

## IMPACT OF URIC ACID ON TOPHUS TENDON INVOLVEMENT

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### Abstract

**Background:** The prevalence of hyperuricemia and the burden of gout have increased worldwide in recent decades. When serum uric acid levels exceed certain thresholds, monosodium urate (MSU) crystals nucleate and deposit in tissues and around joints in individuals with long-standing hyperuricemia. However, before crystal deposition and other manifestations of gout occur, there is always subclinical inflammation. **Materials and Methods:** For this study, 200 patients diagnosed with gout according to the criteria set by the American College of Rheumatology (ACR) were randomly selected and enrolled. **Result:** In this study, it was found that 112 (56%) patients had serum uric acid levels exceeding 7 mg/dl. Among these patients, 34 (30.4%) had previously been diagnosed with high serum uric acid levels. The most common location for intra-tendinous tophus was the patellar tendon, observed in 18 (9%) patients. This was followed by involvement of the quadriceps tendon in 16 (8%) patients, and the Achilles tendon and peroneus tendon in 6 (3%) cases, respectively. Among the patients, 14 (7%) had tophi in both the quadriceps and Achilles tendons, while 10 (5%) had involvement of both the quadriceps and patellar tendons, and 6 (3%) had involvement of both the patellar and Achilles tendons. **Conclusion:** Based on the findings of this study, it can be concluded that ultrasound examination revealed that intra-tendinous tophus was the most common presentation among tendons of the lower limb. The patellar tendon was the most frequently affected, followed by the quadriceps and Achilles tendons.

## INTRODUCTION

In recent decades, there has been a reported increase in the global prevalence of hyperuricemia and the burden of gout. Numerous studies have highlighted the association between hyperuricemia and the prevalence of gout, as well as its link to cardiovascular disease and its outcomes. Additionally, research has shown that early treatment measures can have beneficial effects on disease outcomes.<sup>[1]</sup> When serum uric acid levels exceed certain threshold levels, it leads to the formation of monosodium urate (MSU) crystals and their deposition in tissues and around joints, particularly in cases of long-standing hyperuricemia. However, it is important to note that subclinical inflammation always precedes the crystal deposition and other manifestations of gout. Therefore, early intervention in cases of hyperuricemia or gout should be considered as a new approach to treatment.<sup>[2]</sup> The concentration of serum urate (SU) levels is determined by the breakdown of purines, the rate of uric acid excretion by the kidneys, and the balance between these mechanisms. When the serum levels of

SU reach the solubility threshold (7 mg/dl), it results in oversaturation of SU concentration in both the serum and interstitial fluids.<sup>[3]</sup> This oversaturation leads to the deposition of MSU crystals in tissues and fluids.

The formation of tophi and gouty arthritis, as well as the development of urate nephropathy and urolithiasis, are the result of the deposition of MSU crystals. However, the majority of cases are subclinical, and the use of urate-lowering drugs in these cases is still a topic of debate. On the other hand, the effectiveness of these drugs in treating clinically symptomatic patients has been well established.<sup>[4]</sup> Limited research has been conducted on the musculoskeletal involvement in subclinical cases, and further studies are needed to explore this aspect.<sup>[5]</sup> Previous studies have reported the use of ultrasound technique to detect monosodium urate crystal deposits in cases of hyperuricemia and gout. However, the detection of MSU crystals in subclinical cases using ultrasound is not yet well established. In clinically symptomatic patients, ultrasound findings show hyperechoic spots and hyperechoic enhancement (double contour sign) in

soft tissues and tendons, indicating the presence of tophi, as well as erosions in bone and hyaline cartilage.<sup>[6]</sup> In our present study, we aim to evaluate the impact of serum uric acid on tendons and tophi.

## MATERIALS AND METHODS

The current prospective study was conducted at Nalanda Medical College and Hospital. The study spanned one year, from January 2020. to december 2021. A sample size of 200 was determined with a 90% confidence interval and a maximum allowable error of 10%. Patients who met the diagnostic criteria for gout according to the American College of Rheumatology (ACR) were selected for the study using simple random sampling. Prior to commencing the study, clearance was obtained from the Institutional Ethics Committee, and written informed consent was obtained from each participant. Patients with neurologic diseases, poorly controlled diabetes mellitus, cancer, and chronic alcoholism were excluded from the study. Ultrasound (US) examinations were performed on all enrolled participants to assess tendon involvement. The presence of tophus was recorded for each studied tendon according to the guidelines set by the European League Against Rheumatism (EULAR).<sup>[7]</sup> All patients underwent a comprehensive examination, received treatment, and were scheduled

for follow-up visits. Serum uric acid levels were measured in all study participants at the beginning of the study and during each follow-up visit. Data analysis was conducted using SPSS v22. All tests were performed with an alpha level of significance set at 5%, indicating a significant association if the p-value was less than 0.05.

## RESULTS

In the current investigation, we recruited a total of two hundred gout patients with ages ranging from 24 to 68 years. The average age of the participants in the study was  $36.88 \pm 9.24$  years. Among the entire patient population, the majority fell within the age group of 31-50 years. When considering gender, it was observed that the majority of patients were male, accounting for 148 (74%) individuals, while 52 (26%) patients were female. For this study, we specifically enrolled patients with a serum uric acid level of  $9.0$  mg/dl. Among the 112 (56%) patients, their serum uric acid levels were found to be above 7 mg/dl. Out of these patients, 34 (30.4%) had previously been diagnosed with high serum uric acid levels (above 7 mg/dl). Additionally, out of the total patient population, 128 (64%) individuals had a history of pain at the entheses site prior to their enrollment in the study. [Table 1]

**Table 1: Distribution of research participants based on age and sex.**

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) entheses site		128 (64%)
Previously diagnosed high uric acid (7 mg/dl and above)		34 (30.4%)

**Table 2: Participants' distribution based on 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%)

The current study examined the deposition of tophi through ultrasound examination, with a thorough analysis and documentation of all the findings related to hyperechoic aggregates. Our findings revealed that the most common presentation of tophi was within the tendons. Specifically, the patellar tendon showed the highest prevalence among 18 (9%) patients, followed by the involvement of the quadriceps tendon among 16 (8%) patients, and the Achilles tendon and peroneus tendon among 6 (3%) cases, respectively. In addition to isolated intra-tendinous tophus involvement, our study also reported cases where more than one tendon was affected. We observed tophi in both the quadriceps and Achilles tendon among 14 (7%) patients, followed by

involvement of both the quadriceps and patellar tendon among 10 (5%) patients, and both the patellar and Achilles tendon among 6 (3%) patients. [Table 2]

## DISCUSSION

In the event that serum urate (SU) levels reach the solubility threshold of 7 mg/dl, oversaturation of SU concentration occurs in both serum and interstitial fluids. This oversaturation leads to the deposition of MSU crystals in tissues, resulting in tophi formation. For this study, we included two hundred gout patients aged between 24 to 68 years, with a mean age of  $36.88 \pm 9.24$  years. The majority of patients fell within the age group of 31-50 years. In terms of

gender, 148 (74%) patients were male, while 52 (26%) were female. Patients with serum uric acid levels ranging from 5.5 to 9.0 mg/dl were enrolled, with 112 (56%) having levels exceeding 7 mg/dl. Among these, 34 (30.4%) had previously been diagnosed with high serum uric acid levels. Additionally, 128 (64%) patients reported a history of pain at entheses sites prior to study enrollment.

A study conducted by Eloy D et al among 31 patients with hyperuricemia found similar outcomes to the present study. The study revealed that patients exhibited intra-tendinous tophus involvement, which indicated the deposition of monosodium urate crystals during ultrasound examinations.<sup>[9]</sup> Additionally, Terslev L et al conducted a study on patients with hyperuricemia and reported similar findings to the present study. They also observed intra-tendinous tophus involvement, indicating the deposition of monosodium urate crystals during ultrasound examinations.<sup>[10]</sup> Furthermore, Dalbeth N et al conducted a study on patients with hyperuricemia and gout, and their findings were consistent with the present study. They identified the presence of monosodium urate crystal deposits among the tendons of the feet during ultrasound examinations.<sup>[11]</sup>

The ultrasound examination was utilized in the current study to investigate the deposition of tophi. All findings of hyperechoic aggregates were carefully analyzed and documented. Our study revealed that the most prevalent presentation of tophi was found within the intra-tendinous region. Specifically, among the 18 (9%) patients examined, the patellar tendon exhibited the highest occurrence. This was followed by the involvement of the quadriceps tendon in 16 (8%) patients, and the Achilles tendon and peroneus tendon in 6 (3%) cases, respectively. Furthermore, our study also reported instances where more than one tendon was affected, in addition to isolated intra-tendinous tophus involvement. Among the patients, we observed tophi in both the quadriceps and Achilles tendon in 14 (7%) cases. Additionally, the involvement of both the quadriceps and patellar tendon was observed in 10 (5%) patients, while 6 (3%) patients exhibited involvement of both the patellar and Achilles tendon. These findings align with a study conducted by Peiteado et al, which focused on patients with hyperuricemia and gout. They also identified the presence of the double contour sign and hyperechoic cloudy areas on ultrasound examination within the tendons of the lower limb, attributed to the deposition of monosodium urate crystals. Similarly, another study conducted by Weinger et al, which examined patients with hyperuricemia and gout, reported intra-tendinous tophus as the most common presentation

within the extensor and flexor tendons of the hand, again due to the deposition of monosodium urate crystals.<sup>[12,13]</sup>

## CONCLUSION

Based on our study findings, it was determined that the ultrasound examination revealed the presence of hyperechoic aggregates of intra-tendinous tophus as the prevailing presentation among tendons in the lower limb. The patellar tendon exhibited the highest frequency of involvement, followed by the Quadriceps and Achilles tendons.

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