International Journal of Multidisciplinary Research and Development
Online ISSN: 2349-4182, Print ISSN: 2349-5979
Impact Factor: RJIF 5.72
Received: 03-08-2018; Accepted: 09-09-2018
www.allsubjectjournal.com
Volume 5 Issue 9; September 2018; Page No. 129-133

Subclinical entheseal involvement in lower limbs in patients with type 2 diabetes mellitus: An ultrasound study

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Abstract
Objective: This study aims to detect subclinical lower limb enthesitis in type 2 DM by musculoskeletal ultrasonography & its relation to poor glycemic control & disease duration.
Methods This study was carried out on 80 persons selected from those attending the outpatient clinics of internal medicine department of Al-azhar university hospital, Assuit. From November 2017 till May 2018.
The persons were divided into two groups: Group (A): forty diabetic patients diagnosed according to ADA diagnostic criteria (13 males and 27 females); with age ranges from 20 to 67 years. Group (B): Forty apparent healthy volunteers as a control group (16 male and 24 female) age & sex matched used as a control group.
Results: About 67.5% of patients were females & 32.5% of the patients were males.
About 42.5% of patients had disease duration of 3-5 years, 37.5% of patients had disease duration of 5-10 years, 10% of patients had disease duration of 10-20 years, 5% of patients had disease duration of >20 years. About 15% of patients had BMI (18.5-24.9), 57.5% of patients had BMI (25-29.9), 27.5% of patients had BMI (>30).In this study There: There is a statistically significant difference between age and Ultrasound findings p. value <0.05
There is no significant difference between gender and Ultrasound findings. There is a statistically significant difference between disease duration and Ultrasound findings p. value<0.05.
Conclusion Musculoskeletal Ultrasonography is a suitable and reliable method for examining entheseal structures with great resolution because most of these are superficial structures. Entheseal abnormalities can be documented by ultrasonography in clinically asymptomatic patients with Diabetes. These findings could be related to a subclinical entheseal inflammation.

Keywords: subclinical enthesitis, musculoskeletal ultrasonography, diabetes mellitus

Introduction
Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia, which results from defects in insulin secretion, insulin action, or both [1].
DM impacts the connective tissue and causes various changes in peri-articular and articular structures. Both increase in DM incidence and extension of living period in DM patients lead to a more common observation of musculoskeletal problems in these patients. Metabolic disorders such as protein glycosylation, microvascular anomalies, and collagen accumulation in the skin and periarticular structures may be the reason of changes in the musculoskeletal system [2].
Many studies inspected the musculoskeletal complications of DM patients. An increase in enthesopathic complications, such as diabetic cheiroarthropathy in the upper extremity, Dupuytren's contracture, adhesive capsulitis on shoulder, flexor tenosynovitis and carpal tunnel syndrome, diffuse idiopathic skeletal hyperostosis on the spine, diabetic muscle infarcts at the lower extremity, patellar tendinitis and bursitis, Achilles tendinopathy, plantar fasciitis, was observed [3].
Conventional radiography, ultrasonography, and magnetic resonance imaging are used to diagnose tendinopathies, bursitis, and other morphologic pathologies of musculoskeletal system. Musculoskeletal ultrasonography is a widely available and inexpensive imaging tool, and demonstrates fluid collections, soft tissue lesions, and bone surface lesions with sensitivity comparable with magnetic resonance imaging. Sonographic examination is more sensitive and specific than clinical examination for the detection of enthesitis and tendon involvement [4].

Patients and methods
This study was carried out on 80 persons from those attending the outpatient clinics of internal medicine & Rheumatology, Physical medicine & Rehabilitation department of Al-azhar university hospital, Assuit. From November 2017 till May 2018.
Study design and population

The persons were divided into two groups
Group (A): forty diabetic patients diagnosed according to ADA diagnostic criteria (13 males and 27 females); with age ranges from 20 to 67 years.
Group (B): Forty apparent healthy volunteers as a control group (16 male and 24 female) age & sex matched used as a control group.

The inclusion criteria were as follows

Having diagnosis of Type2 DM for a minimum of 2 years
Age >18 years

Exclusion criteria

Duration of DM of < 2 years
With a history of lower extremity operations; who were exposed to any trauma that might damage the anatomic structure of the lower extremities. Who have another endocrinologic disease (thyroid disorders, etc.).
Who have chronic kidney disease and are undergoing dialysis treatment. Having any of the musculoskeletal symptoms of pain, limitation of range of motion, erythema, swelling, or edema in the lower limbs

Statistical analysis

The collected data were revised, organized, tabulated and statistically analyzed using statistical package for social sciences (SPSS) version 23.0 for windows. Data are presented as the Mean ± standard deviation (SD), frequency, and percentage. Categorical variables were compared using the chi-square ($\chi 2$) and Fisher's exact tests (if required). Continuous variables were compared by the Student t test (two-tailed) and one – way ANOVA test for parametric data with Bonferroni post hoc test to detect differences between subgroups. Pearson correlation test was used to study the correlation between the studied variables. The level of significance was accepted if the P value < 0.05.
The P value is a statistical measure for the probability that the results observed in a study could have occurred by chance

Results

This study was carried out on 80 persons: 40 with DM (13 males and 27 females); with age ranges from 20 to 67 years, (mean age 40.38+12.75 years), the disease duration ranges from 3 to 22 years (7.83+5).

Table 1: Characteristics of the studied patients

Parameters	No. (n= 40)	%
Age	N	%
<30 years	2	5.0
≥30 years	38	95.0
Mean ± SD (Range)	50.38+10.8 (27-69)	

Comment

Age ranged from 27 to 69 years with mean age (50.38+10.8) years.
The highest percentage of the patients was at the age of ≥30years (95%). The lowest percentage of the patients was at the age of < 30 years (5%), with mean age (50.38+10.8) years.

Table 2: Sex distribution of the studied patients

Gender	No. (n= 40)	%
Male	13	32.5
Female	27	67.5

Comment

About 67.5% of patients were females and 32.5% of the patients were males.

Table 3: Disease duration

Disease duration	(n= 40)	%
3-5 years	17	42.5
5-10 years	15	37.5
10-20 years	6	15.0
>20 years	2	5.0
Mean ± SD (Range)	7.83+5 (3-22)	

Comment

42.5% of patients had disease duration of 3-5 years.
37.5% of patients had disease duration of 5-10 years.
10% of patients had disease duration of 10-20 years.
5% of patients had disease duration of >20 years.

Table 4: Musculoskeletal Ultrasound findings of in the diabetic group

	No. (n= 40)	%
Quadriceps enthesis	30	75
Proximal patellar enthesis	28	70
Distal patellar enthesis	22	55
Achilles enthesis	27	67.5
Plantar aponeurosis enthesis	25	62.5

Comment

The Quadriceps enthesis had the highest number of ultrasonic signs of enthesopathy (75%), followed by proximal patellar enthesis (70%), Achilles enthesis (67.5%), Plantar aponeurosis entheses (62.5%), and Distal patellar enthesis (55%).

Table 5: Musculoskeletal Ultrasound findings in the diabetic & control groups

	No. (n= 40) of diabetic group	No. (n= 40) of control group	P-Value
Quadriceps tendon thickness > 6.1 mm Mean± SD	30(75%) 6.87±1.3	24(60%) 6.27±0.9	0.019 S
Proximal patellar tendon thickness >4mm Mean± SD	28(70%) 4.22±0.79	14(35%) 3.76±0.54	0.003 S
Distal patellar tendon thickness >4mm Mean± SD	22(55%) 3.94±0.73	13(32.5) 3.88±0.4	0.66 NS
Achilles tendon thickness > 5.29 Mean± SD	27(67.5) 5.24±0.7	8(20%) 4.85±0.46	0.005 S
plantar aponeurosis thickness > 4.4 Mean± SD	25(62.5) 4.39±0.78	7(17.5) 3.92±0.65	0.005 S

Comment

This table showing: in the diabetic group: The Quadriceps enthesis had the highest number of ultrasonic signs of enthesopathy (75%), followed by Proximal patellar enthesis (70%), Achilles enthesis (67.5%), Plantar aponeurosis entheses (62.5%), and Distal patellar enthesis (55%). While in the control group, The Quadriceps enthesis had the highest number of ultrasonic signs of enthesopathy (60%), followed by proximal patellar enthesis (35%), distal patellar enthesis (32.5%), Achilles enthesis (20%), and plantar aponeurosis enthesis (17.5%).
* Independent sample t-test was used S: Statistically significant difference, P<0.05. NS: Statistically non-significant difference, P>0.05.

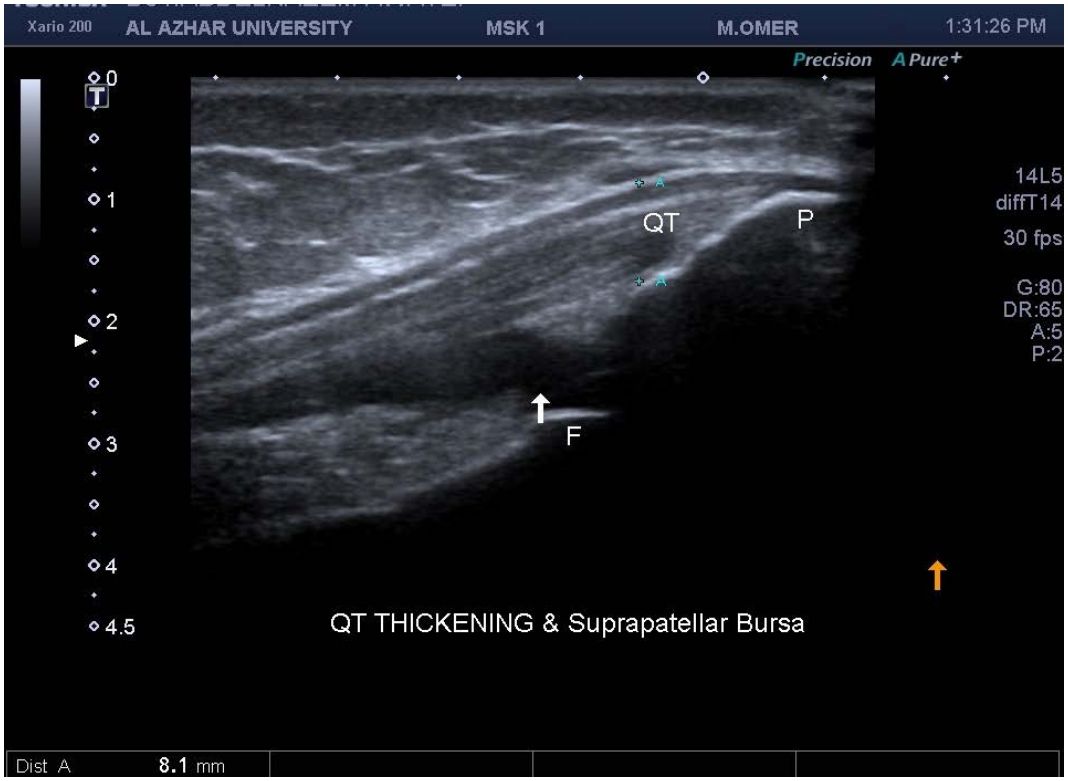

Fig 1: Male patient aged 58 years with diabetes, shows:

Quadriceps tendon enthesopathy with increase in the tendon diameter about 8.1 mm Longitudinal scan of Quadriceps tendon showing, suprapatellar bursa (arrow).

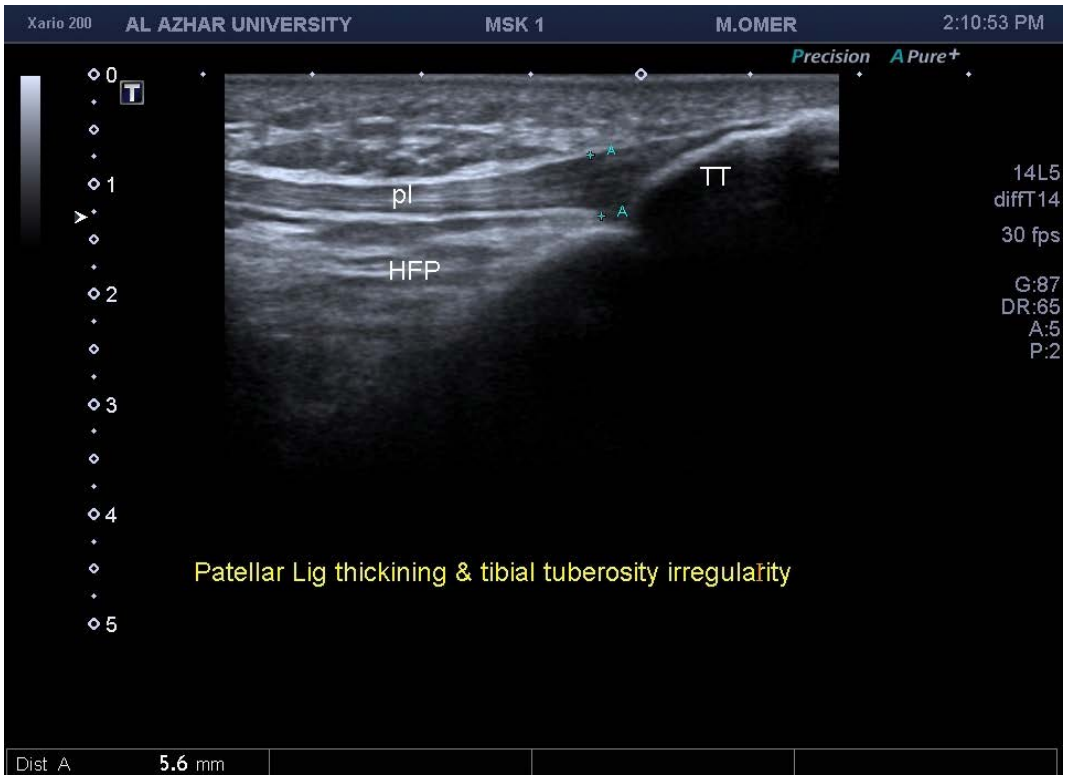

Fig 2: Female patient aged 45years with diabetes, shows:

Distal patellar ligament enthesopathy. Longitudinal scan of Patellar Ligament tendon showing: Increase of tendon thickness. Tibial Tuberosity irregularity at insertion site

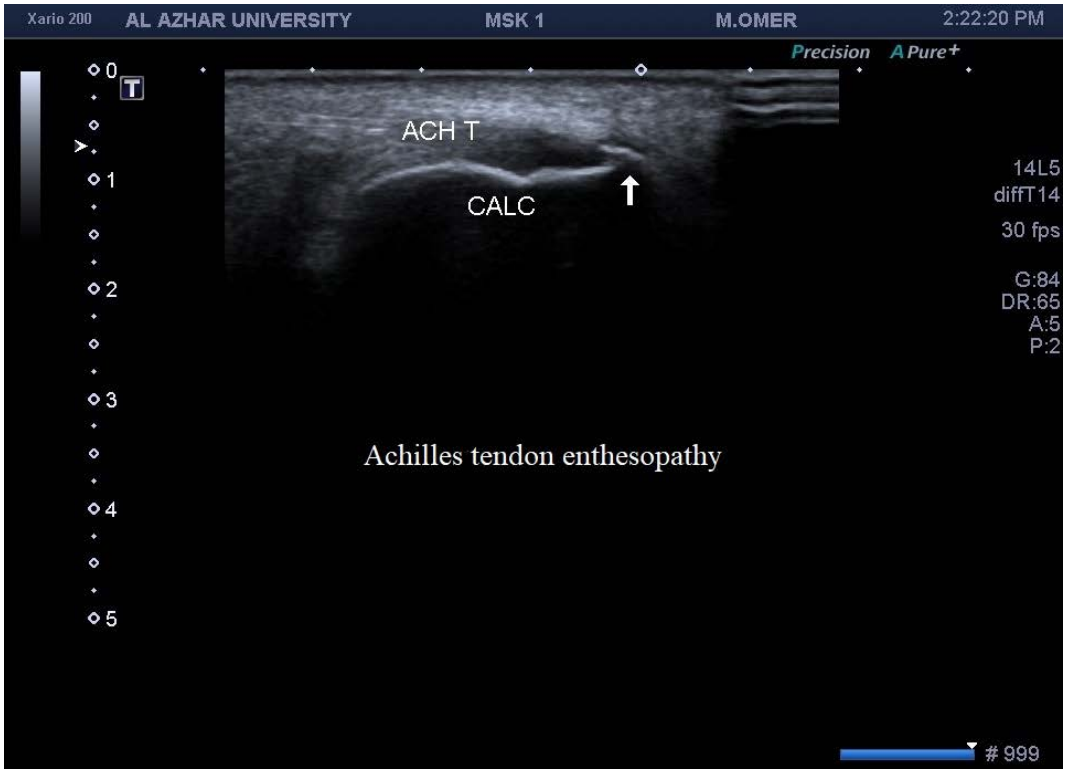

Fig 3: Female patient aged 54 years with DM, shows:

Achilles tendon enthesopathy. Longitudinal scan of Achilles tendon showing: Enthesopathy at Achilles enthesis level

Discussion

By analysis of our results, we found the prevalence of diabetes-related musculoskeletal system problems (Total GUESS Score) is statistically significant difference with the patient's age, DM duration & BMI. There was a significant correlation between total GUESS scores and age in our study. Aging positively effects degenerative changes. However, in our study there is increase of total GUESS scores with the duration of diabetic status. In the agreement with our study Okur and his colleague in 2017 [1] they found that The prevalence of diabetes-related musculoskeletal system problems increases in direct correlation with the age, DM diagnosis age, and DM duration. Also we agree with the study done by Abate and his colleague in 2010 [5] they found that Ageing and diabetes mellitus are conditions frequently associated.

In our study we found statistically significant correlation between disease duration and (proximal patellar ligament, Achilles tendon, quadriceps tendon and plantar fascia) thickness. In the agreement with our study Abate and his colleague in 2012 [6], found that an increase in tendon thickness and disruption in tendon morphology along with the disease time. Also In agreement with our study Batista and his colleague in 2008 [7] found that deterioration of tendon morphology and an increase in tendon thickness correlated with the diabetes period. Also In agreement with our study Okur and his colleague in 2017 [1] & Altinel & his colleague in 2007 [8] found that an increase in the thicknesses of tendons (proximal patellar ligament,, Achilles tendon, and plantar fascia) but In disagreement with our study they found significant correlation between disease duration& distal patellar ligament thickening & also they didn't find significant correlation between disease duration& Quadriceps tendon thickness.

In our study we found a significant statistical correlation between disease duration and supra patellar, retrocalcaneal bursae. In agreement with our study Okur and his colleague in 2017 [1] they found a positive correlation between diabetes duration and bursitis frequency, which is particularly evident for suprapatellar bursitis scores. In disagreement with our study they couldn't find a correlation for retrocalcaneal bursitis & they found a significant correlation for infrapatellar bursitis.

In our study we found a significant statistical correlation between disease duration and enthesophyte formation in agreement with study done by Okur and his colleague in 2017 [1], Abate & his college in 2014 [9].

In our study we found a statistically significant correlation between FBS, HbA1C & total guess score in agreement with Attar 2012 [10]. In disagreement with our study Okur and his college in 2017 [1] didn't find significant correlation between FBS & total guess score.

In our study we found a statistically significant difference between diabetic patients & control group as regard to Quadriceps tendon thickness, proximal patellar ligament thickness, Achilles tendon & planter aponeurosis thickness.

Conclusion

Musculoskeletal Ultrasonography is a suitable and reliable method for examining entheseal structures with great resolution because most of these are superficial structures. Entheseal abnormalities can be documented by

ultrasonography in clinically asymptomatic patients with Diabetes. These findings could be related to a subclinical entheseal inflammation

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