ORIGINAL ARTICLE

EPIDEMIOLOGY AND MANAGEMENT OF GOUT PATIENTS ATTENDING RHEUMATOLOGY TERTIARY CENTRE IN PERAK, MALAYSIA.

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Abstract

Introduction: Gout is the most common treatable inflammatory arthritis worldwide. There is yet any prevalence study on gout on Malaysian population. The management of gout appears to be affected mostly by multiethnic perceptions, knowledge and awareness as well as variation in the treatment by different health care professionals and limitations in treatment modalities. The aim of this study is to describe the epidemiology and management of gout in rheumatology center in Perak state, Malaysia. **Methods:** All patients who were diagnosed as having gouty arthritis based on the 2015 American College of Rheumatology (ACR) classification criteria for gout and who had attended the rheumatology clinic, Hospital Raja Permaisuri Bainun, Perak, Malaysia were selected. Patient's information was retrieved from the clinical records. **Results:** Fifty-four gout patients who were studied were predominantly from the Malay ethnic group followed by Chinese and Indian. The mean age was 53 years and the duration of disease was more than 10 years with male predominance. Forty-two patients had comorbidities which were hypertension, dyslipidemia, diabetes mellitus and ischemic heart disease. The most common manifestation was multiple joint pain, first metatarsophalangeal joint being most affected. Majority of the patients presented with tophi as well as other symptoms and signs of gout. The mean baseline serum uric acid (sUA) was 567.3 umol/L and 469.3 umol/L was six months after the treatment. The mean difference shown between sUA for males and females was statistically significant ($P = 0.012$) although the male patients were outnumbered. Majority of the patients were on urate-lowering therapy (ULT) namely allopurinol and probenecid. However, despite being advised, educated and given counselling sessions on allopurinol and diet, only half of them had shown good compliance. **Conclusion:** The targeted sUA as recommended in the guideline had yet to be achieved in our rheumatology clinic. The identification of reversible risk factors such as non-adherence to treatment, limited availability and accessibility of newer ULT, and dietary compliance in this study will provide guidance for better clinical management of gout in this region.
Keywords: *Gout, Serum uric acid, Clinical presentation, Compliance, Urate-lowering therapy.*

Introduction

Gout is one of the most common and treatable crystal arthropathy with increasing prevalence globally especially in developed countries which predominantly affects men and postmenopausal women[1,2,3,4,5]. Prospective epidemiological studies has shown that high purine diet, obesity, the metabolic syndrome, diuretics, are the risk factors for causing hyperuricemia and gout [6,7].

The American College of Rheumatology (ACR) and European League against Rheumatism (EULAR) have recommended for optimal management of gout with emphasis on patient's education and lifestyle modifications[8, 9].

The objectives of this study were to determine the prevalence and management of gout in tertiary referral center for rheumatic disease in Perak State, Malaysia.

Materials and Methods

This was a hospital-based descriptive study done between October to November 2016 in Rheumatology clinic, Hospital Raja Permaisuri Bainun, Ipoh, State of Perak, Malaysia. Patient's socio-demographic and clinical information were retrieved from rheumatology outpatient clinic record. The management of gout including advice and education on treatment and diet were also evaluated.

Diagnosis of gout was based on the validated definition in previous population-wide epidemiological studies on gout i.e. if patient has been prescribed allopurinol, colchicine or presence of tophi, tophus or podagra[10,11,12,13]. The 2015 ACR-EULAR classification criteria for gout was also applied and used for newly diagnosed gout during the period of this study [14].

Gout patients who had been discharged from the rheumatology clinic, asymptomatic hyperuricemia, and other type of arthritis such as rheumatoid arthritis (RA), psoriatic arthritis (PsA), systemic lupus erythematosus (SLE), calcium pyrophosphate disease (CPPD) or pseudogout, suspected tumor lysis syndrome were excluded.

Ethical clearance was obtained from the institutional, Clinical Research Centre (CRC) Hospital Raja Permaisuri Bainun and Malaysian Research Ethic Committee (MREC).

Statistical analysis

The data was analyzed by using SPSS 23.0. Descriptive statistics and Pearson's chi-square test was used to determine the significance of difference from different categorical variables. $P < 0.05$ was considered statistically significant.

Results

There were a total of 54 cases of gout had been diagnosed and under follow-up at the rheumatology clinic Hospital Raja Permaisuri Bainun, Ipoh. Majority were men from Malay ethnicity followed by Chinese and Indian with mean age and the duration of the disease of 53.1 ± 13.6 SD years and 7 years respectively. The age range was from 26-year old to 80-year old with peak between 40 and 60 year old (**Table 1** and **Table 2**).

The common risk factors for gout identified in our patients were hypertension (44.4%), hyperlipidemia (53.7%), ischemic heart disease (83.3%), and diabetes mellitus (75.9%), and alcohol intake (9.3%), family history of gout (22.2%).

Majority of patients had most of the common signs and symptoms of gout at presentation (**Table 2**). However, crystal analysis under polarized microscope, plain x-ray assessment and musculoskeletal ultrasonography were performed in few patients. The Mean sUA at different intervals was not significantly correlated across

genders, and comorbid including family history (**Table 3**).

More than 80% of patients were prescribed allopurinol and colchicine. Febuxostat was prescribed in 2 patients who developed allergic to allopurinol and have nephrolithiasis. 8 patients have allergic to allopurinol with quarter of them developed Steven Johnson Syndrome. 40.7% of patients had poor medications adherence despite advice and education were given in 64.8% patients documented. 46.3% of patients had defaulted follow-up without any specific reason documented. (**Table 4** and **Table 5**).

Discussion

The prevalence of gout remained higher in men compared to women across all age groups with ratio ranges from 2: 1 to 4: 1 [7, 15]. Among the three major ethnic groups in Malaysia, the incidence of gout is shown to be predominantly occurs in Malay as evidenced from our hospital-based study and other observational studies in Malaysia [16, 17, 18].

Ageing is the major risk factor in developing gout for both genders. Therefore, this attributes to multifactorial causality which then leads to hyperuricemia hence, predispose to crystal deposition [19.20]. It is consistent with our study which shows that the sUA level and gout are increasing with age above 40 years old.

Genetic i.e family history [21] and environmental factors i.e. smoking and alcohol intake besides age, gender, and high purine diet, have been implicated in the development of gout[22]. There was a higher number of patients who smoke observed in our study. Chen MY et al has demonstrated the significant association among sUA and smoking and alcohol consumption[23]. However, alcohol consumption contributed only small percentage in this study due to majority of gout patients were Malays whereby alcohol drinking is not a usual practice.

The significant association between hyperuricemia, gout with comorbidity including metabolic disorders is well established[24, 25]. We observed similar association between gout and hypertension and hypercholesterolemia comparable to previous prevalent gout studies although it was under-powered[24, 26, 27]. Despite high prevalence of ischemic heart disease and diabetes mellitus observed in this study, it was found that these comorbidities were not independent risk factors for gout [5].

There were only 2 urate lowering therapy (ULT) readily available in Malaysia i.e. allopurinol and probenecid. Febuxostat was not readily available and accessible in our hospital and it is used as a second-line ULT. Losartan which has uric acid lowering properties, although it is insignificant, was added to patients' treatment who had hypertension, diabetes with nephropathy. In our study, 91% of gout patients were prescribed allopurinol as it is recommended as first-line ULT for management of gout in accordance to international guidelines [8, 9]. We observed in our study, sUA concentration did not achieve recommendation target[28]. As mentioned, added to the presence of comorbidities i.e. metabolic disorders, hypertension, and non-adherence to treatment have become a major challenge in managing gout patients. The findings showed that almost half of the patients had defaulted follow-up without a good reason documented although 65% of them were aware of the importance of compliance to the treatment.

Besides a small sample size in our study, there were other limitations that results in discrepancy in the statistical analysis. Poorly documented important information such as smoking, alcohol consumption, dietary habit, weight and height led to variation in distribution of gout risk.

Conclusion

Gout, being one of the most common preventable and treatable crystal arthropathy, it is still sub optimally managed with current standard of care even in a tertiary center. Our study shows that poor adherence or poor knowledge of treatments are the factors probably contribute to failure to achieve targeted serum uric acid. Unavailability of the alternative ULT, inappropriate use of allopurinol, different perception of healthcare professionals on gout are among the other barriers towards effective management of gout. This study also highlights the importance of recognizing this common disease which is poorly managed and may be the first step in improving management of gout in future.

Conflict of interest

The authors declare that they have no competing interests.

Table 1: Baseline socio-demographic characteristics

N = 54	n (%)
Ethnicity:	
Malay	46 (85.2)
Chinese	3 (5.6)
Indian	4 (7.4)
Others	1 (1.9)
Gender:	
Male	49 (90.7)
Female	5 (9.3)
Mean age $\pm$ SD (years)	53 $\pm$ 13.6
[a] Comorbidities:	
Nil	12 (22.2)
Hypertension	24 (44.4)
Diabetes mellitus	41 (75.9)
Hypercholesterolemia	29 (53.7)
Ischemic Heart Disease	45 (83.3)
Numbers of comorbidities per patient:	
1 – 2	32 (69.3)
More than 2	10 (18.5)
Family history of gout	12 (22.2)
Smoking	35 (64.8)
Alcohol intake	5 (9.3)
Employment status:	
Currently employed	17
Unemployed	4
Retiree (not due to health)	16
Disabled and /or retired due to health	2

a:Comorbities: any of these conditions: hypertension, diabetes mellitus, ischemic heart disease, hypercholesterolemia.

Table 2: Clinical characteristics of gout patients

N = 54	n (%)
Duration of disease	7 ± 5.6
(Mean ± SD years)	
Clinical presentation:	
Joint involvement:	20 (37.0)
- First MTP[a]	30 (55.6)
- Knee	25 (46.3)
- Ankle	8 (14.8)
- DIP[b]	17 (31.5)
- Other joints	
Signs of gout:	8 (14.8)
- Monoarthritis	4 (7.4)
- Unilateral first MTP	6 (11.1)
- Unilateral tarsal	41 (75.9)
- Frequency of attack (> 1 episode of acute attack)	
- Presence of tophi	37 (72.5)
- Presence of podagra	9 (16.7)
- Maximum inflammation within 1 day	36 (66.7)
Radiological imaging:	
Plain X-ray:	
- Erosion	8 (14.8)
- Subcortical cyst without erosion	1 (1.9)
Microscopy:	
Presence of negative birefringent MSU[c] crystals	6 (11.1)
Ultrasound kidneys:	
Presence of renal calculi	14 (25.9)

a. MTP = Metatarsophalangeal, b. DIP = Distal Interphalangeal, c. MSU = Monosodium urate

Table 3: Serum uric acid and comorbidities at different interval

	Baseline	3 months	6 month	p
	Mean sUA ± SD, µmol/L			
Male	543.44 ± 152.03	507.32 ± 138.94	478.58 ± 182.77	ns
Female	767.44 ± 365.34	325.00 ± 325.50	365.00 ± 339.73	
Hypertension	550.82 ± 170.48	463.13 ± 148.70	148.70 ± 185.95	ns
Ischemic Heart Disease	586.53 ± 219.42	383.00 ± 183.10	384.50 ± 200.72	ns
Diabetes Mellitus	618.72 ± 255.99	379.17 ± 158.08	383.00 ± 210.29	ns
Hypercholesterolemia	575.69 ± 204.38	503.22 ± 147.66	483.04 ± 171.31	ns
Smoking	544.58 ± 198.51	458.49 ± 166.35	382.06 ± 208.67	ns
Family history of gout	535.12 ± 256.91	421.36 ± 187.32	376.11 ± 215.58	ns

sUA = serum uric acid; $p < 0.05$ is considered statistically significant; ns = not significant

Table 4: Uric acid lowering medication used

N=54	n (%)
Allopurinol	49 (90.9)
Febuxostat	2(3.8)
Colchicine	43(79.7)
Probenecid	11(20.4)
Losartan	20(37.2)

Table 5: Medication and high purine diet adherence

	(%)
High purine diet non adherence	29 (53.7)
Medication	
- Compliance	24 (44.4)
- Non compliance	22 (40.7)
Main reasons for non-compliance:	
Forgetful	1 (1.9)
Defaulted follow-up	25 (46.3)
Education on allopurinol	35 (64.8)
Allergy to allopurinol	8 (14.8)

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