Original Article

Lower Limb Enthesopathy in Patient with Diabetes Mellitus without Clinical Signs of Arthropathy

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ABSTRACT:

Background: *Diabetes mellitus is a leading cause of death and disability worldwide. Its global prevalence was about 8% in 2011 and is predicted to rise to 10% by 2030. DM has great impact on the connective tissue and prolongation of diabetes period increases the degree of complications. Musculoskeletal ultrasonography using the Glasgow Ultrasound Enthesitis Scoring System (GUESS) is a validated and useful tool to quantify articular and periarticular changes of lower extremity.*

Objectives: *The objective of this study is to findout the correlation between Glasgow Ultrasound Enthesitis Score in diabetic patients and duration of DM.*

Materials and Methods: *This Cross sectional study was carried out in the Department of Radiology and Imaging, BIRDEM, Dhaka, during July 2017 to June 2019 period. For this purpose, a total of 120 diabetic patients were included in this study.*

Observation and Results: *Results revealed the mean age (±SD) was 49.46±7.99 years ranging from 35-64 years. Male to female ratio was 1:1.1. There was positive significant correlation found between duration of DM with the suprapatellar bursitis (r=0.637; p=0.001), infrapatellar bursitis (r=0.319; p=0.001) retrocalcaneal bursitis(r=0.715;p=0.001), quadriceps tendon thickness (r=0.583;p=0.001), proximal patellar ligament thickness(r=0.441;p=0.001) and Achilles tendon thickness (r=0.343;p=0.001).*

On the other hand, there was a negative correlation (r=-0.176; p=0.055) was found between the plantar aponeurosis thickness with duration of DM. There was a significant positive correlation (r=0.941; p=0.001) was found between the total GUESS score with duration of DM.

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There was also a positive correlation was found between duration of diabetes with total enthesophyte score (r=0.734; p=0.001) and total erosion score (r=0.791; p=0.001). The receiver-operator characteristic (ROC) curves of duration of DM had area under curve 0.988; 95% confidence interval, 0.974–1.00, with a cut off value 20 years having 57.6% sensitivity and 100.0% specificity for prediction of severe entheseal damage.

Conclusion: *This study indicates that Ultrasonographic evaluation of lower extremity entheseal sites in diabetic patient by using Glasgow Ultrasound Enthesitis Scoring System (GUESS) significantly correlated with duration of diabetes.*

Key words: *Diabetes mellitus, Enthesitis, lower extremity entheseal sites, retrocalcaneal bursitis, Glasgow Ultrasound Enthesitis Scoring System (GUESS), Non-alcoholic fatty liver disease*

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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]. Diabetes mellitus is a leading cause of death and disability worldwide. Its global prevalence was about 8% in 2011 and is predicted to rise to 10% by 2030 [2]. Enthesitis or enthesopathy is defined as inflammation of the origin and insertion of ligaments, tendons, aponeuroses, annulus fibrosus, and joint capsules[3]. DM has great impact on the connective tissue and causes various changes in periarticular and articular structures[4]. Prolongation of diabetes period increases the degree of complications[5].

The prevalence of enthesopathy is increased in patients with DM compared with euglycemic persons. Several studies have shown increased thickness and stiffness of the plantar fascia and Achilles tendon in Type 2 DM patients[6]. Furthermore, a number of studies showed the influence of hyperglycaemia on metabolic process such as protein glycosylation, microvascular changes and collagen accumulation in the skin and periarticular structures may be the reason for enthesopathy in patients with DM.

Conventional radiography, ultrasonography, and magnetic resonance imaging are used to diagnose tendinopathies, bursitis, and other morphologic pathologies of musculoskeletal system. Musculoskeletal ultrasonography is a non-invasive, widely available and relatively inexpensive technique that can be used to demonstrate fluid collections, soft tissue lesions, and bone surface lesions with sensitivity comparable with magnetic resonance imaging[6].This study was look at the intra-articular and peri-articular soft tissue changes found among patients with DM using real-time musculoskeletal US imaging.

Glasgow Ultrasound Enthesitis Scoring System (GUESS).The Glasgow Ultrasound Enthesitis Scoring System (GUESS) is a validated and useful tool to quantify ultrasonographic finding[7]. GUESS includes evaluation of quadriceps tendon, patellar ligament, achilles tendon, plantar fascia thickness, enthesophytes and erosions at the origin, and attachment sites of the tendons. Suprapateller, infrapateller and retrocalcaneal bursae were also evaluated. Examination of the superior pole of the patella

(quadriceps tendon insertion), inferior pole of the patella (patellar ligament origin), and patellar ligament insertion at the tibial tuberosity are performed
with the patient in the supine position with the knees flexed at 30◦ . The Achilles tendon and plantar aponeurosis are examined with the patient lying prone position with the feet hanging over the edge of the examination table at 90◦ flexion. Bony erosion is defined as discontinuity of the cortex with a defect, an enthesophyte is defined as a bony prominence at the end of normal bone contour. Thickness of ligaments, fascias, and tendons is measured at the point of maximum thickness proximal to the bony insertion. Tendon thickness and the presence or absence of bony erosion, enthesophyte, and bursitis are recorded for each site. One point is scored for each abnormal entheseal site, with a maximum score of 18 for each lower limb examined. The total GUESS score is calculated as the sum of scores of both lower limbs, with a maximum score of 36.Materials and Methods.This Cross sectional study was performed in the department of Radiology and Imaging, BIRDEM, Dhaka, from July 2017 to June 2019 period. A total of 120 diabetic patients both male and female diagnosed case of diabetes mellitus more than 3 years were included in this study. Patients who are obese (body mass index more than 25 kg/m^2), had history of trauma to the lower extremity, had suspected infective or neoplastic lesions of joints of lower extremity are excluded in this study.

Phillips Affinity 50G machine with 12.5 MHz linear transducer and GUESS questionnaire form were used as study materials.

Statistical Analysis

Statistical analyses of the results were obtained by using window based computer software devised with Statistical Packages for Social Sciences (SPSS-20). The results were presented in tables, figures, diagrams. Data were presented as means with standard deviations (SD) or as counts with percentages. Correlation between Glasgow Ultrasound Enthesitis Scoring System and duration of diabetes mellitus was evaluated by correlation - coefficient test. For all tests, a value of $P<0.05$ was considered as significant.

RESULTS

The mean age (±SD) of the patients was 49.46 (± 7.99) years. The age ranged from 35-64 years.

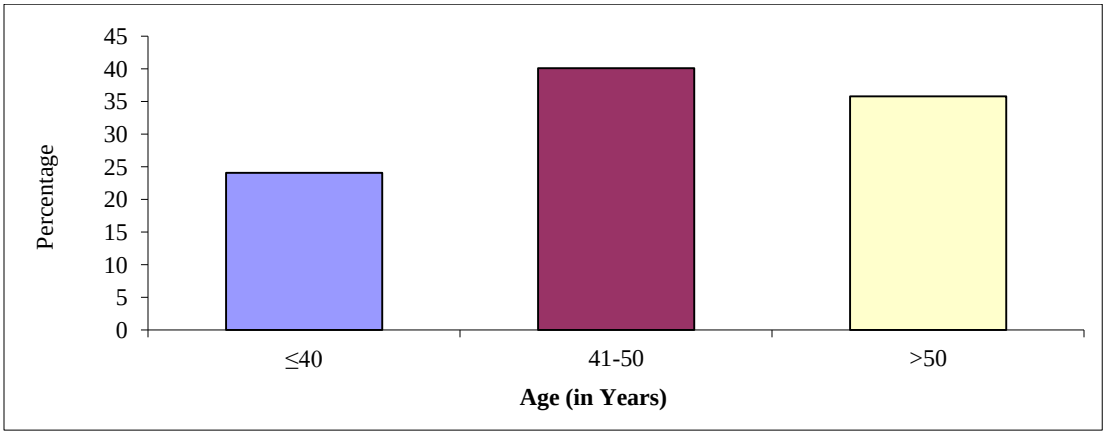

Figure 1: The bar diagram showing age distribution of the study patient

Figure 2 shows the sex distribution of study population. More than half 62 (51.7%) patients were female and 58 (48.3%) were male.

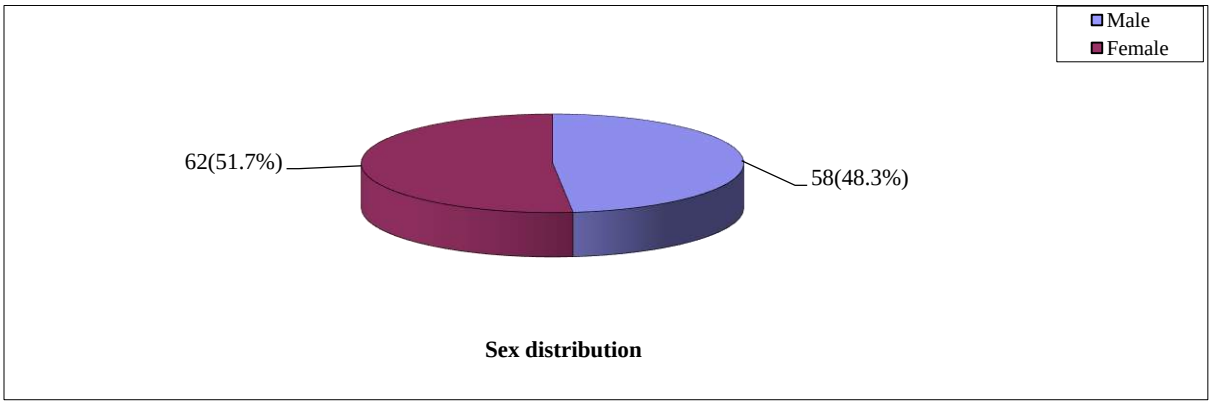

Figure 2: **The pie chart showing sex distribution of the study patients**

Association between demographic profile with duration of diabetes (Table1)

Table1: Association between demographic profile with duration of diabetes

Demographic profile	**Duration of diabetes (years)**				**P value**
	4-5	**5-10**	**10-20**	**>20**	
No of patients	19	39	43	19	
Sex (male/female)	5/14	29/10	20/23	4/15	0.001[s]
Age (min-max)	42(39-50)	47(35-60)	53(42-64)	54(50-60)	0.001[s]

s= significant p value reached from Chi square test

Table II: Association between Glasgow Ultrasound Enthesitis Scoring System with duration of diabetes (n=120)

	Duration of diabetes (years)				**P value**
	4-5 (n=19)	**5-10 (n=39)**	**10-20 (n=43)**	**>20 (n=19)**	
Total GUESS score					
Mean±SD	3.79±2.02	10.92±2.18	15.81±2.48	23.26±1.15	0.001[s]
Range (Min-Max)	1-4	3-8	4-9	10-12	

s= significant p value reached from ANOVA test

Table III Sonographic finding at entheseal sites and duration of diabetes mellitus

	Duration of diabetes (years)			
	4-5 (n=19)	**5-10 (n=39)**	**10-20 (n=43)**	**>20 (n=19)**
Total enthesophyte score				
Mean±SD	3±0.75	4.36±1.25	5.26±1.31	7.95±1.27
Range (min-max)	2-4	3-7	3-7	6-9
Total erosion score				
Mean±SD	0±0	4.54±2.55	6.42±1.69	9.47±0.51
Range (min-max)	0-0	1-9	4-9	9-10
Quadriceps tendon thickness(Mean±SD)	3.64±0.37	4.29±0.86	4.81±1.13	6.54±1.89
Ranged(Min-Max)	3.25-4.15	3.5-5.45	3.5-6.76	4.95-9.5
Proximal Patellarligament thickness (Mean±SD)	2.83±0.28	3.18±0.76	3.4±0.5	3.80±0.18
Range(Min-Max)	2.5-3.1	2.5-5	2.8-4.5	3.55-4
Distal Patellar ligament thickness (Mean±SD)	2.66±0.26	2.97±0.42	3.09±0.74	3.29±0.38
Range(Min-Max)	2.25-2.9	2.5-3.9	2-4.55	2.65-3.55
Achilles tendon thickness (Mean±SD)	3.43±0.39	3.64±0.53	4.35±0.97	4.36±0.96
Range(Min-Max)	3-4	3-4.45	2.5-6.3	3-5.5
Plantar aponeurosis thickness (Mean±SD)	2.85±0.16	3.3±0.6	3.37±0.72	2.66±0.60
Range(Min-Max)	2.75-3.1	2.5-4.35	2-4.45	2.15-3.75
Suprapatellar bursitis score (Mean±SD)	0.00±0.0	0.26±0.442	0.44±0.52	1.0±0.0
Range(Min-Max)	0-0	0-1	0-1	1-1
Infrapatellar bursitis score (Mean±SD)	0.00±0.0	0.26±0.442	0.23±427	0.47±513
Range(Min-Max)	0-0	0-1	0-1	0-1
Retrocalcaneal bursitis score (Mean±SD)	0.00±0.0	0.00±0.0	0.53±0.50	0.79±0.419
Range(Min-Max)	0-0	0-0	0-1	0-1

s= significant, p value reached from ANOVA test

Correlation between the total GUESS score and duration of DM

Figure 3 shows significant positive correlation (r=0.941; p=0.001) between the total GUESS score and duration of DM.

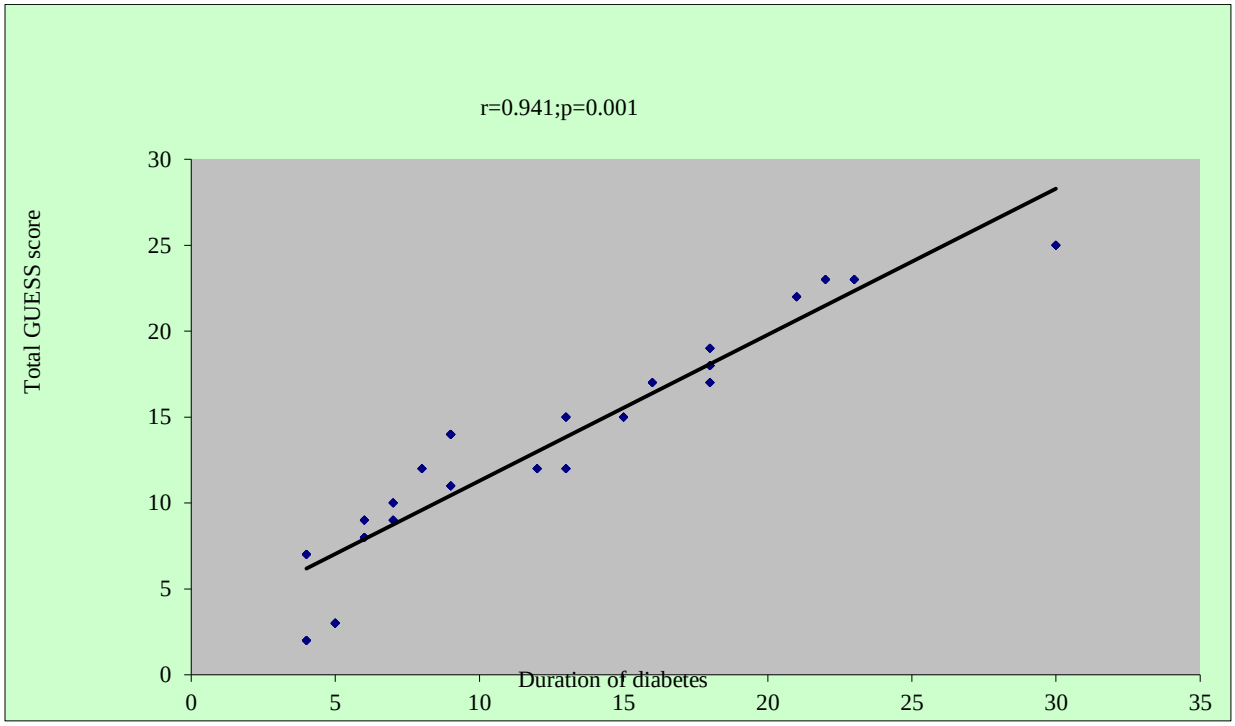

Figure 3: Scatter diagram showing positive significant correlation (r=0.941; p=0.001) between the total GUESS score and duration of DM.

Receiver-operator characteristic (ROC) curve of duration of DM for prediction of severe entheseal damage.

	Cut of value	Sensitivity	Specificity	Area under the ROC curve	95% Confidence interval (CI)	
					Lower bound	Upper bound
Duration of DM (year)	20	57.6	100.0	0.988	0.974	1.000

DISCUSSION

In this present study, it was observed that 40.1% patients belonged to age 41-50 years. The mean age (±SD) was 49.46±7.99 years with ranged from 35-64 years (Figure-1). Simialrly Kerimoglu et al. (2007) found the mean age of the patients was 50 years varied from 18–74 years[8] . On the other hand, Okur et al. (2017) found the

mean age was 55 years with ranged from 38 to 77 years[7].

In this current study, it was observed that 51.7% patients were female and 48.3% were male (Figure 2). Worldwide estimates suggested that 9.6% of men and 18.0% of women aged 60 years have enthesopathy of the hips or knees in diabetic patients[9].

In this present study, it was found that the mean (min-max) age was 42(39-50) years in duration of DM belonged to 4 – 5 years, 47(35-60) years in duration of DM belonged to 5 – 10 years, 53(42-64) years in duration of DM belonged to 10 – 20 years and 54(50-60) years duration of DM belonged to more than 20 years, which was statistically significant ($p<0.001$) (Table-I). Similarly, Okur et al. (2017) study found that the ages of their participant were comparable among the four groups and a statistically significant difference was observed ($p<0.001$)[7].

It was observed in this current study that the mean total GUESS score was 3.79±2.02 in 4-5 years of diabetes, 10.92±2.18 in 5-10 years of diabetes, 15.81±2.48 in 10-20 years of diabetes and 23.26±1.15 in >20 years of diabetes. The mean total score was significantly ($p<0.05$) higher in patients having duration of diabetes more than 20 years followed by 10 – 20 years, 5- 10 years and 4 – 5 years (Table II). This result is similar to Okur et al. (2017) study [7].

Regarding the correlation between total GUESS score with duration of DM, it was observed that there was significant positive correlation ($r=0.941$; $p=0.001$) was found between the total GUESS score with duration of DM (Figure 3). Musculskeletal ultrasound has greater advantage for evaluation and identification of enthesophytes and/or erosions, measurement of thickness of tendons/ligaments and bursal collections around the joints particularly in diabetic patients with a history of 10 years or longer disease period[10]. Okur et al. (2017) also identified enthesophytes in the Achilles tendons and increased frequency of bursitis development in diabetic patients [7]. Unlu et al. (2003) revealed deterioration in the tendon morphology and bursitis in 14 out of 23 diabetic patients [11].

The prevalence of diabetes-related musculoskeletal complications increases in direct correlation with the patient's age and duration of DM [12,14]. It is believed that collagen thickening due to the deterioration of DM neoangiogenesis, nonenzymatic glycosylation of peritendinous collagen, and basal membrane damage further aggravates diabetes-related musculoskeletal complications[13,15]. In this current study, it is observed that the receiver-operator characteristic (ROC) curves of duration of DM had area under curve 0.988; 95% confidence interval, 0.974–1.00, with a cut off value 20 years having 57.6% sensitivity and 100.0% specificity for prediction of severe enthesal damage.

CONCLUSION

In this study it observed that there is significant positive correlation between Glasgow Ultrasound Enthesitis Scoring System (GUESS) and duration of diabetes. It can be concluded in the present study that Glasgow Ultrasound Enthesitis Scoring System (GUESS) is a useful, effective and inexpensive tool for early diagnosis of

musculoskeletal complications of diabetic patients**.**

LIMITATIONS OF THE STUDY

1. The study population was selected from one selected hospital in Dhaka city, so that the results of the study may not reflect the exact picture of the country.
2. Reference values of Glasgow Ultrasound Enthesitis Scoring System (GUESS) score were based on European population.
3. Further study can be carried out on normal healthy subjects to find out the normal reference values.

REFERENCES

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus. 2008. *Diabetes Care*. **31**, pp.55-60.

2. International Diabetes Federation (IDF) [Internet]. Country estimates table 2011. IDF diabetes atlas**. 6th ed**. 2012. Available from:

3. Papanas, N., Courcoutsakis, N., Papatheodorou, K., Daskalogiannakis, G., Maltezos, E. & Prassopoulos, P., 2009. Achilles tendon volume in type 2 diabetic patients with or without peripheral neuropathy: MRI study. *Experimental and clinical endocrinology & diabetes*. **117**(10), pp.645-648.

4. Aydeniz, A., Gursoy, S. & Guney, E., 2008. Which musculoskeletal complications are most frequently seen in type 2 diabetes mellitus? *Journal of International Medical Research*. **36**(3), pp.505-511.

5. Balint, P.V. & Sturrock, R.D., 2001. Intraobserver repeatability and interobserver reproducibility in musculoskeletal ultrasound imaging measurements. *Clinical and experimental rheumatology*. **19**(1), pp.89-92.

6. Abate, M., Schiavone, C. & Salini, V., 2010. Sonographic evaluation of the shoulder in asymptomatic elderly subjects with diabetes. *BMC Musculoskeletal Disorders*. **11**(1), p.278.

7. Okur, S.C., Dogan, Y.P., Mert, M., Aksu, O., Burnaz, O. & Caglar, N.S., 2017. Ultrasonographic Evaluation of Lower Extremity Entheseal Sites in Diabetic Patients Using Glasgow Ultrasound Enthesitis Scoring System Score. *Journal of medical ultrasound*. **25**(3), pp.150-156.

8. Kerimoglu, U., Hayran, M., Ergen, F.B., Kirkpantur, A. & Turgan, C., 2007. Sonographic evaluation of entheseal sites of the lower extremity in patients undergoing hemodialysis. *Journal of Clinical Ultrasound*. **35**(8), pp.417-423.

9. Batista, F., Nery, C., Pinzur, M., Monteiro, A.C., de Souza, E.F., Felippe, F.H., Alcântara, M.C.& Campos, R.S., 2008. Achilles tendinopathy in diabetes mellitus. *Foot Ankle Int*. **29**(1), pp-498-501.

10. Abate, M., Di Carlo, L., Salini, V. & Schiavone, C., 2014. Metabolic syndrome associated to non-inflammatory Achilles enthesopathy. *Clinical rheumatology*. **33**(10), pp.1517-1522.

11. Unlu, Z., Ozmen, B., Tarhan, S., Boyvoda, S. & Goktan, C., 2003. Ultrasonographic evaluation of pes anserinus tendino-bursitis in patients with type 2 diabetes mellitus. *The Journal of rheumatology*. **30**(2), pp.352-354.

12. Wyatt, L.H. & Ferrance, R.J., 2006. The musculoskeletal effects of diabetes

mellitus. *The Journal of the Canadian Chiropractic Association*. **50**(1), pp.43-50.
13. Battery, L. & Maffulli, N., 2011. Inflammation in overuse tendon injuries. *Sports medicine and arthroscopy review*. **19**(3), pp.213-217
14. De Oliveira, R.R., Lemos, A., de Castro Silveira, P.V., Da Silva, R.J. & De Moraes, S.R.A., 2011. Alterations of tendons in patients with diabetes mellitus: a systematic review. *Diabetic Medicine*. **28**(8), pp.886-895.
15. Serban, O., Porojan, M., Deac, M., Cozma, F., Solomon, C., Lehghel, M., Micu, M. & Fodor, D., 2016. Pain in bilateral knee osteoarthritis–correlations between clinical examination, radiological, and ultrasonographical findings. *Medical ultra-sonography*. **18**(3), pp.318-325.