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Original Article

Demographic, clinical, and laboratory features of Turkish patients with gouty arthritis: A prospective cohort study

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Abstract

Objective: We have conducted this study to evaluate clinical and laboratory findings and to gather and evaluate information that would be useful in clinical practice, such as demographics, joint involvement patterns, laboratory anomalies, treatments applied, and responses obtained in patients diagnosed with gout.

Methods: In our study, the demographic, clinical, and laboratory characteristics of 94 patients diagnosed with gout were evaluated. The patients were re-evaluated with regard to their clinical and laboratory findings at the end of the 1st and 3rd months, their responses to the treatment were observed, and where necessary, new treatment adjustments were made.

Results: Seventy-nine (84%) of the patients were men, and 15 (16%) were women. The ages of the patients ranged between 22 and 86 years with the average age being 57.5 years. The joint involvement during a gouty arthritis attack was most frequently observed in the 1st metatarsophalangeal joint (87.2%), followed by the ankle joint (26.9%), and the knee joint (23.7%). The joint involvement pattern was evaluated to reveal that the acute monoarticular arthritis was observed in 87 patients (93.5%), followed by acute oligoarticular arthritis coming in second in terms of frequency (26.9%). An average attack was determined to last 10.7 days, and the average number of attacks in a year was 2.69. In our study, the colchicine treatment in 24 of our patients, in whom it was determined during the admission and follow-up process that they have not had gouty arthritis attack in the past 3 months, was stopped. Five (20.8%) patients whose colchicine treatment was stopped later developed gouty arthritis attacks, and the colchicine treatment was restarted. On the other hand, 10 out of 38 patients (26.3%), who have either been continuing or had never been on colchicine treatment, were observed to experience a gouty arthritis attack during their 1st and 3rd month check-ups.

Conclusion: In patients with gout, it is recommended that the related diseases, as well as the triggering factors (alcohol, drug use, and dietary effect), be determined, the necessary lifestyle changes be made, and the treatments started.

Keywords: Arthritis, uric acid, lifestyle

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Introduction

Gout is a self-restrictive ailment that develops secondary to hyperuricemia and causes repetitive arthritis attacks. The prevalence of the disease is higher in men compared to women, and it is more frequently observed in the middle aged and elderly men, as well as post-menopausal women. In addition to the genetic factors, hypertension, diabetes mellitus, metabolic syndrome, chronic renal failure, alcohol consumption, myeloproliferative diseases, hypertriglyceridaemia, diet, and drug use (especially diuretics, low-dose aspirin, cyclosporine) also contribute to the development of gout (1-4). In the recent years, an increase has been observed in patients with gout due to the metabolic syndrome, obesity, changes in the dietary preferences, and increase in the use of diuretic antihypertensive agents. The management of this disease that is being more frequently observed in population, as well as its comorbidities, is important. Using this as our starting point, we have conducted this study to evaluate clinical and laboratory findings and to gather and evaluate information that would be useful in clinical practice, such as demographics, joint involvement patterns, laboratory anomalies, treatment, and responses obtained, in patients who applied to the rheumatology clinic and were diagnosed with gout as per the 2015 American College of Rheumatology/European Leage Against Rhetumatology (ACR/EULAR) criteria.

Methods

This prospective cohort study has been conducted on patients who presented to the Training and Research Hospital Rheumatology outpatient clinic and were diagnosed with gout as per the 2015 ACR/EULAR criteria. This study was approved by the local ethics committee on January 4, 2016, approval number 2015-256. Out of 94 patients who participated in the study, 71 patients were present during the 1st month check-up, and 62 were present during the 3rd check-up.

Inclusion criteria were the following:

1. Patients between 18 and 90 years of age
2. Patients diagnosed with gout as per the 2015 ACR/EULAR criteria

The following were the exclusion criteria:

1. Having another inflammatory rheumatologic disease

During the first admission phase, the following information regarding the patients selected as per the foregoing criteria was evaluated: age, gender, disease longevity, average body mass index (BMI), number of attacks experienced in the last year, average attack duration, joint involvement pattern (acute/chronic, mono-arthritis/oligo-arthritis/polio-arthritis), joints involved, the first MTF joint involvement, concomitant diseases (diabetes mellitus [DM], hypertension [HT], chronic renal failure [CRF], ischemic heart disease, hyperlipidemia, nephrolithiasis history, etc.), cigarette and alcohol use, physical examination results, medications used, diuretic drug use, urea-creatinine, uric acid, cholesterol, triglyceride levels, erythrocyte sedimentation speed, and c-reactive protein level. The patients were subjected to urinary tract ultrasound (USG) imaging to check for the presence of nephrolithiasis. The patients were sent to the Diet and Nutrition Polyclinic to ensure that they were put on an appropriate low-protein diet. Upon their initial admission and at their 1st month and 3rd month check-ups, the patients were subjected to a Health Assessment Questionnaire. Upon the 1st and 3rd month check-ups, the patients were physically examined, new attacks and patient compliance with the diet were questioned, the urea, creatinine, uric acid, cholesterol, triglyceride, sedimentation, and CRP levels were evaluated, and the necessary adjustments were made depending on patient responses to the treatment.

Statistical analysis

The Number Cruncher Statistical System 2007 (Kaysville, Utah, USA) program was employed for statistical analyses. In addition to identifying the statistical methods (averages, standard deviation, median, frequency, ratios, minimum, maximum) used in the study data evaluation, Student's t-test was been employed in comparing two groups of normally distributed parameters, and the Mann-Whitney U test was used for non-normally distributed parameters where quantitative data were concerned. On the other hand, the Kruskal-Wallis test was used for the comparison of three or more groups that did not display normal distribution, while Pearson's chi-square test, the Fisher-Freeman-Halton test, Fisher's exact test, and Yates' continuity correction test were used in the comparison of qualitative data. The Friedman test was used for the intra-group comparison of the parameters displaying non-normal distribution, whereas Wilcoxon signed-ranks test was used in making paired comparisons. The level of significance was considered to be $p<0.05$.

Results

A total of 94 patients participated in the study: 15 women (16%) and 79 men (84%). The average age of the participants was 57.06±13.62 years (the average age of women was 65.1 and men 56.3). Demographic characteristics of patients and information on their average age, BMI, concomitant diseases, and physical examination findings are shown in Table 1. The number of attacks the patients suffered, joint involvement patterns, and distribution of the joints involved are shown in Table 2; the distribution related to the findings upon patients' first admission to the polyclinic is shown in Table 3; changes found on the 1st and 3rd month check-ups are shown in Table 4; and the treatments the patients received are shown in Table 5. The initial uric acid value was on average 8.08±1.82 mg/dL; the 1st and 3rd month average uric acid values were 6.83±1.65 mg/dL and 6.74±1.57mg/dL, respectively. In the paired comparisons, the decrease in the uric acid levels in the 1st ($p=0.001$) and 3rd ($p=0.001$) month check-ups in comparison to the initial results was considered significant ($p<0.01$). The Initial Health Assessment Questionnaire Disability Index (HAQ-DI) measurements of the subjects was on average 0.57±0.51; the 1st and 3rd month measurements on the other hand were 0.35±0.42 and 0.28±0.42, respectively. The decrease in the 1st ($p=0.001$) and 3rd ($p=0.001$) month HAQ-DI measurements in comparison to the initial values was considered to be statistically significant ($p<0.01$) The uric acid levels of 32.2% (n=19) of the subjects from among 59, who initially displayed high uric acid levels, were below 6 mg/dL by the 3rd month. Fifteen (24.2%) of the 62 subjects who were followed up for three months displayed new gouty arthritis attacks. While 14.9% (n=14) of the subjects did not receive colchicine treatment, 59.6% (n=56) continued with their treatments, and the colchicine treatment in 25.5% (n=24) was stopped during the time they were monitored. A statistically significant difference has not been determined regarding the rate of the attacks suffered within the 3rd month based on whether the colchicine treatment was stopped ($p=1.000$; $p>0.05$) (Table 6). The number of attacks and BMI of patients did not demonstrate a statistically significant difference based on patients' age ($p>0.05$) The urinary stone history and urinary tract ultrasound results did not display a statistically significant difference on the basis of age ($p=0.05$). The initial uric acid levels and the 3rd month uric acid levels did not show a statistically significant difference with regard to age ($p>0.05$).

The number of attacks and BMI of patients did not demonstrate a statistically significant difference with regard to gender ($p>0.05$) The history of urinary stones and urinary tract ultrasound results did not display a statistically significant difference with regard to gender ($p=0.05$). The initial uric acid levels and the 3rd month uric acid levels did not show a statistically significant difference with regard to gender ($p>0.05$). The number of attacks and BMI did not demonstrate a statistically significant difference with regard to the existence of CRF ($p>0.05$), although the initial uric acid levels and the 3rd month uric acid levels did not show a statistically significant difference based on the existence of CRF. The initial uric acid levels of the subjects with renal failure were higher than in subjects without renal failure ($p>0.05$).

Discussion

Comprehensive studies on gout employing different methods have been conducted. Gout is a disease that can coexist with many other ailments. In the study by Primatesta et al. (5) in the United States, where a total of 177,637 patients with gout were evaluated retrospectively, the following chronic comorbidities have been found: HT at the rate of 36.1%, DM at the rate of 15.1%, CRF at the rate of 3.2%, ischemic heart disease at the rate of 10.2%, and dyslipidemia at the rate of 27.0% (5). On the other hand, in our study, HT was determined to coexist with gout at the rate of 35.2%, DM 27.5%, CRF 40.2%, ischemic heart disease 18%, and dyslipidemia 35.1%. In our study, the ratio of patients with gout and CRF was high. This fact was attributed to the existence of the nephrology clinic and dialysis unit. Thus, there was a joint follow-up of the patients at the study site,

Table 1. Demographic characteristics of patients

		Min.-Max. (Median)	Avg±Ss
Age (year)		22-86 (57.5)	57.06±13.62
Height (m)		1.45-1.9 (1.7)	1.70±0.09
Weight (kg)		40-116 (85)	85.42±14.43
BMI (kg/m^2)		19-44.8 (29)	29.64±4.51
Duration of the Disease (months)		0-720 (48)	76.96±117.67
		N	%
Age (year)	<40 years	12	12.8
	40-65 years	50	53.2
	≥65 years	32	34.0
Gender	Female	15	16.0
	Male	79	84.0
BMI (kg/m^2)			
>30		37	39.3
25-30		41	43.6
<25		11	11.7
Unknown		5	5.3
Concomitant Diseases			
Hypertension	49	54.4	
Ischemic heart disease	17	18.7	
Hyperlipidemia	32	35.2	
Chronic kidney disease	37	40.2	
Diabetes mellitus	25	27.5	
Habits			
Smoking	Never smoked	30	34.5
	Quit smoking	43	49.4
	Still smoking	14	16.1
Alcohol	Drinks alcohol	62	75.6
	Social drinker	12	14.6
	Habitual drinker	8	9.8
Diuretic Use	28	30.8	
-Nephrolithiasis History	25	27.5	
-Nephrolithiasis in Urinary Tract USG	12	15.0	
-Patients With Nephrolithiasis History			
Determined to Have Stones in USG (n=25)	9	36.0	
Physical Examination Upon Admission			
Swelling	29	32.2	
Redness	18	20.0	
Pain	44	48.9	
Tophus	6	6.7	
Bursit	5	5.6	

as well as a low number of subjects included in the study. In the study by Alvarez-Nemegyei et al. (6) including 104 primary gout patients on urolithiasis risk factors and their prevalence in patients with gout, 55 subjects (39%) were diagnosed with nephrolithiasis. Thirty-seven patients (26%) were diagnosed via their medical history, while 18 patients were diagnosed via USG (13%). On the other hand, in the study conducted by Shimizu and Hori (7), the presence of stones was determined in 103 of 383 gout patients using computed tomography (CT). While 65 (17%) of these 383 patients had a history of urinary stones, 64 (62%) of the 103 patients who were diagnosed with urolithiasis via a CT scan had no previous history.

As such, a total number of patients with a positive history for stones and stones as determined by CT was 126 (32.8%). In our study, 25 of 91 patients (27.5%) whose medical histories were obtained in detail had a history of urinary stones. Nephrolithiasis was determined in 12 of the 83 (15%) patients who had a urinary tract USG. Nine of these patients had already had a history of nephrolithiasis. Therefore 28 patients in total (30.7%) were determined to have nephrolithiasis. The use of diuretics contribute to the development of gout. In our study, 28 patients (30.8%) were using diuretics (8 patients used furosemide, and 20 patients used thiazide group diuretics). The diuretic use ratio of the patients in our study was in conformity with previous studies (3, 4). In terms of the joint involvement pattern, 87 of our patients (93.5%) displayed acute monoarthritis, while acute oligo-arthritis was observed secondarily in 26.9% of the patients in terms of the involvement pattern. Joint involvement in the form of polyarthritis and chronic joint involvement (monoarthritis/ oligoarthritis/ polyarthritis) were determined at lower rates. In terms of joint involvement during a gout attack, the involvement of the first metatarsophalangeal joint was observed with the highest frequency (87.2%), followed by the ankle (26.9%) and knee involvement (23.7%). Tophus was determined in six patients and bursitis in five patients. In the SUGAR study conducted on 346 gout patients by Taylor et al. (8), the patients were divided into four groups in terms of joint involvement, and the first group with the highest prevalence displayed the metatarsophalangeal joint involvement (39.4%), the second group demonstrated the knee or ankle/center-foot involvement (37.1%), the third group the elbow, wrist, and hand involvement (14.8%), and the fourth group the polyarticular involvement (8.7%). However, the patients included in this study with gouty arthritis have not been evaluated in terms of other joint involvements developed at differ-

Table 2. Number of attacks, involvement pattern, and distribution regarding joints involved

	Min.-Max. (Median)	Avg±Ss
Attack Duration (days)	0-90 (7)	10.72±13.06
Number of Attacks in the Last Year	0-20 (2)	2.69±2.99
	N	%
-Involvement Pattern		
Acute monoarthritis	87	93.5
Acute oligoarthritis	25	26.9
Acute polyarthritis	5	5.4
Chronic monoarthritis	5	5.4
Chronic oligoarthritis	2	2.2
Chronic polyarthritis	4	4.3
-Joints Involved		
MTF arthritis	82	88.2
Knee	22	23.7
Ankle	25	26.9
Elbow	11	11.8
Metacarpophalangeal	8	8.6
Other	22	23.7

•More than one joint involvement is observed

Table 3. Distribution of the laboratory findings at the time of first admission

	Min.-Max. (Median)	Avg±Ss
Uric acid (mg/dL)	3.4-13 (7.75)	7.96±1.80
LDL cholesterol (mg/dL)	53.8-204 (127.5)	125.26±39.20
HDL cholesterol (mg/dL)	21-71 (40.5)	41.39±12.64
Triglyceride (mg/dL)	53-832 (167)	208.18±133.7
Erythrocyte sedimentation rate (mm/hour)	1-82 (13)	21.54±20.43
C-reactive protein (mg/dL)	0.02-11 (0.5)	1.11±1.75

•More than one joint involvement is observed

ent times or for different involvement patterns (oligoarthritis/polyarthritis). In the meta-analysis study by Stewart et al. (9) involving 44 different studies, the first metatarsophalangeal joint involvement was observed at the rate of 73%, which was similar to the rate we obtained in our study.

The HAQ-DI score is a measurement index that has been developed to evaluate rheumatic diseases led by rheumatoid arthritis. This includes eight activities (items) making up 20 questions. The HAQ-DI questions daily activities, such as putting on clothing, straightening up, eating, walking, hygiene, grasping objects, etc. Each response is evaluated on a scale from 0 to 3. The HAQ-DI is a survey reflecting the functional state, and the resultant score has been shown to be in correlation with disease activity indicators (10). In our study, the HAQ-DI score of our patients was obtained upon their initial admission, as well as on their 1st and 3rd month check-ups. The HAQ-DI score average in the initial admission was 0.57, with the 1st and 3rd month averages being 0.35 and 0.28, respectively, and as such, the decrease in the HAQ-DI measurements in the 1st and 3rd months in comparison to the initial measurements was considered to be significant. In our study, it has been observed that the decrease in the functional capacity of geriatric patients due to additional diseases, independent of the presence of a gout attack or complications, could cause an increase in the HAQ-DI scores. In the study conducted by Alvarez-Hernandez et al. (11) on 206 patients with gout, the HAQ-DI scores of patients were taken at their initial admission and during their 6 month check-up. The HAQ-DI score average was observed to be 0.59±0.77 at the time of the initial admissions, and after 6 months, a drop to 0.31±0.58 was observed on the average. The results obtained are similar to ours. An evaluation of the patients in terms of the treatments they received showed that 81 patients (86.2%) received colchicine treatment, 86 patients (91.5%) allopurinol, and 28 patients (29.8%) corticosteroid treatment. Corticosteroid treatment was prescribed to patients with severe gouty arthritis or those who applied with acute attacks where the NSAII use was contraindicated. In a retrospective study in which the treatment methods of gout were evaluated, a NSAII was used at the rate of 41.7%, colchicine 16.7%, corticosteroid 21%, probenecid 1.4%, and allopurinol 31.8%, and 39% of the patients reported that they did not receive any treatment (5).

In our study, colchicine application was discontinued in 24 patients who had no any arthritis attacks in the past 3 months. Five (20.8%) patients whose colchicine treatment was stopped developed gouty arthritis attacks, as determined at their 3rd month check-up, and they were restarted on the colchicine treatment. On the other hand, 10 of 34 (26.3%) patients, who came for their 1st and 3rd month check-ups and have either been continuing or never have been on colchicine treatment, were observed to have been going through a gouty arthritis attack at their 3rd month check-up. A statistically significant difference has not been determined regarding the rate of the attacks suffered within the 3rd month based on whether the colchicine treatment was stopped or not. A newly started anti-hyperuricemia treatment can increase the risk of an acute attack due to the fluctuation caused in the uric acid levels in the serum and tissue. To prevent this, it is recommended to use colchicine or NSAII for a period shorter than 6 months. Due to its potential toxic effects (myopathy or neuropathy) and the fact that it has no effect in preventing the sedimentation of uric acid, colchicine treatment is not indicated as the long-term prophylaxis (12). In the prospective, double-blind study conducted by Borstad et al. (13), patients with chronic gout were given colchicine and a placebo drug to prevent an acute gouty attack before they were started on allopurinol treatment, and the existing treatment was continued for another 3 months after the serum uric acid value dropped below 6.5 mg/dL. When the attacks that developed in the 6-month period were evaluated in terms of their number and duration, the group receiving colchicine

Table 4. Evaluation of the change in laboratory findings: Initially, at the 1st, and 3rd month check-ups

		n	Min.-Max. (Median)	Avg±Ss	[a]p	Paired comparisons; [b]p
Uric acid (mg/dL)	Baseline	59	3.4-12.4 (8.0)	8.08±1.82	0.001**	0.001**
	1st Month		2.6-10.4 (6.7)	6.83±1.65		0.001**
	3rd Month		3.2-10.7 (6.3)	6.74±1.57		0.434
LDL Cholesterol (mg/dL)	Baseline	38	53.8-204 (130)	129.26±40.87	0.046*	0.001**
	1st Month		49-216 (130)	122.39±38.73		0.014*
	3rd Month		35-188 (118)	119.60±35.72		0.001**
HDL Cholesterol (mg/dL)	Baseline	38	27-71 (46.5)	45.10±10.65	0.666	0.740
	1st Month		28-73 (42.5)	45.37±11.62		0.378
	3rd Month		27-87 (44.0)	47.16±13.95		0.150
Triglyceride (mg/dL)	Baseline	38	53-641 (150.5)	180.50±109.37	0.184	0.303
	1st Month		57-490 (158)	162.47±77.46		0.191
	3rd Month		58-370 (128.5)	157.63±84.84		0.091
Erythrocyte sedimentation rate (mm/hour)	Baseline	43	4-73 (15)	23.33±21.24	0.008**	0.016*
	1st Month		2-87 (8)	18.84±20.62		0.008**
	3rd Month		1-77 (8)	18.35±20.38		0.755
C-Reactive protein (mg/dL)	Baseline	51	0.02-11.0 (0.44)	1.13±2.03	0.381	0.157
	1st Month		0.08-10.0 (0,36)	0.78±1.47		0.330
	3rd Month		0.03-8.77 (0.35)	0.71±1.26		0.776

[a]Friedman test; [b]Wilcoxon signed ranks test; *p<0.05; **p<0.01

Table 5. Distributions pertaining to the treatments

	N	%
Gouty Arthritis Treatment		
Colchicine	4	4.3
Allopurinol	8	8.5
Prednisolon	1	1.1
Colchicine + prednisolon	3	3.2
Colchicine + allopurinol	54	57.4
Allopurinol + prednisolon	4	4.3
Colchicine + allopurinol + prednisolon	20	21.3

Table 6. Evaluation of attack sufferers at 3-month follow-up based on Colchicine treatment

		Colchicine Treatment (n=62)		
		Not Stopped n=38	Stopped n=24	p
Attack Sufferers at 3-Month Follow-Up	None	28 (73.6%)	19 (79.1%)	1.000
	Yes	10 (26.3%)	5 (20.8%)	

Fisher's exact test

treatment was observed to have developed lesser attacks (13). In a meta-analysis conducted by Roughley et al. (14) involving 17 studies determining the prevalence of CRF and nephrolithiasis in patients with gout, the rate of patients with CRF was determined to be 24% (>stage 3, GFR<60 mL/min.), and a positive nephrolithiasis history was determined to be 14%. In the study conducted by Jing et al. (15) on 5085 patients with CFR, the gout prevalence in all CFR patients was determined to be 24.3%, while the gout prevalence in patients with GFR≥60 mL/min was 16%, which increased to 35.6% in patients with GFR<30 mL/min. 30.7% of the patients with a previous gout diagnosis were not receiving any treatment, while 47.2% of the patients receiving an urate-lowering treatment were observed to have ongoing hyperuricemia.

In conclusion, gout characterized by recurring acute arthritis attacks could also display a chronic course, but it would always require continued clinical check-ups. Several factors affect the development of this disease. The elimination of risk factors, especially those that are lifestyle based (obesity, sedentary life style), must take precedence. The follow-up of the uric acid level after an arthritis attack, and when necessary the administration of uric-acid-lowering treatments, and achieving the targeted uric acid level are of a great importance in patients with gout.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of University of Health Sciences, Bakırköy Dr. Sadi Konuk Training and Research Hospital (Decision Date: January 4, 2016; Approval Number: 2015-256).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

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