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Original Research Article

Association of enthesopathy among patients diagnosed with Rheumatoid arthritis

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Abstract

Aim & Objective: The purpose of this study was to use ultrasonography at Tezpur Medical College and Hospital in Assam to assess the prevalence and distribution of enthesopathy in RA patients.

Background: Rheumatoid arthritis (RA) is a widely occurring autoimmune disorder that primarily targets the synovial membranes of small joints. However, it can also present with symptoms outside the joints. One such symptom, enthesopathy, is often difficult to diagnose clinically. Ultrasonography has emerged as a newer technique for identifying enthesopathy.

Materials and Methods: There were 14 healthy controls and 29 RA patients in the study. Six entheses sites were graded using the Madrid Sonography Enthesitis Index (MASEI) and analyzed using Doppler ultrasound and a linear transducer in order to evaluate enthesopathy.

Results: Enthesopathy in RA patients was successfully identified by ultrasonography. The enthesopathy scores at the plantar aponeurosis and Achilles tendon insertions showed statistically significant variations. Compared to healthy controls, RA patients had a significantly higher overall enthesopathy score.

Conclusion: Enthesal abnormalities were shown to be highly prevalent in RA patients assessed by ultrasonography.

Keywords: Rheumatoid arthritis, Enthesitis, Ultrasonography, Enthesopathy.

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1. Introduction

An abnormally hypoechoic (loss of normal fibrillar architecture) and/or thickening of tendons or ligaments at the site of bone attachment (sometimes containing hyperechoic foci, such as calcifications) appearance in two perpendicular planes on Doppler imaging is known as enthesopathy.[1] Enthesopathy has two causes, which are divided into two categories: inflammatory and non-inflammatory.[2]

Trauma, degenerative, autoimmune, metabolic and and genetic factors are examples of non-inflammatory causes. The location where tendons, ligaments, joint capsules, or fascia adhere to the bone is known as enthesis. Entetikos, an ancient Greek term meaning "that which is put in from the outside," is where the word "enthesis" originates.[3]

Multiple joint pain, swelling, and stiffness are hallmarks of rheumatoid arthritis (RA), which has an estimated global age-standardized point prevalence of 246.6 and an yearly incidence rate of 14.9 per lakh population, respectively.[4] Handicap is widespread and significant; in a big US research, after ten years, 35% of RA patients had an employment-related handicap.[5] Early diagnosis and treatment are linked to better clinical and radiographic results and a higher chance of remission; delays in diagnosis longer than three months may be harmful.[6] Around 1% of individuals globally are afflicted with rheumatoid arthritis (RA), a chronic, systemic inflammatory autoimmune disease. It affects the synovial membranes resulting in synovitis as a primary abnormality and subsequently leads to bone destruction such as erosions and cartilage damage.[7,8]

Inflammation at the location of tendons or ligaments in the bone is linked to enthesopathy. Seronegative spondyloarthropathy frequently exhibits this characteristic.[9] However, it might be challenging to clinically detect enthesopathy due to the limited sensitivity and specificity of clinical diagnostics.[10]

In Rheumatoid arthritis (RA), inflammation in the tendon sheaths can eventually spread to the tendons themselves. This inflammatory process weakens the tendons, making them more prone to injury. Initially, this may result

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in partial tears, but over time, these tears can progress to complete ruptures. Spontaneous tendon rupture is a common feature of RA, particularly in the later stages of the disease.

Sometimes the clinical examination for enthesitis and enthesopathy is unclear, and ultrasound can help detect aberrant enthesis. But as of yet, neither histological nor imaging studies have identified any morphologic characteristics that would allow for the distinction between inflammation and entheses degeneration, microinjury, and chronic overuse.[16,17] Furthermore, there are a number of theories as to the origin of enthesitis, including genetic, autoimmune, inflammatory, and mechanical factors.[18] McGonagle along with associates.[19] Suggested an enthesitis-based model for the pathophysiology of spondyloarthritis, which occurs when the innate immune response (e.g., to bacterial products) interacts with biomechanical variables. Recent research has highlighted the significance of stromal cells and demonstrated that mechanical strain plays a significant role in enthesitis and bone formation in SpA.[20] Because of its inflammatory edema, structural intra-tendinous rips, and scarring, an ultrasound image typically shows a thicker and inhomogeneous attachment regardless of the pathophysiology. Cysts and erosions in the bone attachment are visible, along with vessels of the inflammatory-repair process.[21] However, based on Feydy and colleagues' study. The differential diagnosis includes enthesopathy from overuse and traumatic lesions, and neither power doppler ultrasound nor magnetic resonance imaging can distinguish between patients with and without SpA.

When enthesopathy occurs, ultrasound (US) and magnetic resonance imaging (MRI) can be used to identify the symptoms of inflammation and long-term alterations.[11] However, the US appears to be superior because to its low cost, ease of detection, and lack of technical changes.[12] Information about the connection between enthesitis and RA is scarce. Therefore, it is essential to determine how enthesopathy is related to RA. The purpose of this study was to determine how common entheses involvement was in RA patients.

2. Materials and Methods

Twenty-nine successive RA patients were chosen from our outpatient clinic, all over the age of 18, who met the study's inclusion criteria. Individuals who had lower limb peripheral neuropathy, had used fluoroquinolones during the previous six months, were athletes, or had diabetes, spondyloarthropathy, or other associated connective tissue disorders, diabetes, Gout were not included in the study. Fourteen healthy controls, matched by age and free of musculoskeletal conditions, were also included. The study was approved by the local ethics committee, and informed consent was obtained from both the patients and controls. All patients' RA disease activity was evaluated using the Disease Activity Score 28 (DAS28).

The distal Achilles tendon, the distal quadriceps tendon, the distal triceps tendon, the distal plantar aponeurosis, and the distal and proximal patellar ligament insertion were the six entheses sites at which bilateral scans were conducted in perpendicular plane, according to de Miguel. The Madrid Sonography Enthesitis Index (MASEI) was used to score the entheses.

The following lesions were assessed using this scoring system: bursitis, erosions calcifications, power Doppler signals in enthesis sites, and the thickness and structure of tendons and ligaments. A score of 0 indicated the absence of calcifications, 1 indicated the presence of a modest calcification or ossification, 2 indicated the obvious presence of enthesophytes, and 3 indicated the presence of substantial calcifications and ossifications. If there was no bursitis or if a well-defined, localized anechoic or hypoechoic region was seen at the site of a bursa, the score was 0. A cortical rupture accompanied by a step-down bone contour defect was referred to as bony erosion (rated as 0 if absence and 3 if present). The following lesions were assessed using this scoring system: bursitis, calcifications, erosions, power Doppler signals in enthesis sites, and the thickness and structure of tendons and ligaments. All measurements and scores were taken during the examination. A score of 0 indicated the absence of calcifications, 1 indicated the presence of a modest calcification or ossification, 2 indicated the obvious presence of enthesophytes, and 3 indicated the presence of substantial calcifications and ossifications.

If there was no bursitis or if a well-defined, specific area that is either anechoic or hypoechoic was seen at the site of a bursa, the score was 0. A cortical rupture accompanied by a step-down bone contour defect was referred to as bony erosion (rated as 0 if absence and 3 if present). Doppler signals were given a score of 3 if they were present or 0 if they weren't The structure of the tendon or ligament was deemed aberrant (rated 0 or 1) if the fibrillar pattern was lost, the appearance was hypoechoic, or there was fusiform thickening ligament and tendon thicknesses.(**Figure 1**) Calcifications received a score of 0 for non-existence, 1 for a little calcification or ossification, 2 for the obvious presence of enthesophytes, or 3 for large ossifications and calcifications. If there was no bursitis score 0 or if a well-defined, specific area that is either anechoic or hypoechoic was seen at the site of a bursa, the score was 1. A cortical rupture accompanied by a step-down bone contour defect was referred to as bony erosion (rated as 0 if absence and 3 if present). A power Doppler signal was given a score of three or zero if it was absent.(**Figure 3**, **Figure 4**)

The ligament and tendon thicknesses were measured at the bone insertion location of greatest thickness. Thick tendons or ligaments were defined as those that measured more than 6.1 mm for the quadriceps tendon, 5.29 mm for the Achilles tendon, 4.4 mm for the plantar aponeurosis, 4.3 mm

for the triceps tendon, and 4 mm for the proximal and distal patellar ligament.(**Figure 2**)

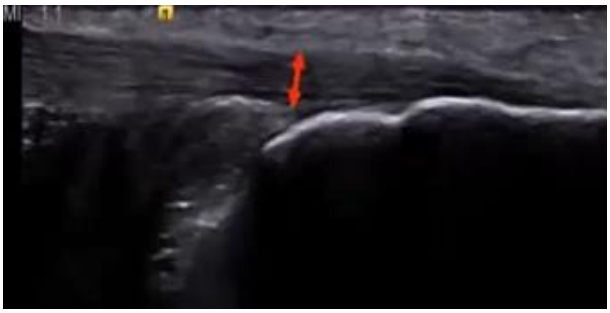

Figure 1: Showing normal thickness and normal fibrillar pattern of Achilles tendon

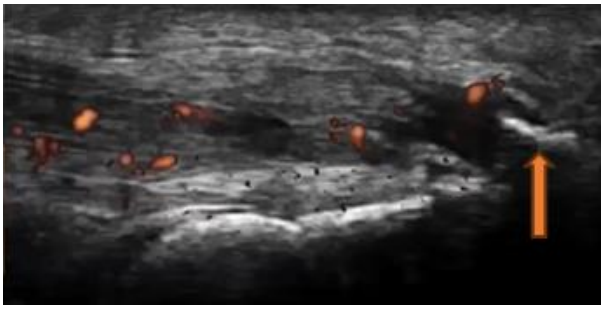

Figure 2: Enthesophyte of planter aponeurosis

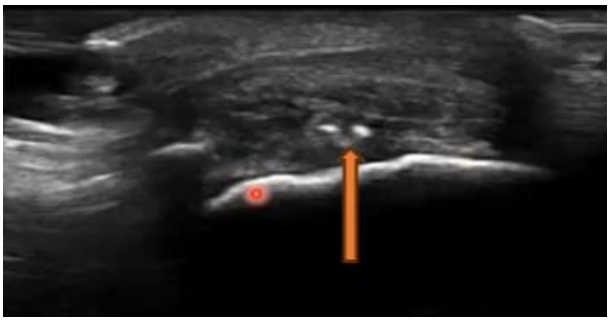

Figure 3: Showing calcification

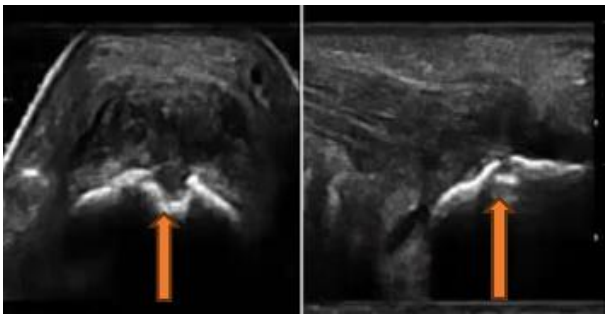

Figure 4: Erosion of calcaneum

3. Results

There were 14 healthy controls and 29 patients with rheumatoid arthritis in the study population. 348 enthesis sites in RA patients and 168 in healthy controls were bilaterally scanned. Nine (64.3%) women and five (35.7%) men made up the healthy controls, whereas 21 (72.4%) women and 8 (27.6%) men made up the RA patients. The mean age of patients with RA and healthy controls was 42.06±15.19 and 41.14±13.75 years, respectively (P=0.156). For the RA group, the range of RA duration were 1– 25 years, mean duration of RA were 5.5±0.87 years. The disease activity score 28 (DAS28−ESR) was 3.5±1.5.(**Table 1**)

The 21 (72.4%) of RA patients were using combined methotrexate and steroid medications, compared to 5 (17.3%) who were taking only methotrexate. Twenty patients having dose of 7.5mg/ weekly, five patients 10mg/weekly, four patients 5mg/weekly dose of methotrexate. The dose of steroid ranges from 5mg to 20mg daily. The percentage of patients on low-dose steroids was just 3 (10.3%).

Table 1: Numbers of males and females affected with rheumatoid arthritis and healthy group

Category	Female	Male
RA patients	21	8
Healthy Control	9	5

Table 2: Madrid Sonographic Enthesitis Index scores and the thickness of tendons or ligaments are compared.

	Rheumatoid arthritis N=58	Control N=28	P value
Plantar aponeurosis thickness (mm	3.7±0.73	3.7±0.86	0.361
Achilles tendon thickness (mm)	4.9±0.71	4.6±0.59	0.402
Distal patellar ligament thickness (mm)	3.8±0.79	3.6±0.71	0.716
Proximal patellar ligament thickness (mm)	4.1±0.66	3.9±0.68	0.817
Quadriceps tendon thickness (mm)	5.9±1.1	6.3±0.67	0.142
Triceps tendon thickness (mm)	4.2±0.74	4.1 ±0.66	0.309
MASEI proximal plantar aponeurosis insertion	0-9	0-4	0.004
MASEI Achilles tendon insertion	0-6	0-2	0.009
MASEI distal patellar ligament insertion	0-5	0-4	0.412
MASEI proximal patellar ligament insertion	0-8	0-6	0.08
MASEI quadriceps tendon insertion	0-6	0-2	0.700
MASEI distal triceps	0-7	0-2	0.651
MASEI total score	0-24	0-6	<0.000

Table 3: Presence of abnormalities suggesting enthesopathy

	Rheumatoid arthritis [n (%)]	Control [n (%)]	P value
At least one thicker tendon/ligament	43 (74.1)	18(64.2)	0.434
At least one structural change	37 (63.8)	9(32.1)	0.004
At least one erosion	14 (24.1)	2(7.1)	0.08
At least one bursitis	6 (10.3)	1(3.6)	0.282
At least one PD signal	19(32.8)	0	0.001
At least one calcification	15(25.9)	3(10.7)	0.143

Tendon and ligament thickness did not differ statistically significantly between RA patients and the control group. Patients with RA had higher MASEI values for the Achilles tendon and plantar aponeurosis than those in the control group. However, there was no statistically significant difference in MASEI scores of distal and proximal patellar tendon, quadriceps tendon insertion, nor distal triceps tendon insertion. However,

Patients with RA had a higher MASEI total score than the control group (**Table 2**). Abnormalities suggestive of enthesopathy are shown in **Table 3**.

4. Discussion

Rheumatoid Arthritis (RA) is the most common form of inflammatory arthritis, affecting around 1% of the global population [11]. The main clinical feature of RA is synovitis, though extra-articular structures such as bursae and tendon sheaths may also be impacted. RA patients can experience a range of clinical manifestations, some of which may be subclinical,[12] such as entheseal abnormalities. Despite this, there is limited research on enthesopathy in RA patients. Enthesopathy is considered the primary lesion in spondyloarthropathies (SpA).[6] As clinical exams and conventional radiography are neither sensitive nor specific for assessing entheses, ultrasound (US) has become a valuable tool for detecting signs of enthesopathy.[13] US provides detailed insight into both active and chronic lesions affecting the entheses.[14] Two key sonographic indices for enthesitis are GUESS[15] and MASEI,[6] with MASEI being preferred due to its ability to assess the upper limbs as well. In this study, both gray scale and power Doppler ultrasound were used to examine six enthesis sites. No significant differences in tendon thickness were observed between RA patients and the control group. However, the MASEI scores for the proximal insertion of the plantar aponeurosis and Achilles tendon were significantly higher in RA patients.

In a study done by Genc et al.[11] enthesophytes observed in plantar aponeurosis enthesis were not found more often in RA patients than healthy controls. MASEI score of Achilles tendon insertion was significantly higher in patients with RA in comparison with the control group. Also, total MASEI score was significantly higher in RA patients.

When entheses were evaluated using ultrasound, 74.1% of RA patients had at least one structural alteration affecting their ligaments or tendons, compared to healthy controls. 32.8% of rheumatoid arthritis patients had at least one Power Doppler signal at the entheses.

The study lacked a comparative group of spondyloarthropathy patients, which would have been valuable for a more meaningful comparison. Additionally, a longitudinal design would have been better than a cross-sectional one since it would have made it possible to identify predictors and shed light on the long-term consequences of enthesopathy in RA patients.

5. Conclusion

Ultrasonography (US) entheseal abnormalities are present in a high percentage (around 3/4th cases) of Rheumatoid arthritis (RA) patients.

6. Ethical No.

086/2023/TMC&H.

7. Conflict of Interest

None.

8. Source of Funding

None.

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