 30	11.672	1	0.009	0.944	2.457
Age	<60 (base)		2	0.001>		
	60-80	12.370	1	0.001>	0.811	2.654
	>=80	19.711	1	0.001>	0.777	2.972
HbA1c		1.74	1	0.011	0.218	0.555
Smoking	Nonsmoker (base)	6.987	1	0.001>	0.561	1.944
	smoker					

least one musculoskeletal disorder. The important point in these studies is that although the rate of occurrence is significant in all these studies, the statistical differences might be due to the diversity of the disorders studied; for example, osteoarthritis, which has not been considered in the present study, as well as the differences in demographic characteristics, such as the patient's age range, lifestyle, and living place. The most common complication in this study was carpal tunnel syndrome (26.4%). In the study conducted by Fatemi *et al.*,[14] the prevalence rate of carpal

tunnel syndrome in diabetic and pre-diabetic people was estimated to be 48% and 36%, respectively. In the study conducted by Clarke *et al.*,[15] some complications, such as carpal tunnel syndrome and hand joints limitations, were more common due to higher transfer and richer sedimentation of sugar metabolites in hand tissues, which have more mobility.

However, in contrast to our study, Cagliero *et al.*[16] reported that the most common musculoskeletal complication was shoulder capsulitis (52.5%), followed by carpal tunnel

syndrome. Linsay *et al.*[17] also reported that the most common musculoskeletal complication in the diabetic patients was shoulder capsulitis (53.8%), possibly because of sedimentation of glucose metabolites in capsule and cartilage tissues. The higher incidence of carpal tunnel syndrome might be related to neuropathy caused by diabetes, emerging with symptoms similar to carpal tunnel, thus, electromyography (EMG)-NCV is needed to differentiate them. Various studies have been carried out in order to evaluate the relationship between the underlying risk factors and musculoskeletal disorders in diabetic patients. For example, in the study conducted by Kyani *et al.*,[18] factors, including age, being female, smoking, and the duration of diabetes were associated with various types of musculoskeletal disorders. Similar to our study, Fatemi[14] showed that age, gender, and BMI were important indicators for the development of musculoskeletal disorders in all diabetic and pre-diabetic people. Moreover, Fatemi[11] suggested that age and BMI were two factors with a significant association with musculoskeletal disorders in both diabetic and prediabetic people. In addition, in the study conducted by Akulovar *et al.*,[19] and other similar studies,[20,21] a significant relationship was found between the occurrence of carpal tunnel syndrome and being female, which is consistent with results of our study, which contrasts with the results of some other studies.[22]

With regard to the relationship between glucose control and rheumatologic complications, controversial results have been reported by different studies. In the present study, a significant relationship was found between the level of HbA1c, as an indicator of glucose control, and the occurrence of rheumatologic complications. The study conducted by Shakibi *et al.*[23] showed that with better control of blood glucose, the incidence of these disorders decreases. In the study of Indian researchers, age, duration of diabetes, and glycosylated hemoglobin showed a significant relationship with these disorders. Their relationship with age and blood glucose control was consistent with the results of our study, but their relationship with the duration of diabetes contradicts the results of our study. It should be noted that this study also examined knee osteoarthritis.[24] Moreover, in the study conducted by Sinagh *et al.*[25] on patients with type I diabetes, no significant relationship was found between carpal tunnel syndrome and glucose control. Other studies have found that there is no significant relationship between serum HbA1c levels and rheumatologic manifestations.[26] Considering a prevalence rate of over 50% for these musculoskeletal complications in many of the studies, it seems that screening for musculoskeletal complications should be included as an essential part of care for patients with type II diabetes. Diabetic patients and related physicians need to be trained on and pay more attention to these debilitating diabetic complications since early diagnosis and timely treatment of these complications

can prevent chronic disabilities. The important point is that better control of diabetes can lead to reduced rheumatologic complications.

Conclusions

Diabetes often affects the musculoskeletal system and its complications have an adverse impact on patients' quality of life and mortality. Hence, diagnosis, prevention, and treatment of these complications are very crucial. It is recommended that musculoskeletal examinations be included as an important part of regular care for these patients. It is also recommended that studies with a higher sample size be conducted by considering other factors, such as job and the effect of geographical factors and living place.

Limitations and recommendations

The type of research and the limitations of the research population limit the range of generalization of the results and interpretations of the variables of the study. Therefore, it is recommended to other researchers interested in rheumatology and its relationship with diabetes to examine the accuracy of these results in a wider population along with a control group.

All Authors reviewed the article and they have agreed with the contents of the paper.

Conflicts of interest

There are no conflicts of interest.

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