ORIGINAL PAPERS

Particularities of Patients Dignosed with Gout in Rheumatology Departament

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Abstract

Gout is a chronic metabolic disease, characterized by joint inflammation caused by monosodium urate monohydrate crystals. The main objective of this study was to identify the prevalence of gout in a rheumatology department in Romania and secondary to describe the characteristics of patients diagnosed with this condition, with emphasis on the comorbidities. This is a longitudinal, retrospective study on 280 patients from the Department of Internal Medicine and Rheumatology, Dr I Cantacuzino Hospital, from January 2017 to May 2019, diagnosed with chronic or acute gout. The prevalence of gout in our hospital in 2 years period was 0.97%. Gouty attack was diagnosed in 38.2% of cases, while 61.8% were evaluated for chronic gout. Male frequency was 69.6%, alcohol consummation was observed in more than half of the cohort (53.2%) and 72.1% were retired persons. The most frequent comorbidity was hypertension (HBP) (82.1%) followed by dyslipidemia (65.3%), atherosclerotic disease(ATS) (55.0%) and chronic kidney disease (53.9%). There was a significant association between HBP, ATS and dyslipidemia with chronic gout ($p=0.038$, $p=0.022$ and $p=0.009$, respectively). The rate of gouty attack significantly increased with the serum level of uric acid ($p<0.001$). The therapeutic approach complies with international recommendations.

Keywords: gout, prevalence, comorbidities, treatment.

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INTRODUCTION

Gout is a chronic, metabolic condition characterized by the presence of monosodium urate monohydrate (MSU) crystals in the joints and the tissues. It predominantly affects men in their second and third decades of age and postmenopausal women[1]. Clinical manifestations of gout include recurrent exacerbations of inflammatory arthritis, accumulation of urate crystals in the form of trophy and kidney damage[2]. The pathogenesis of gout involves the intrinsic formation of uric acid in the form of urate at serum levels high enough to lead to precipitation of urate into crystals consequently deposition in joints, which causes an intense, local inflammatory response. Hyperuricemia is the main cause of gout, food sources that can contribute to this condition are risk factors such as organs and red meat, as well as alcohol consumption. Other factors involved in etiology include advanced age, male sex, obesity, certain medications, genetics. The drugs involved in gout pathogenesis can be diuretics, low-dose aspirin, ethambutol, pyrazinamide and ciclosporin[2].

Worldwide data suggest that the prevalence of gout is increasing, although this varies widely from one nation to another, from 0.3-1.7% in developing countries to 1.2%-4.1%, in developed ones. Men have a higher risk of developing gout than women in all age groups, although the sex ratio tends to become more equal in the elderly people[3,4].

Soluble urate does not induce gout attacks, only crystallized urate promotes acute inflammation by complement activation either the alternate pathway though C3 component, or by classical pathway through C1 component, interleukin-1 (IL-1) being a proinflammatory cytokine that plays an essential role in mediating inflammation in gout[5]. A gout attack or acute gout is characterized by the sudden onset of severe joint pain and edema. Typically, inflammation peaks between 12 and 24 hours, after the onset. More frequent, the initial attacks occur in the joints of the lower limbs and are monoarticular in men. Involvement of the first metatarsophalangeal joint is the most common site of attack, occurring in 50% of patients. Even if any joint can be affected, the more frequent are forefoot, knee, wrist, fingers, and olecranon bursa. After the resolution of the acute attack, the patient enters the intercritical stage. For most patients, the second attack occurs within the first year. The final stage of this condition is known as tophaceous gout. It presents as subcutaneous nodules. Tophaceous gout can appear more than 10 years after the onset of attacks. The most common locations are the fingers, knees, olecranon bursa, Achilles tendon and other tendons[6]. Patients affected by gout are often presenting various other comorbidities, hyperuricemia being associated with high comorbidity burden. More common diseases among those patients are cardiac conditions, such as high blood pressure (HBP), myocardial infarction, stroke, but also metabolic ones like obesity, hyperlipidemia, type 2 diabetes mellitus (DM) and chronic kidney disease (CKD)[7].

Treatment includes general lifestyle and diet modification especially avoidance of high-purine meats and no alcohol consummation. Gout attack's management should be started as soon as possible. Nonsteroidal anti-inflammatory drugs (NSAIDs) and colchicine are first-line medications, while corticosteroids are reserved for patients who either do not respond to or cannot tolerate NSAIDs or colchicine. Biological agents such as IL-1 blockers can be considered for patients with adverse effects or inefficiency to the first line of treatment[8]. For chronic gout, urate-lowering therapy is recommended , hypouricemic drugs being either xanthine oxidase inhibitors (Allopurinol and Febuxostat) or uricosurics (Probenecid, Sulfinpyrazone, Benzbromarone)[9].

The main objective of this study was to identify the prevalence of gout in the rheumatology department of a University Hospital. Second objectives were to describe the characteristics of patients who had acute or chronic gout, paying particular emphasis to the comorbidities that these patients exhibited.

MATERIALS AND METHODS

This is a longitudinal, retrospective study on 280 patients from the Department of Internal Medicine and Rheumatology, Dr I Cantacuzino Hospital, from January 2017 to May 2019. Data was extrapolated from patient's charts. Age older than 18 years old, hospital admission for evaluation of chronic gout or acute gout were the inclusion criteria. The local ethics committee gave its approval and all patients enrolled signed a consent form.

Data was presented as number and percentage for ordinal numbers and as mean and standard deviation for continuous numbers. The analysis was made using Excel and SPSS, a p-value under 0.05 being considered statistically significant.

RESULTS

From January 2017 to May 2019 in our hospital, there were 28.787 patients' hospitalization, of which 280 had an evaluation for chronic or acute gout. Thus, the prevalence of gout in our hospital in 2 years period was 0.97%. Acute gout was present in 38.2% (N=107) of cases, while 61.8% (N=173) were evaluated for chronic gout. As shown in table 1, the male frequency was 69.6%, 72.1% were retired persons. Urban residency was the most prevalent, in 65.7% of cases. The majority of patients with gout, were between 50- and 70-year-old, 63.2%, with a male: female ratio of 2.5:1. Under 50 years old were 12.8% of patients with a male: female ratio of 8:1, while 23.93% were older than 70-year-old with a sex ratio of male: female of 1.2:1.

A BMI at hospital admission higher than 25 kg/m^2, consider overweight and obese, was found in 71.1% (N=199) of cases. Alcohol intake was admitted by 53.2% of subjects.

Table 1 Patients' characteristics

Characteristics	Frequency, N=280	Percentage, %
Age at hospital admission		
<50 y.o	36	12.9%
50-70 y.o	177	63.2%
>70 y.o	67	23.9%
Sex		
Male	195	69.6%
Female	85	30.4%
Working status		
Employee	69	24.6%
Retired	202	72.1%
No working status	9	3.2%
Environment		
Urban	184	65.7%
Rural	96	34.3%
BMI at hospital admission		
Underweight (BMI<18.5)	6	2.1%
Normal weight (BMI ≥18.5 and<25)	75	26.8%
Overweight/obese (BMI ≥25)	199	71.1%
Alcohol status		
Yes	149	53.2%
No	131	46.8%
Smoking status		
Yes	70	25.0%
No	210	75.0%

Analyzing the presence of the comorbidities (Table 2), high blood pressure is the most frequent disease in this cohort affecting 82.1% of patients. Chronic gout was more frequently associated with hypertension than acute gout, with a statistical validation, p=0.038. The patients suffering from atherosclerotic disease were those with a history of at least 1 of the following: coronary artery disease, acute heart attack or ischemic stroke. Thus, in this study, 55% of patients were affected by atherosclerotic events, 61.3% (N=106) being diagnosed with chronic gout with a statistically significant association, p=0.022. Chronic kidney disease was present in 53.9% of cases, while heart failure in 25.0%, with no statistical difference between acute and chronic gout.

Table 2 Patients' comorbidities and comparison between acute and chronic gout

Comorbidity	Total N=280	p- value comparison between Acute (N=107) and Chronic gout (N=173)
Atherosclerotic disease	154, 55.0%	0.022*
Heart failure	70, 25.0%	0.776
High blood pressure	230, 82.1%	0.038*
Dyslipidemia	183, 65.3%	0.009*
Non-alcoholic fatty liver disease	153, 54.6%	0.618
Diabetes mellites type II	84, 30.0%	0.196
Chronic kidney disease	151, 53.9%	0.983
History of solid neoplasm	23, 8.2%	-

*= statistically significant

Diabetes mellites type II was registered in 30.0% of cases, without a significant difference between those having acute and chronic gout. More than half of the cohort, 65.3%, were diagnosed with dyslipidemia, this condition being significantly associated with chronic gout, p=0.009. Regarding the presence of neoplasm, 8.2% of patients had a history of solid neoplasm, hematologic malignancy was not registered in our study.

As for the prevalence of comorbidities among female patients, shown in Figure 1, 88% suffered from HBP, 55% had chronic kidney disease, 30.5% heart failure and 65% atherosclerotic disease. Three comor-

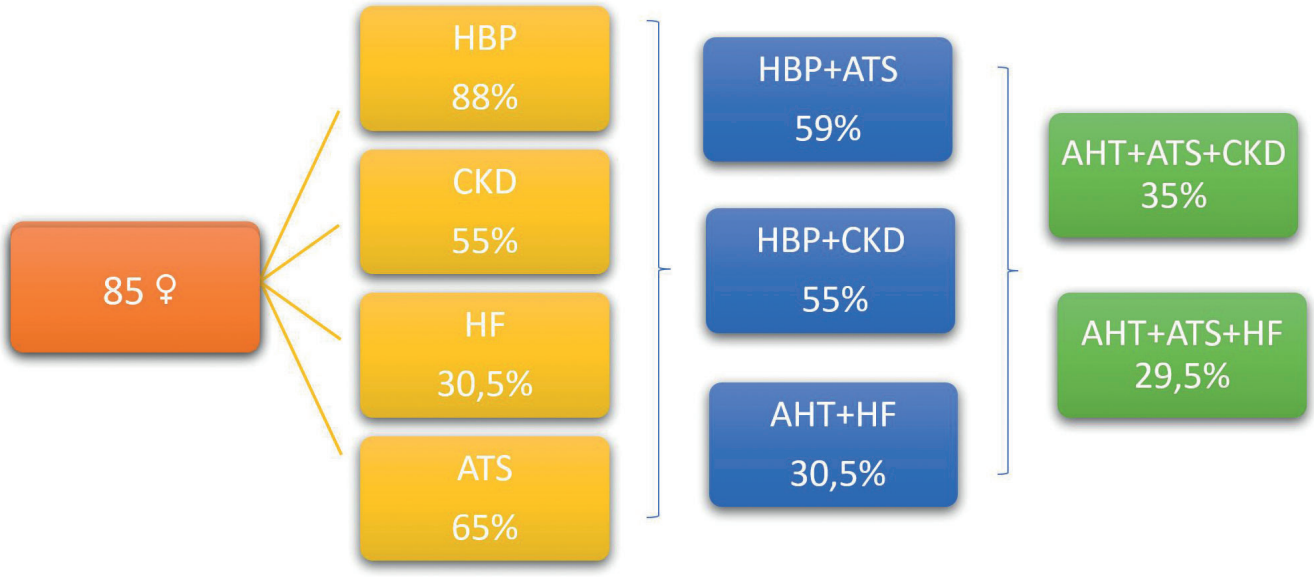

Figure 1. Comorbidities prevalence among the female patients; AHP= high blood pressure; CKD=chronic kidney disease; HF=heart failure; ATS=atherosclerotic disease.

bidities simultaneously were registered in 35% and 29.5% of cases, having HBP associated with atherosclerotic disease and chronic kidney disease, and hypertension associated with atherosclerotic disease and heart failure, respectively. All four comorbidities were present in 19% of patients.

Table 3. Serum Uric acid analyses in the cohort

	N	sUA mean±SD mg/dL	P-value
Alcohol intake			
Yes	149	7.1±1.9	0.054
No	131	6.7±1.9	
Sex			
Male	195	6.9±1.8	0.827
Female	85	6.8±1.9	
Acute Gout			
Yes	107	7.6±1.9	<0.001*
No	173	6.5±1.7	

*= statistically significant, SD= standard deviation, N= number

The upper limit of normal for uric acid was considered 7mg/dL. Analyzing the level of serum uric acid (sUA) (Table 3), the results showed that males and patients drinking alcohol regularly had a higher value of sUA than females and those without alcohol intake (6.9±1.8 vs 6.8±1.9, 7.1±1.9 vs 6.7±1.9, respectively), with no statistically difference for sex, p=0.827, and a borderline result for alcohol intake p=0.054.

In this study, the rate of acute gouty attack significantly increased with higher levels of serum uric acid (p<0.001), 63.5% having acute gout from those with sUA>9 mg/dL, as only 48.91% of patients with sUA within normal range are diagnosed with acute form of the disease (as illustrated in figure 2).

Regarding the treatment, the hygienic-dietary regimen was recommended for all people with gout. NSAIDs were used in 45.7% of patients (N=128), col-

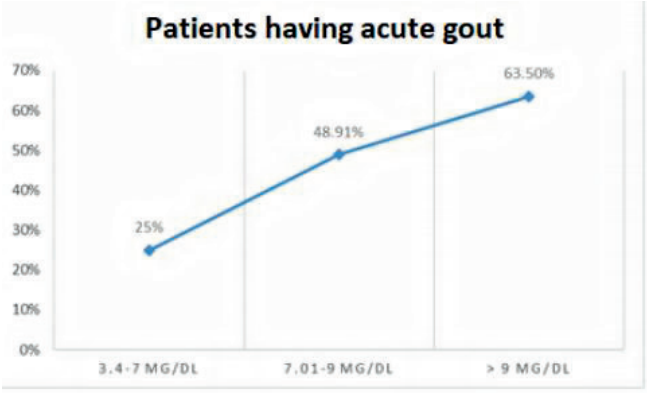

Figure 2. The rate of acute gout cases depending on sUA level

chicine in 51.1% (N=143) and corticosteroids in 10.3% (N=29). Chronic treatment was predominantly represented by Allopurinol, administered in 84% of cases, with an oral dosage between 50 mg and 600 mg per day. Only 2% of patients in this study received Febuxostat (80 mg daily).

DISCUSSIONS

In our cohort the prevalence of gout reached 0,97%, while in the general population, the data from 2018 estimated this prevalence between 1 and 4% worldwide [10]. A study published in 2022 by the team led by Natalie McComick and carried out between 2007-2016 aimed to identify the particularities of gout in the American population according to gender[11]. They demonstrated that the rates of the gouty attacks among both men and women were higher in black population than the white American population, OR 1.3 and 1.8, respectively. The current study did not identify elements related to race, but in the studied population, men proportion was three times higher than the female subgroup[11]. In the current study, the upper limit of normal for uric acid was considered 7mg/dL, but the ACR/EULAR guideline sets this limit at 6mg/dL, which would mean that 65% of the participants in this study had elevated uric acid values[8]. The American Cohort Analysis revealed that in the female population, economic issues, diet, obesity, and renal disorders are connected to gout, whereas in the male population, chronic kidney disease and diet are the main risk factors[11]. Although the link between lipid profile and uric acid has not been sufficiently researched, a study conducted by Nurshad Ali in 2019 in Bangladesh established a statistically significant, directly proportional link between uric acid levels and those of total cholesterol, triglycerides and LDL and an inversely proportional link with HDL cholesterol[12]. Thus, also in the present work, it is noted that 55% of the patients who presented for a gout attack were dyslipidemia, the vast majority associating increased or greatly increased values of both uric acid and total cholesterol and triglycerides[12]. The comorbidities identified among analyzed population were: atherosclerotic disease, congestive heart failure, hypertension, dyslipidemia, hepatic disease, diabetes mellites type II, chronic kidney disease, history of solid neoplasm. In the data published in 2018 the associated diseases were quite similar, even the proportions of each entity were comparable, for example hypertensive population reached 82% in our cohort while in general population was higher than 75%[10]. The CKD proportion identified in our studied population was 53%, while the NHAHNES survey described a proportion of 70% CKD[13]. More than half of the analyzed population consumes alcohol, as it is known internationally that alcohol consumption increases the risk of hyperuricemia and gout attacks[14]. 38% of our cohort population was registered as acute gouty attack, the medication used being in accordance with EULAR Recommendation, based on Colchicine, NSAIDS and corticotherapy[8]. The data from the NOR GOUT study, which aimed to follow up for 2 years the patients with a recent gout attack, showed that in the first 3-6 months the flares are frequent despite the maximum hypouricemic therapy, but they become rare in the second year, the crystals identified ultrasonographical at baseline being a negative prognostic factor for the recurrence of gout attacks even after 2 years of follow up[15]. Long-term hypouricemic medication (allopurinol, febuxostat) was recommended to 86% of the patients in this study, allopurinol being in almost all cases the specific therapy. The most popular ULT in Sweden is allopurinol, but probenecid and febuxostat are other options. 98% of all ULT prescribed in 2021 was allopurinol[16].

According to a 2018 meta-analysis, allopurinol reduces the risk of acute myocardial infarction and stroke by 60% and cuts the risk of kidney disease development in half. These additional advantages of allopurinol are beneficial given the high incidence of these comorbidities and among the individuals examined in this article[17].

CONCLUSION

In conclusion, the study carried out shows that the prevalence of gout in the rheumatology clinic in Romania reaches data comparable to the general population. The identified comorbidities are from the cardiovascular, renal, hepatic and diabetic spectrum in variable proportions. The therapeutic approach complies with international recommendations. Extending the analysis to the national level could be useful to highlight the particularities of this disease among the Romanian population.

Compliance with ethics requirements: For the publication of this article the authors declare that there is no

conflict of interest and the patient's informed consent was obtained for the publication of images and personal data, preserving the patient's anonymity.

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