

Effects of serum uric acid on tophus involvement of tendon?Jay Satish Bhatt^{1*}, Naveen Rathor²^{1,2}Assistant Professor, Department of Orthopedics, American International Institute of Medical Sciences, Udaipur, Rajasthan, India

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Abstract

Background: The worldwide prevalence of hyperuricemia and burden of gout is reportedly increased in last few decades. Serum uric acid levels above threshold levels result in nucleation of monosodium urate (MSU) crystals and leads to deposition of crystals in tissues and around joints among cases of long-standing hyperuricemia. However, subclinical inflammation always precedes the deposition of crystals and other manifestation of gout. **Material & Methods:** In the present study 200 Patients who were diagnosed with gout by ACR (American College of Rheumatology) criteria were enrolled for the study by simple random sampling. Clearance from Institutional Ethics Committee was taken before start of study. Written informed consent was taken from each study participant. **Results:** In the present study, 112 (56%) patients the serum uric acid levels were found more than 7 mg/dl. Out of these patients 34 (30.4%) were previously diagnosed with high serum uric acid (more than 7 mg/dl). We found that intra-tendinous tophus is most common in patellar tendon among 18 (9%) patients which is followed by involvement of quadriceps tendon among 16 (8%) patients and involvement of Achilles tendon and peroneus tendon among 6 (3%) cases respectively. tophi in both quadriceps and Achilles tendon among 14 (7%) patients which is followed by involvement of both quadriceps and patellar tendon among 10 (5%) patients and 6 (3%) patients had involvement of both patellar and Achilles tendon. **Conclusion:** We concluded from the present study that the ultrasound examination and all the hyperechoic aggregates of intra-tendinous tophus was the most common presentation among tendons of lower limb. Involvement of patellar tendon was the most common presentation which is followed by Quadriceps and Achilles tendon.

Key words: Uric acid, Tophus, Tendon.

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Introduction

The worldwide prevalence of hyperuricemia and burden of gout is reportedly increased in last few decades. Several studies reported the association between hyperuricemia and prevalence gout and also reports that the association of hyperuricemia with cardiovascular disease and its outcomes. Studies also reports the early treatment measures have been shown benefits in disease outcome [1].

Serum uric acid levels above threshold levels result in nucleation of monosodium urate (MSU) crystals and leads to deposition of crystals in tissues and around joints among cases of long-standing hyperuricemia. However, subclinical inflammation always precedes the deposition of crystals and other manifestation of gout therefore, early intervention in hyperuricemia or gout cases should be considered as new approach in treatment [2].

The breakdown of purines and the rate of uric acid excretion by kidneys and balance of both mechanisms represents the concentration of serum urate (SU) levels. Whenever the serum levels of serum urate (SU) reaches its solubility threshold levels (7 mg/dl) result in oversaturation of SU concentration in serum as well as interstitial fluids [3]. This oversaturation of SU levels in serum and interstitial fluids leads to deposition of MSU crystals in tissues. This deposition of MSU

Correspondence*Dr. Jay Satish Bhatt**Assistant professor,
Department of Orthopedics,
American International Institute of Medical Sciences,
Udaipur, Rajasthan, India.**E-mail:** jay9bhatt@gmail.com

crystals result in tophi formation and gouty arthritis and sometimes urate nephropathy and urolithiasis. However, majority of cases are subclinical and use of urate-lowering drugs in these subclinical cases is still debatable, but usefulness of these drugs in clinically symptomatic patients is well established [4]. The data regarding musculoskeletal involvement among subclinical cases is also limited and elaborated researches are required for these cases [5].

The detection of monosodium urate crystals deposits among cases of hyperuricemia and gout is done by application of ultrasound technique is reported in previous studies. However, detection of MSU crystals in subclinical cases by ultrasound is not well established. In clinically symptomatic patients hyperechoic spots and hyperechoic enhancement (double contour sign) are reported in soft tissues and tendons on USG finding which indicates the presence of tophi and bone and hyaline cartilage erosions [6]. We conduct the present study to evaluate the effects of serum uric acid on tendon and tophus.

Materials & Methods

The present prospective study was carried out in Department of Orthopedics at our tertiary care centre. The study duration was of one year from July 2019 to June 2020. A sample size of 200 was calculated at 90% confidence interval at 10% of maximum allowable error. Patients who were diagnosed with gout by ACR (American College of Rheumatology) criteria were enrolled for the study by simple random sampling. Clearance from Institutional Ethics Committee was

taken before start of study. Written informed consent was taken from each study participant.

Patients with neurologic diseases, poorly controlled diabetes mellitus, cancer patients and chronic alcoholic were excluded from the study. Ultrasound (US) examination done in all enrolled participants for tendon involvement. Findings for presence of tophus were recorded as per EULAR guidelines for each studied tendon [7]. All patients were fully examined and treatment was given and scheduled follow-up was conducted. serum uric acid levels were estimated in all study participants at the time of study and at each follow-up visits. Data analysis was carried out using SPSS v22. All tests were done at alpha (level significance) of 5%; means a significant association present if p value was less than 0.05.

Results

In present study, we enrolled two hundred patients of gout who were aged between 24 to 68 years. The mean age of study participants was 36.88 ± 9.24 years. Out of the total patients, the majority of them were belong to the age group of 31 -50 years. On the basis of gender, majority of patients were male i.e. 148 (74%) and 52 (26%) patients were females. In the present study we enrolled patients with serum uric acid level of 5.5 -9.0 mg/dl. Among 112 (56%) patients the serum uric acid levels were found more than 7 mg/dl. Out of these patients 34 (30.4%) were previously diagnosed with high serum uric acid (more than 7 mg/dl). Out of total patients 128 (64%) had history of pain at enthesi site before enrollment in the study. (Table 1)

Table 1: Distribution of study participants according to age and gender

Parameters		No. of patients (%)
Gender	Male	148 (74%)
	Female	52 (26%)
high uric acid (7 mg/dl and above)		112 (56%)
Pain in (at least one) enthesi site		128 (64%)
Previously diagnosed high uric acid (7 mg/dl and above)		34 (30.4%)

In the present study, tophi deposition was studied by the ultrasound examination and all the hyperechoic aggregates findings were analyzed and recorded. We found that intra-tendinous tophus was the most common presentation in our study. In our study, we found that intra-tendinous tophus is most common in patellar tendon among 18 (9%) patients which is followed by involvement of quadriceps tendon among 16 (8%) patients and involvement of Achilles

tendon and peroneus tendon among 6 (3%) cases respectively. other than isolated intra-tendinous tophus involvement more than one tendon involvement was also reported in present study. We found tophi in both quadriceps and Achilles tendon among 14 (7%) patients which is followed by involvement of both quadriceps and patellar tendon among 10 (5%) patients and 6 (3%) patients had involvement of both patellar and Achilles tendon. (Table 2)

Table 2: Distribution of study participants according to tophi deposition

Tophi deposition	No. of patients (%)
Isolated patellar tendon	18 (9%)
Isolated quadriceps tendon	16 (8%)
Isolated Achilles tendon	6 (3%)
Isolated peroneus tendon	6 (3%)
Both quadriceps and Achilles tendon	14 (7%)
Both quadriceps and patellar tendon	10 (5%)
Both patellar and Achilles tendon	6 (3%)
Total	76 (38%)

Discussion

In Whenever the serum levels of serum urate (SU) reaches its solubility threshold levels (7 mg/dl) result in oversaturation of SU concentration in serum as well as interstitial fluids. This oversaturation of SU levels in serum and interstitial fluids leads to deposition of MSU crystals in tissues. This deposition of MSU crystals result in tophi formation [8]. In present study, we enrolled two hundred patients of gout who were aged between 24 to 68 years. The mean age of study participants was 36.88 ± 9.24 years. Out of the total patients, the majority of them were belong to the age group of 31 -50 years. On the basis of gender, majority of patients were male i.e. 148 (74%) and 52 (26%) patients were females. In the present study we enrolled patients with serum uric acid level of 5.5 -9.0 mg/dl. Among 112 (56%) patients the serum uric acid levels were found more than 7 mg/dl. Out of these patients 34 (30.4%) were previously diagnosed with high serum uric acid (more than 7 mg/dl). Out of total patients 128 (64%) had history of pain at entheses site before enrollment in the study.

Similar results to the present study were reported in a study conducted by Eloy D et al among 31 patients with hyperuricemia and found that intra-tendinous tophus involvement representing the monosodium urate crystals deposition among patients on the ultrasound examination [9]. Similar results to the present study were also reported in a study conducted by Terslev L et al patients with hyperuricemia and found that intra-tendinous tophus involvement representing the monosodium urate crystals deposition among patients on the ultrasound examination [10]. Similar results to the present study were also reported in a study conducted by Dalbeth N et al patients with hyperuricemia and gout and found the deposits of monosodium urate crystals among tendons of feet on the ultrasound examination [11].

In the present study, tophi deposition was studied by the ultrasound examination and all the hyperechoic aggregates findings were analyzed and recorded. We found that intra-tendinous tophus was the most common presentation in our study. In our study, we found that intra-tendinous tophus is most common in patellar tendon among 18 (9%) patients which is followed by involvement of quadriceps tendon among 16 (8%) patients and involvement of Achilles tendon and peroneus tendon among 6 (3%) cases respectively. other than isolated intra-tendinous tophus involvement more than one tendon involvement was also reported in present study. We found tophi in both quadriceps and Achilles tendon among 14 (7%) patients which is followed by involvement of both quadriceps and patellar tendon among 10 (5%) patients and 6 (3%) patients had involvement of both patellar and Achilles tendon. Similar results to the present study were reported in a study conducted by Peiteado et al patients with hyperuricemia and gout and found the double contour sign and hyperechoic cloudy areas on ultrasound examination among tendons of lower limb due to monosodium urate crystals deposition [12]. Similar results to the present study were reported in a study conducted by Weinger et al patients with hyperuricemia and gout and found intra-tendinous tophus as the most common presentation among extensor tendons and flexor tendons of the hand due to monosodium urate crystals deposition [13].

Conclusion

We concluded from the present study that the ultrasound examination and all the hyperechoic aggregates of intra-tendinous tophus was the most common presentation among tendons of lower limb. Involvement of patellar tendon was the most common

presentation which is followed by Quadriceps and Achilles tendon.

References

1. Kuo C-F, Grainge MJ, Zhang W, Doherty M. Global epidemiology of gout: prevalence, incidence and risk factors. *Nat Rev Rheumatol* 2015 Nov 7;11(11):649–62.
2. Stewart S, Dalbeth N, Vandal AC, Rome K. Characteristics of the first metatarsophalangeal joint in gout and asymptomatic hyperuricaemia: a cross-sectional observational study. *J Foot Ankle Res* 2015;8:41.
3. Maiuolo J, Oppedisano F, Gratteri S, Muscoli C, Mollace V. Regulation of uric acid metabolism and excretion. *Int J Cardiol* 2016 Jun 15;213:8–14.
4. Martillo MA, Nazzari L, Crittenden DB. The crystallization of monosodium urate. *Curr Rheumatol Rep* 2014 Feb;16(2):400.
5. Pasalic D, Marinkovic N, Feher-Turkovic L. Uric acid as one of the important factors in multifactorial disorders--facts and controversies. *Biochemmedica* 2012;22(1):63–75.
6. Chowalloor PV, Siew TK, Keen HI. Imaging in gout: A review of the recent developments. *Ther Adv Musculoskelet Dis* 2014 Aug;6(4):131–43.
7. Gutierrez M, Schmidt WA, Thiele RG, Keen HI, Kaeley GS, Naredo E, et al. International Consensus for ultrasound lesions in gout: results of Delphi process and web-reliability exercise. *Rheumatology* 2015 Oct;54(10):1797–805.
8. Naredo E, Uson J, Jiménez-Palop M, Martínez A, Vicente E, Brito E, et al. Ultrasound-detected musculoskeletal urate crystal deposition: which joints and what findings should be assessed for diagnosing gout? *Ann Rheum Dis* [Internet]. 2014 Aug;73(8):1522–8.
9. De Ávila Fernandes E, Sandim GB, Mitraud SA V, Kubota ES, Ferrari AJL, Fernandes ARC. Sonographic description and classification of tendinous involvement in relation to tophi in chronic tophaceous gout. *Insights Imaging* 2010 Jul;1(3):143–8.
10. Terslev L, Gutierrez M, Christensen R, Balint P V., Bruyn GA, DelleSedie A, et al. Assessing Elementary Lesions in Gout by Ultrasound: Results of an OMERACT Patient-based Agreement and Reliability Exercise. *J Rheumatol* 2015 Nov;42(11):2149–54.
11. Dalbeth N, Kalluru R, Aati O, Horne A, Doyle AJ, McQueen FM. Tendon involvement in the feet of patients with gout: a dual-energy CT study. *Ann Rheum Dis* 2013 Sep 1;72(9):1545–8.
12. Peiteado D, De Miguel E, Villalba A, Ordóñez MC, Castillo C, Martín-Mola E. Value of a short four-joint ultrasound test for gout diagnosis: a pilot study. *Clin Exp Rheumatol*;30(6):830–7.
13. Weniger FG, Davison SP, Risin M, Salyapongse AN, Manders EK. Gouty flexor tenosynovitis of the digits: report of three cases. *J Hand Surg Am* 2003 Jul;28(4):669–72.

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