

Features of the Clinical and Laboratory Course of Gout

Shodikulova G. Z, Pulatov U. S, Karimov A. Kh.

Samarkand State Medical University

Abstract: Interest in the problem of gout is associated with its high prevalence and rapid growth among men and women of working age. In the study, 75 patients with primary gout were examined. The average age of the patients was 55.9±8 years (ranging from 29 to 65 years). It has been substantiated that it is necessary to conduct a comparative analysis of articular syndrome with liver and kidney damage in patients with gout.

Keywords: gout, liver pathology, chronic kidney disease, clinical and laboratory features.

INTRODUCTION

Gout is a disease associated with inflammation of the joints and the accumulation of uric acid crystals in various tissues, which leads to severe pain, swelling, and inflammation. Gout is one of the most ancient diseases known to mankind. Among rheumatic diseases, gout is considered the most studied, well-understood, and controllable nosological entity [2]. According to Dehlin, M. et al. (2020), the prevalence and incidence of gout are influenced by various factors (such as the localization of the study group, genetics, research methodology, etc.). However, it is known that the indicators range from less than 1% to 6.8% per 1000 person-years and vary between 0.58–2.89. Gout is more common in men than in women, increases with age, and is more frequent in certain ethnic groups [9,11].

From a clinical perspective, gout is characterized by recurrent acute arthritis and the appearance of tophi. This disease mainly occurs in men, but recently its prevalence has also been observed to increase among women. For treatment, drugs that affect the pathogenetic mechanisms of gout are used [1,6,13].

The increase in gout incidence among young people is associated with the widespread prevalence of environmental factors related to gout, while the genetic aspects of the disease's etiology and pathogenesis remain insufficiently studied. It is noted that in Russia, hyperuricemia is found in 4–12% of the population, but gout is diagnosed in only 0.1% of people. In Eurasia and America, the prevalence of gout is about 2%, and among men over 50–60 years old, 4–6% suffer from gout [4,8,10,16]. In this regard, in recent decades, searches have been conducted for genes associated with hyperuricemia and gout risk, and the influence of genetic factors on the regulation of uric acid synthesis and excretion has been studied.

The chronic progressive nature of gout requires physicians to diagnose it as early as possible. However, detecting this pathology in its early stages presents significant difficulties. To date, no specific laboratory test has been found to identify gout. Only the combination of numerous clinical and laboratory signs can help in diagnosing this disease. Therefore, the search for diagnostic methods that make it possible to distinguish gout from degenerative diseases of the musculoskeletal system remains a pressing issue.

MATERIALS AND METHODS

The research was conducted at the Central Hospital of the Samarkand City Medical Association. To carry out the dissertation work, a comprehensive approach was used, which included clinical, laboratory, biochemical, immunological, ultrasound, radiological, CT, and statistical research methods.

In the study, 75 patients with primary gout were examined and divided into 3 groups:

- ➤ Group 1 (n=31): patients diagnosed with primary gout without internal organ involvement.
- ➤ Group 2 (n=20): patients with primary gout and liver and kidney involvement.
- > Group 3 (n=24): patients with primary gout and kidney involvement.

Biochemical research methods included the assessment of renal and hepatic parameters, lipid spectrum, rheumatic tests, uric acid level, IL-6, IL-10, and TNF-α levels.

The functional state of the joints was evaluated using a special questionnaire, including:

- ➤ The Foot Function Index,
- The American Orthopedic Foot and Ankle Society (AOFAS) scale (9,12).

The AOFAS scale evaluates parameters such as pain, functional limitations, mobility, and certain aspects of quality of life (11,13,14).

Quality of life was assessed using the European Quality of Life Questionnaire (EQ-5D), as this questionnaire is universal and allows a realistic assessment of the patient's psychometric state (reliability, validity, sensitivity) and general health status.

Pain intensity was assessed using the Visual Analogue Scale (VAS) (6–8).

In addition, the Gout Impact Scale (GIS) was used, which is a specific method for assessing not only the quality of life but also the impact of gout during attacks and in general. The questionnaire included five scales.

Statistical data processing was carried out using the "Statistica 6.0" software package on a personal computer, calculating the arithmetic mean (M), standard error of the mean (m), Student's t-test, and equality of variances (F – Fisher's test). A significance level of p=0.05 was considered statistically significant. For the statistical analysis of the obtained results, Statistica 12.0 and Microsoft Excel 2010 packages were used.

RESULTS AND DISCUSSIONS

The average age of the patients was 55.9 ± 8 years (ranging from 29 to 65 years). Patients under 43 years old numbered 16 (21.33%), those between 44 and 58 years — 39 (52%), and those between 59 and 65 years — 20 (26.67%). The average age at the onset of the disease was 44.8 ± 8 years. In the majority of patients (71.1%), the disease began between the ages of 35 and 52.

The average duration of the disease at the time of presentation was 5.2 years (1.0–10.0 years). The general characteristics of the patients according to age and disease duration are presented in Table 1.

Number (n) **% Indicators** 100.0 **Total** 75 Age Up to 43 years 16 21.33 52.00 44-58 years 39 59–65 years 20 26.67 Disease duration (years) <1 year 12 16.00 2–5 years 28 37.33 6–10 years 35 46.67

Table 1 General characteristics of patients with gout

Patients who were taking uricosuric drugs, those with severe renal failure, advanced cardiopulmonary failure, or oncological diseases were excluded from the study.

According to patient history, signs of arthritis were present before the diagnosis of gout was established. At the initial examination, acute gouty arthritis was recorded in 12 patients, prolonged

arthritis (lasting 3 weeks to 3 months) in 28 patients, and chronic arthritis (lasting more than 3 months) in 35 patients. During the last year, the average number of relapses was 3.0 (1.0–6.0). Additionally, during the last year, 64 patients had between 1 and 6 attacks of arthritis, while 11 patients experienced between 6 and 9 attacks.

The general characteristics of joint syndrome are presented in Table 2, according to the classification of M.G. Astapenko and E.G. Pihlaka. Recurrent arthritis was observed in 36 patients (48%), and chronic arthritis in 39 patients (52%).

The mean age of patients with recurrent arthritis was 52.6 ± 8.8 years, while in those with chronic arthritis it was 47.2 ± 8.7 years. The average duration of joint attacks was 1-3 weeks. On average, 9 joints (5–13) were affected during the course of the disease. In 52 patients, up to 11 joints were affected, while in 23 patients between 11 and 28 joints were involved. Subcutaneous tophi were detected in 26 patients, with an average of 6 nodules (ranging from 1 to 14). Intraosseous tophi were revealed radiologically in 35 patients.

Table 2 Frequency of joint syndrome in patients with gout (n=75)

Indicators	Number (n)	%
Arthritis type		
Recurrent	36	48.0
Chronic	39	52.0
Arthritis form		
Monoarthritis	16	21.33
Oligoarthritis	14	18.67
Polyarthritis	45	60.00
Duration of joint attack		
5–7 days	11	14.67
8–21 days	33	44.00
22–30 days	22	29.33
1–3 months	9	12.00
Number of attacks per year		
1–2	16	21.33
3–5	48	64.00
≥6	11	14.67
Radiological stage		
0	7	9.33
I	27	36.00
II	35	46.67
III	6	8.00

At the time of examination, 35 patients were taking medications (allopurinol) that affect uric acid levels. The duration of treatment ranged from 1 week to 1 year.

During the study, it was found that patients often had comorbid conditions, particularly cardiovascular, renal, and hepatic diseases. A comparative analysis of patients with gout and joint syndrome was performed between those with hypertension, hepatosis, and chronic kidney disease, and those without such conditions. The frequency of comorbid diseases was as follows: Group 1 - 41.3% (n=31), Group 2 - 26.7% (n=20), and Group 3 - 32% (n=24).

Table 3 Relationship between gout severity index, its components, and comorbid conditions

Indicators	Group 1 (n=31)	Group 2 (n=20)	Group 3 (n=24)
Age (years)	54.9 (48.6; 60.5)	55.6 (51.0; 61.8)	57.2 (50.2; 63.5)
Tophi, %	22.6	55.0	33.3
Number of tophi	3.0 (2.0; 5.0)	3.0 (2.0; 7.0)	4.0 (1.0; 8.0)
Joints affected during disease	12.0 (5.0; 18.0)	12.0 (8.0; 14.0)	12.0 (5.0; 15.0)
Joints affected at examination	4.0 (2.0; 9.0)	5.0 (3.0; 9.0)	5.0 (3.0; 9.0)
Frequency of arthritis per year	3.0 (1.0; 6.0)	3.0 (2.0; 5.0)	3.0 (2.0; 7.0)
Duration of last attack (weeks)	5.0 (1.0; 6.0)	6.0 (2.0; 9.0)	6.0 (1.0; 9.0)
Uric acid (µmol/L)	570.0 (428.0; 623.0)	580.0 (490.0; 623.0)	587 (433; 624)
Severity index score	3.31 (2.71; 3.8)	3.3 (2.8; 4.1)	3.4 (2.9; 4.3)

*Note: p < 0.001, significant differences between groups

Analysis of joint syndrome in gout revealed a number of differences between patients with and without comorbid conditions (Table 3). In patients with liver and kidney disease, the number of affected joints and the severity index were higher (p=0.05).

Gouty tophi occurred more frequently in patients with hepatic and renal pathology (p<0.01). Subcutaneous tophi and the number of affected joints were significantly higher in Groups 2 and 3 compared with Group 1 (p<0.01).

During the examination of patients, it was revealed that they often had comorbidities, particularly cardiovascular, renal, and hepatic diseases. Among the patients, only 32% were diagnosed with chronic renal failure. When analyzing the laboratory indicators of the group of patients with gout and renal impairment, the following results were obtained (Table 4).

Table 4 Laboratory indicators of patients with gout and renal impairment

Indicators	Value	р
Uric acid, µmol/L	587 (436;624)	< 0.01
CRP, mg/L	9.81 ± 5.1	< 0.05
Total cholesterol, mmol/L	6.832 ± 1.10	< 0.05
HDL-C, mmol/L	1.591 ± 0.47	< 0.05
LDL-C, mmol/L	4.892 ± 1.11	< 0.05
Triglycerides, mmol/L	2.845 ± 1.06	< 0.001
Urea, mmol/L	5.678 ± 1.7	< 0.001
Creatinine, µmol/L	93.2 ± 15.6	< 0.001

In patients with gout and both liver and kidney damage, the disease began at almost the same age $(46.81 \pm 8.7 \text{ and } 46.52 \pm 9.6 \text{ years}$, respectively, p<0.001). In these patients, gout started significantly earlier, and the number of affected joints was higher (p<0.001 and p<0.05, respectively). They also experienced more frequent gouty arthritis attacks during the last year (p<0.01).

Among the examined gout patients, 24 showed signs of renal impairment. Of these, 16 had a recurrent course of the disease, while 8 had a chronic course. The most common renal-related symptoms were urolithiasis, dysuric complaints, lumbar pain, macrohematuria, and hypertension.

In the recurrent form of the disease, macrohematuria was observed in a lower percentage of patients, whereas in the chronic course it was clearly manifested. Dysuric complaints were present in one-third of patients with recurrent gout but were observed in all patients with the chronic course. Urolithiasis was found in 12 patients in both groups. The most frequent complaint in both groups was lumbar pain (62.5% of patients with recurrent gout and 50% with the chronic course). Arterial hypertension was the most common manifestation in gout patients with nephropathy, occurring in 70.8% of cases (Figure 1).

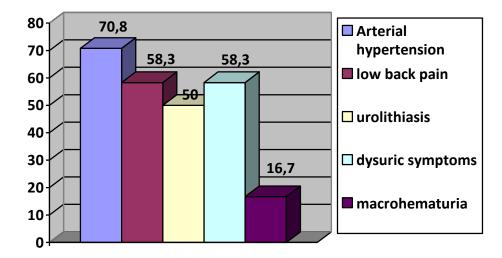


Figure 1. Frequency of clinical signs of renal impairment in patients with gout.

In a long-term general urinalysis of 75 examined patients, approximately 40% were found to have proteinuria. In most cases, proteinuria was mild and transient.

Among the 75 patients, 23 showed a single urine sample protein content ranging from 0.0333–0.0991‰. In the majority of patients, the protein concentration was 0.033–0.066‰. Only 2 patients had proteinuria of 0.1322‰, and 1 patient had 0.258‰.

Daily proteinuria analysis revealed an average level of 0.172–0.451 g/L, with only 3 patients exceeding 0.451 g/L.

Leukocyturia was detected in 27 patients: 19 had mild leukocyturia, while 8 had pronounced leukocyturia. Hematuria was observed in 32% of cases: 15 had mild hematuria and 9 had pronounced hematuria. In addition, urate salts were found in 32% of patients.

The diagnostic value of ultrasound (US) in detecting gouty nephropathy was high. These findings were confirmed by other examinations, with an accuracy rate of 93%. Ultrasound revealed renal pathology of various types in 78.5% of patients. Most commonly, urolithiasis was diagnosed.

Renal cysts were detected in 8 patients, with diameters ranging from 0.5 to 3.2 cm, and numbering 1 to 3 per kidney. Changes in the renal pelvis and calyces, together with stones, were observed in 24 patients. With leukocyturia taken into account, an additional diagnosis of pyelonephritis was made in 14 patients.

Thus, in patients with gout, a comprehensive approach is advisable, prescribing hypouricemic therapy while considering clinical and laboratory indicators as well as comorbid conditions. In addition to pharmacological treatment aimed at correcting arterial hypertension and lipid metabolism disorders, lifestyle modifications such as weight reduction and elimination of harmful habits should be recommended. This approach will improve the quality of life of gout patients, reduce the frequency and duration of relapses, and decrease the cumulative risk factors associated with comorbid conditions.

CONCLUSION

We considered it necessary to carry out a comparative analysis of joint syndrome in patients with gout, with and without liver and chronic kidney disease. It was revealed that in patients with gout who also had hypertension, hepatic, and renal pathology, the number of affected joints and the severity index were higher compared to patients without such comorbidities.

The obtained results demonstrated a relationship between the duration of the disease and arterial blood pressure. Among the main risk factors, the following were more pronounced: increased systolic blood pressure, decreased levels of high-density lipoproteins (HDL), and elevated total cholesterol.

From these findings, it can be concluded that in patients with gout, the presence of comorbid conditions is consistently associated with higher risk factors.

REFERENCES

- Abhishek A, Valdes AM, Jenkins W, Zhang W, Doherty M. Triggers of acute attacks of gout, does age of gout onset matter? A primary care based cross-sectional study. *PLoS One*. 2017 Oct 12;12(10):e0186096. doi:10.1371/journal.pone.0186096.
 PMID: 29023487; PMCID: PMC5638318.
- 2. Adashek ML, Bourji KI. Pegloticase Induced Hemolytic Anemia in a Patient With G6PD Deficiency. *J Hematol.* 2018 May;7(2):83-85. doi:10.14740/jh402w. Epub 2018 May 10. PMID: 32300419; PMCID: PMC7155862.
- 3. Alghubayshi A, Edelman A, Alrajeh K, Roman Y. Genetic assessment of hyperuricemia and gout in Asian, Native Hawaiian, and Pacific Islander subgroups of pregnant women: biospecimens repository cross-sectional study. *BMC Rheumatol.* 2022 Jan 6;6(1):1. doi:10.1186/s41927-021-00239-7. PMID: 34986901; PMCID: PMC8734301.
- 4. Alrajeh KY, Roman YM. Pharmacogenetic Perspective for Optimal Gout Management. *Future Pharmacol*. 2022;2:135–152. doi:10.3390/futurepharmacol2020011.
- 5. Amatucci AJ, Padnick-Silver L, LaMoreaux B, Bulbin DH. Comparison Between Early-Onset and Common Gout: A Systematic Literature Review. *Rheumatol Ther*. 2023 Aug;10(4):809-823. doi:10.1007/s40744-023-00565-x. Epub 2023 Jun 19. PMID: 37335432; PMCID: PMC10326179.
- 6. Beringer PM, Kriengkauykiat J, Zhang X, Hidayat L, Liu S, Louie S, et al. Lack of effect of P-glycoprotein inhibition on renal clearance of dicloxacillin in patients with cystic fibrosis. *Pharmacotherapy*. 2008 Jul;28(7):883-94. doi:10.1592/phco.28.7.883. PMID: 18576903.
- 7. Bezalel Y, Gershoni-Baruch R, Dagan E, Lidar M, Livneh A. The 3435T polymorphism in the ABCB1 gene and colchicine unresponsiveness in familial Mediterranean fever. *Clin Exp Rheumatol.* 2009 Mar-Apr;27(2 Suppl 53):S103-4. PMID: 19796545.
- 8. Borić-Bilušić AA, Božina N, Lalić Z, Lovrić M, Nađ-Škegro S, Penezić L, Barišić K, Trkulja V. Loss of Function ABCG2 c.421C>A (rs2231142) Polymorphism Increases Steady-State Exposure to Mycophenolic Acid in Stable Renal Transplant Recipients: An Exploratory Matched Cohort Study. *Adv Ther.* 2023 Feb;40(2):601-618. doi:10.1007/s12325-022-02378-w. PMID: 36434147.
- 9. Bortolotti M, Polito L, Battelli MG, Bolognesi A. Xanthine oxidoreductase: One enzyme for multiple physiological tasks. *Redox Biol.* 2021 May;41:101882. doi:10.1016/j.redox.2021.101882. PMID: 33578127; PMCID: PMC7879036.
- 10. Bowden RG, Richardson KA, Richardson LT. Uric acid and metabolic syndrome: Findings from national health and nutrition examination survey. *Front Med (Lausanne)*. 2022 Dec 14;9:1039230. doi:10.3389/fmed.2022.1039230. PMID: 36590930; PMCID: PMC9795410.
- 11. Brigham MD, Milgroom A, Lenco MO, Wang Z, Kent JD, LaMoreaux B, et al. Immunosuppressant Use and Gout in the Prevalent Solid Organ Transplantation Population. *Prog Transplant*. 2020 Jun;30(2):103-110. doi:10.1177/1526924820913514. PMID: 32208882.
- 12. Cai N, Chen M, Feng P, Zheng Q, Zhu X, Yang S, Zhang Z, Wang Y. Relationships between obesity and prevalence of gout in patients with type 2 diabetes mellitus: a cross-sectional population-based study. *BMC Endocr Disord*. 2024 Aug;24(1):137. doi:10.1186/s12902-024-01672-8. PMID: 39090627.
- 13. Cai N, Chen M, Wu L, Feng P, Ye X, Liu Q, Zhu X, et al. Association between physical activity and the prevalence of gout among patients with type 2 diabetes mellitus and hyperuricemia: a two-center population-based cross-sectional study. *Clin Rheumatol*. 2024 Sep;43(9):2955-2961. doi:10.1007/s10067-024-07081-5. PMID: 39060811.

- 14. Cao L, Zhao T, Xie C, Zheng S, Wan W, Zou H, Zhu X. Performance of Ultrasound in the Clinical Evaluation of Gout and Hyperuricemia. *J Immunol Res.* 2021 Apr 5;2021:5550626. doi:10.1155/2021/5550626. PMID: 33884273; PMCID: PMC8041551.
- 15. Card-Gowers J, Retat L, Kumar A, Marder BA, Padnick-Silver L, LaMoreaux B, et al. Projected Health and Economic Burden of Comorbid Gout and Chronic Kidney Disease in a Virtual US Population: A Microsimulation Study. *Rheumatol Ther*. 2024 Aug;11(4):913-926. doi:10.1007/s40744-024-00681-2. PMID: 38836994.
- 16. Carroll MB, Smith DM, Shaak TL. Genomic sequencing of uric acid metabolizing and clearing genes in relationship to xanthine oxidase inhibitor dose. *Rheumatol Int.* 2017 Mar;37(3):445-453. doi:10.1007/s00296-016-3592-2. PMID: 27798726.