Addis Ababa University

College of Health Sciences

Department of Internal Medicine

Clinical Profile, and Treatment Pattern and Factors Affecting Treatment outcomes of Patients with Gouty Arthritis Attending the Rheumatology Clinic of Tikur Anbessa Specialized Hospital and Lancet General Hospital, Ethiopia

A Three Year Multicenter Retrospective Study

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Abbreviations and Acronyms

AAU-Addis Ababa University

ACR -American College of Rheumatology

BMI-Body Mass Index

CI – Confidence Interval

CKD- Chronic Kidney Disease

CVD- Cerebrovascular Disease

DM- Diabetes Mellitus

eGFR- Estimated Glomerular Filtration Rate

EULAR- European Alliance of Associations of Rheumatology

FMoH: Federal Ministry of Health

GA- Gouty Arthritis

HF- Heart Failure

HTN- Hypertension

IHD- Ischemic Heart Disease

M: F- Male to Female Ratio

MSU- Monosodium Urate

MTP- Metatarsophalangeal Joint

NGO- Non-Governmental Organization

NSAIDs- Non-Steroidal Anti-Inflammatory Drugs

OR- Odds Ratio

SPSS- Statistical Package for the Social Sciences

TASH- Tikur Anbessa Specialized Hospital

UA- Uric Acid

ULT-Urate Lowering Therapy

Acknowledgment

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ABSTRACT

Background

Gout is a chronic disease condition characterized by intermittent flares of acute inflammatory arthritis. Although it is said to be the most prevalent inflammatory arthritis in adults, there have been limited number of literature from some African countries and no previous studies has been done on gout in Ethiopia.

Objective

The Objective of this study is to assess the prevalence, clinical features, and treatment pattern and factors affecting treatment outcomes of patients with gouty arthritis having follow-up at rheumatology clinic of Tikur Anbessa Specialized Hospital (TASH) and Lancet General Hospital.

Methods

Hospital based retrospective cross-sectional study was conducted on patients diagnosed with gouty arthritis and having follow-up with the same diagnosis at the rheumatology clinic of TASH and Lancet General hospital from December 1, 2024 to February 28, 2025GC. Structured questionnaire was used to collect data from the electronic medical recording system for all the patients who were seen at the two rheumatology clinic from September, 1, 2022 to August 31, 2024GC. The collected data was checked for completeness and descriptive as well as correlation analysis was made using (SPSS) version 26.0.

Results

A total of 233 patients were included and the study found that majority of the patients with gouty arthritis were male with male to female ratio of 12.7:1. The mean age of the patients was 55.14 years. Comorbid disease condition was identified in 45% of the studied patients. The First MTP joint was involved in 58.8% of the patients and 39.5% of the patients had polyarticular GA. 40% of the patient had tophaceous gout and joint deformity is seen in 10.7% of patients. Serum uric acid level was found to be below 6mg/dl in 19% of the patients during the acute gout flare. 41.3% those who had x-ray and 71.1% among the U/S group were found to have imaging changes characteristics of gouty arthritis. ULT therapy was prescribed for approximately 74% of the patients. Allopurinol is the most commonly prescribed ULT. The dose of ULT used were 100mg or less for allopurinol and 40mg or less for febuxostat in 48% and 78.3% patients respectively**.** Concomitant anti-inflammatory medications were prescribed for 82% of the patients. Only 30% of the patients achieved target UA level of 6mg/dl. Acute gout flare is documented in 60% percent of patients while on treatment of whom more than 56% had two or more flare. Age, use of anti-inflammatory medication and involvement of more than 4 joints were found to affect serum UA level and recurrent gout attack in patients with GA.

Conclusion

The socio-demographic characteristics of our patients with GA are similar to their counterpart elsewhere except high M: F and slightly younger mean age. Clinically our patients have more polyarticular and tophaceous gout. Treatment pattern is also similar to other setting except the higher percentage of patients on ULT. Older age, polyarticular gout and use of anti-inflammatory medication prophylaxis are factors identified to affect treatment outcome.

Key words: Gouty Arthritis, Hyperuricemia, Crystal Induced Arthritis, Inflammatory Arthritis

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1. Introduction

1.1. Background

Gout is a chronic disease condition which results from deposition of monosodium urate crystal (MSU) arising in the setting of hyperuricemia.[1,2] The deposition of these crystals trigger intermit-tent flares of acute inflammatory arthritis often presenting as an acute monoarthritis, although oligo- or polyarticular presentations can occur.[3] The first metatarsophalangeal joint (Podagra) is a common site for the first presentation of gout. Other frequently affected sites are the mid-foot, ankle, and knee joint.[4,5] In some patients with hyperuricemia, tophi can also form; these lesions can lead to joint damage and deformity.[1]

It is the most common inflammatory arthritis affecting adults. The disease is more prevalent in men than women and its prevalence in western countries is estimated to be between 3% and 6% in men and 1% and 2% in women.[6]

The prevalence of gouty arthritis in Africa is not well studied in the available literature. However, some studies have provided insights into arthritis in general which may include gouty arthritis. A systematic review and meta-analysis of estimated prevalence of six types of arthritis in Africa, including rheumatoid arthritis and Osteoarthritis, but it did not specifically focus on gouty arthritis. The review found that gout was reported in only two studies from South Africa, with prevalence of 1784 cases per 100,000 people in rural and urban areas combined.[15]

The disease is found to be more prevalent in certain patient population with predisposing risk factors. These identified risk factors include chronic kidney disease, obesity, cardiovascular disease, diabetes, hypertension, dyslipidemia, hypertriglyceridemia, kidney stones, cardiovascular disease, type 2 diabetes, and heart failure and dietary factors such as intake of high purine foods such as red meat, seafood, and beer, and intake of sugar sweetened beverages.[7,8]

The gold standard for gout diagnosis is MSU crystal identification. On polarizing light microscopy of synovial fluid, MSU crystals appear as negatively birefringent needle-shaped crystals and are 1 to 20 μm in length. MSU crystals may be both intra-cellular and extra-cellular. Synovial fluid during a gout flare has an inflammatory pattern, with high numbers of neutrophils (sometimes >50,000 cells/mm^3).[27] There are certain characteristic radiographic features which can re-enforce the diagnosis if found during patient evaluation.[26,31]

Patients with recurrent gout flares and tophi have high disability scores and poor health-related quality of life.[32] Work productivity is also reduced in patients with severe gout, with an estimated mean work day loss of 25.1 days per year.

Numerous studies from many different countries have demonstrated low rates of ULT prescription, infrequent serum urate monitoring, suboptimal dosing of ULT when prescribed, and poor attainment of serum urate targets in those who do have serum urate testing.[35–36]

1.2. Statement of the problem

Gouty arthritis is the most common inflammatory arthritis and have a significant impact on quality of life on those affected with resultant development of disability in those who are not properly treated.[33, 34] It can also lead to lost work productivity and increased healthcare costs and significant psychological impact on those with the disease.[35] Additionally, the diagnosis of gout in a patient is associated with an increased risk of cardiovascular disease and mortality.[10,11,12]

Studies have shown that appropriate management of gouty arthritis and prevention of subsequent flare of disease is associated with reduced joint damage and overall quality of life.[11,12] Despite the high prevalence of the disease and its impact on the general public health and productivity; there is a paucity of studies and research on its prevalence, identified risk factors, treatment outcome and factors affecting response to treatment.

Therefore, studies like this one will help in identifying peculiarities of the clinical characteristics of patients with gouty arthritis in our setting and also help identify gaps in the management of patients with the disease. We believe that the result of the study will be utilized to improve patient care and outcome.

1.3. Significance of the Study

Despite being the most common inflammatory arthritis in adults, there is paucity of research on gouty arthritis patients regarding their socio-demographic characteristics, treatment profiles and outcomes. The result of this study will fill some of this gaps concerning the prevalence of gouty arthritis, clinical profiles of patients with the disease, treatment response and factors affecting treatment outcome in patients with gouty arthritis having follow-up in the rheumatology clinics of Tikur Anbessa Specialized hospital and Lancet General Hospital. We also believe that the result of this study will serve to design care plan to improve treatment outcomes of patients with the disease and also serve as an input for furthering studies on this topic at local and regional level.

2. Objectives:

2.1. General Objectives:

To assess the clinical profile, and treatment patterns and factors affecting treatment outcomes of patients with gouty arthritis having follow-up at rheumatology clinic of Tikur Anbessa Specialized Hospital (TASH) and Lancet General Hospital.

2.2. Specific Objectives:

1. To describe the socio-demographic characteristics of patients with gouty arthritis having follow-up at rheumatology clinic of Tikur Anbessa Specialized Hospital (TASH) and Lancet General Hospital.
2. To identify comorbid conditions and diseases found in these patients
3. To describe pharmacologic treatment used during the study period
4. To examine the treatment outcome and factors associated with treatment outcomes

3. Methodology:

3.1. Study Design:

A retrospective cross-sectional study design was used to study the socio-demographic and clinical characteristics, treatment outcome and determinants of treatment outcome among gouty arthritis patients seen at TASH and Lancet General hospital in three-year period.

3.2. Study area:

The study area was conducted at the rheumatology clinics of Tikur Anbessa Specialized Hospital and Lancet General Hospital.

Tikur Anbessa Specialized Hospital is the largest teaching hospital in Ethiopia located in the capital Addis Ababa with more than 700 beds and the hospital is known for its highest level of diagnostic and treatment services in the country[18]. The Hospital serves more than 500,000 patients each year and it is the only government hospital in the country with dedicated rheumatology clinic where only patients with rheumatic disease are seen.

Lancet General Hospital is established by the union of top level experts in the field of medical practice in the country in September 2019. It is one of the largest private hospital located at Megenagna, Addis Ababa with over 180 patient beds including VIP and Private rooms. The Hospital provides more than 36 sub-specialty services.[19]

3.3. Study Period:

The study was conducted from December 1, 2024GC to February 28, 2025GC.

3.4. Study Population:

3.4.1. Source Population:

All patients diagnosed to have gouty arthritis and were seen and had follow-up at the rheumatology clinic of TASH and Lancet General hospital within three years period from September 1, 2022 to August 31, 2024 GC were included in the study.

3.4.2. Study Subjects:

All patients diagnosed with gouty arthritis and were having follow-up for it at the rheumatology out-patient clinic in TASH and Lancet General hospital within the study period who fulfilled the inclusion criteria were included.

3.4.3. Sampling Method:

Since this is an institution-based study, the plan was to include all patients seen during the specified study period. Accordingly, all adult (aged 18 years or more) patients diagnosed with gouty arthritis who were seen from September 1, 2022 to August 31, 2024 GC, fulfilling the inclusion criteria were included in the study.

3.5. Data collection

3.5.1. Inclusion Criteria:

- All adult patients aged 18 years and more who meet the 2015 ACR/EULAR classification criteria for gouty arthritis and being treated as such from September 1, 2022GC to August 31, 2024GC.

3.5.2. Exclusion Criteria:

- Patients who are being treated for GA at rheumatology clinic without fulfilling the ACR/EULAR diagnostic criteria
- Patient who does not meet the ACR/EULAR criteria for initiation of ULT
- Patients with incomplete follow-up data.
- Patients who meet the criteria but have less than 6 months of follow-up in during the study period
- Patients who presented with their first ever episodes of gout attack
- Patients who have transient cause for the gout attack specifically highly proliferative hematologic malignancy

3.5.3. Study Variables

Independent Variables

- Age
- Sex
- Family history of GA
- Alcohol Intake
- Comorbid disease condition
- Number of Joint involved
- MTP involvement
- Presence of tophi
- Presence of joint deformity
- Uric acid level at diagnosis and at 6 months
- Presence of x-ray changes
- Use of ULT and the dose of ULT used
- Use of Anti-inflammatory medications
- Adherence to ULT and anti-inflammatory medications
- Use of diuretics

Dependent Variables

- Achievement of target uric acid level below 6mg/dl
- Any Gout flare after initiating treatment

4.5.4. Operational Definition

- Adult: Any one with age of ≥18 years
- Gout flare: A clinically evident episode of acute inflammation induced by monosodium urate crystals
- Tophus: An ordered structure of monosodium urate crystal and the associated host tissue response
- Mono-articular Gout: Gout attack involving only single joint
- Oligo-articular Gout: Gout attack involving 2 to 4 joints at presentation
- Polyarticular Gout: Gout attack involving ≥5 joints at presentation
- U/S evidence of Gout: Presence of double contour sign, tophi, snowstorm sign and bone erosion
- X-ray evidence of gout: Erosion is defined as a cortical break with sclerotic margin and overhanging edge, excluding distal interphalangeal joints and gull wing appearance
- Remission: Resolution of gouty arthritis without any flare for 6 consecutive months or more
- Alcohol intake: Any amount of alcohol intake reported by the patient
- Inadequate adherence to medication: Admission of patient to missing dose of medication
- Diuretics: Drugs assigned to thiazide or loop diuretics pharmacologic category
- Family History of gout: First degree relative with gout
- Recent Uric Acid level: Serum UA level determined at the last visit of patient at least 6 months after initiation of ULT
- CKD: eGFR below 60ml/1.72m^2/hr.

3.6. Data Collection and Analysis methods

All patients who were diagnosed with gouty arthritis and are being treated as such at the rheumatology clinic of TASH and Lancet general hospital, Addis Ababa, from September 1, 2022 to August 31, 2024GC were screened using the 2015 ACR/EULAR gout classification criteria for fulfillment of the criteria at initiation of care. Those patients who were found to have score of ≥8 are classified as having gout and are included in the study.

Accordingly, a total of 576 patients were identified to be seen at the rheumatology clinic of TASH and Lancet General Hospital. Among these 233 patients were found to fulfill the ACR/EULAR classification criteria and included in the study. 88 patients were excluded because they did not fulfill the ACR/EULAR classification criteria for gout. Most these patients are from TASH. 159 patients actually fulfilled the ACR/EULAR classification criteria however they were excluded from the study because of incomplete data or did not meet ACR/EULAR recommendation for initiation of ULT. 8 of the patients who were having highly proliferative hematologic malignancy at the time of acute gout attack were excluded from study as they had transient hyperuricemia predisposing them to gouty arthritis. We had excluded 86 patients from the study because of wrong diagnosis as they were identified to have other joint disease than like RA, OA, Reactive Arthritis etc. or some I-care number were non-existent and probably were erroneously recorded on the hematology log book. The remaining 12 patients were excluded either because they were lacking adequate follow-up period or only had one clinic visit by the time data collection was performed.

After patients fulfilling criteria were identified questionnaires were filled by trained data collectors, particularly graduate physician and interns who were well familiarized in interpreting the clinical records

of patients. The cases are characterized with respect to age, sex, radio-biochemical characteristics, outcome of treatment and factors affecting treatment outcome. The data collection process was closely supervised by the principal investigator.

After data collection is complete, data was edited and coded for processing and analysis. Data processing and analysis was done manually and using the SPSS statistical software with the assistant of experienced data analyst. Result were reported using descriptive statistical methods such as frequency, percentages, tables and graphs. Association studies were done using Chi-square test for categorical variables, Spearman's Rho method for ordinal variables and ANOVA test for continuous variables. Multinomial logistic regression was also done to assess the effect of different factors on outcome. Level of significance was set at P-value of 0.05 or less in all scenarios.

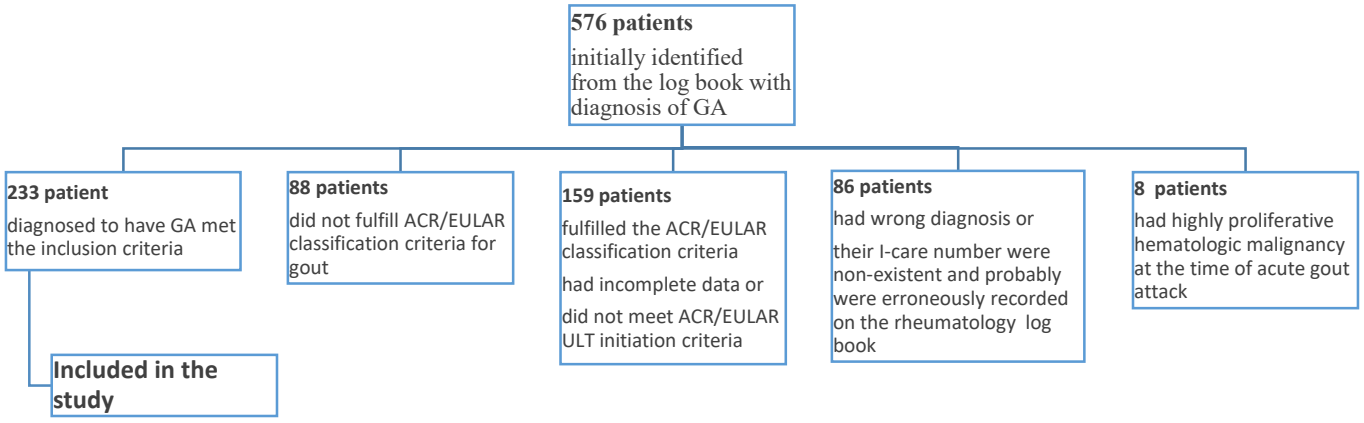


Figure 1. Sampling procedure

4. Ethical Consideration

Ethical clearance was obtained from the ethical review committee of Lancet General hospital and the Department of Internal Medicine and study proposal was approved by the ethical committee of the department of Internal Medicine College of Heath Science, Addis Ababa University before the start of the study.

5. Dissemination of research results

After the completion of the research, the result will be presented to the Rheumatology unit, Department of Internal medicine and possibly to the whole academic society of interest such as College of Health Science. Finding may also be presented on annual conferences and seminars for the medical community at large.

Research findings will be sent to both national and international medical journals for publishing and it will be disseminated through internet to different medical sites. Results will also be disseminated to other national teaching and non-teaching hospitals.

6. Result

6.1. Socio-demographic characteristics

A total of 233 adult patients who were diagnosed with GA at Tikur Anbessa Specialized Hospital (TASH) and Lancet General hospital from September 1, 2022 to August 31, 2024 met the inclusion criteria and were included in the final data analysis. Among the 233 patients 216(92.7%) were males and 17(7.3%) were females with a M: F ratio of 12.7:1. The age of patients ranged between 30 and 93 years. The median age at diagnosis was 53 years whereas the mean age at diagnosis was 55.14±12.45 years. Majority of the patients were in the age category of 46-60 years. Among the studied patients 53% admitted to utilization of alcohol before the first attack of gout and 21.9% them continued to do so even after the diagnosis of GA. Comorbid disease condition/s was reported or discovered during evaluation in nearly 45% of the studied patients. Of the comorbidities identified, hypertension is the most common as it was found among 77.9% of those patients with comorbidity followed by DM in 38.5% and CKD in 20.8%. More than 22% of the patients reported having family history of gout in their first degree relatives.

Table 1. The sociodemographic characteristics of Gouty Arthritis Patients

Variables	Frequency	Percentage
Age in years		
30-45	64	27.5
46-60	94	40.3
61-75	60	25.8
>75	15	6.4
Sex		
Female	17	7.3
Male	216	92.7
Family history of gout		
Yes	52	22.3
No	32	13.7
History of alcohol intake when you had the first attack?		
Yes	123	52.8
No	59	25.3
Patient report ongoing use of Alcohol?		
Yes	51	21.9
No	153	65.7
Comorbidity disease		
Yes	104	44.6
No	129	55.4

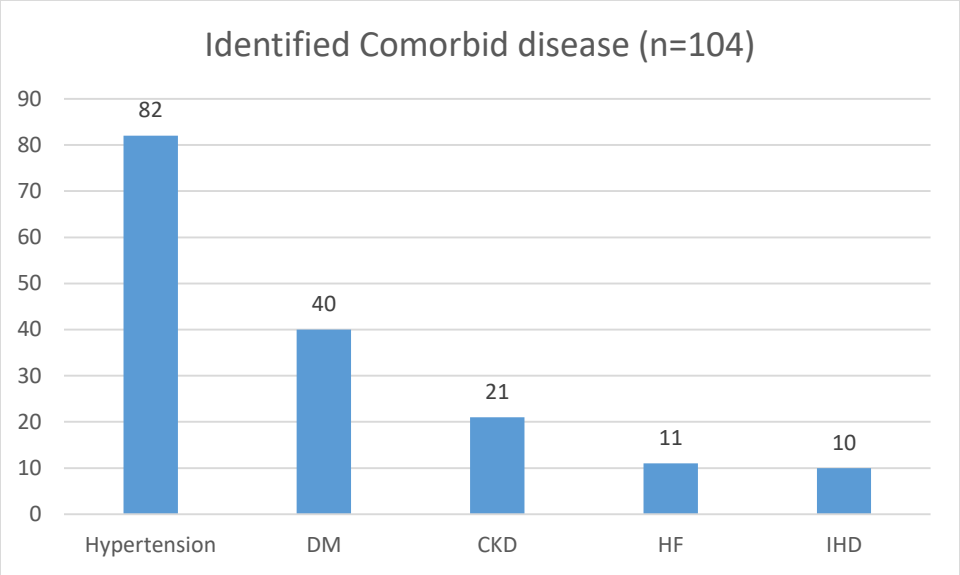


Figure 2. Identified comorbid disease

6.2. Clinical Characteristics of Patients

Among the 233 patients, at the time of initiation of care, 65 of them had only one joint involvement while 76 of them had two to four joints involvements. 39.5% of the patients were found to have involvement of more than 4 joints. The First MTP joint was found to be affected by symptomatic crystal deposition in 58.8% of the patients. Physical palpable subcutaneous tophi gout was found among 40% of the studied patients and 10.7% of the patients were found to have joint deformity from the disease.

Table 2. Gout related clinical characteristics of patients

Variable	Frequency	Percentage
Number of involved joints documented at entry of care		
1	65	27.9
2-4	76	32.6
>4	92	39.5
First MTP joint involved		
Yes	137	58.8
No	96	41.2
Tophi Present		
Yes	94	40.3
No	139	59.7
Joint deformity		
Yes	25	10.7
No	208	89.3

6.3. Radio-Biochemical Characteristics of Patients

When the radio-biochemical characteristics of these 233 patients who were included in the study was explored, 211 of them had determination of serum UA at the initial visit while they were having acute attack of gout. And among these 211 patients, serum uric acid level was found to be below 6mg/dl for 18.9% of patients and it was found to be between 6 and 10mg/dl and above 10mg/dl in little more than 70% and 10.4% of the patients respectively during the acute gout flare. Involved joint X-ray image was obtained for 44.6% of the patients and imaging changes which are characteristics of GA was seen in 41.3% of the patients. U/S scanning of involved joint was performed for 37% of the patients; 71.1% the scanned patients had sonographic findings which are highly suggestive of gouty arthritis.

Table 3. Radio-Biochemical Characteristics of Patients with Gout.

Variable	Frequency	Percentage
Uric acid level at the diagnosis of gouty arthritis		
<6mg/dl	40	18.95
Between 6 and 10mg/dl	149	70.62
≥10mg/dl	22	10.43
Patient had involved joint X-ray		
Yes	104	44.6
No	129	55.4
X-ray changes consistent with gout arthritis (n=104)		
Yes	43	41.3
No	61	58.7
Patient had involved joint ultrasound during acute attack		
Yes	90	38.6
No	143	61.4
Sonographic finding consistent with GA (n=90)		
Yes	64	71.1
No	26	28.9

6.4. Treatment Profile and Outcomes of patients

Looking at the treatment profile of the 233 patients involved in this study, ULT therapy was prescribed for a little less than 74% of the patients. Among these 172 patients for whom ULT was prescribed; most of them are put on Allopurinol as it is prescribed for 65.1% them and Febuxostat is the second most commonly used ULT as it is used to lower the serum uric acid level in 34.9% of the patients. The dose of ULT used were 100mg or less for Allopurinol and 40mg or less for Febuxostat in 48% and 78.3% of patients respectively. 5.4% of the patients were taking Allopurinol at dose of ≥300mg per day. The daily dose of Febuxostat prescribed was between 40 and 80mg in 21.7% of the patients. Concomitant anti-inflammatory

therapy as a prophylaxis of flare was given for 06 months for 82% of the patients. Colchicine is the most commonly used medication for this purpose followed by Prednisolone and its analog as they were given for 68.1% and 33.5% respectively. NSAIDs were used in 25.5% of the patients. 31.8% of the patients who were put on ULT therapy admitted to missing to variable doses of the medication prescribed for them to take.

Table 4. Treatment Profile of patients

Variable	Frequency	Percentage
Patient is on any form of ULT		
Yes	172	73.8
No	61	26.2
ULT therapy used (n=172)		
Allopurinol	112	65.1
Dose of Allopurinol (n=112)		
≤100mg	54	48.2
100-300mg	52	46.4
≥ 300mg	6	5.4
Febuxostat (n=172)	60	34.9
Dose of Febuxostat		
≤40mg	47	78.3
40-80mg	13	21.7
Patient was given additional anti-inflammatory medication for six months in addition to ULT		
Yes	190	81.5
No	43	18.5
Type of anti-inflammatory medication(n=190)		
NSAIDs	48	25.5
Colchicine	128	68.1
Prednisone or its analogs	63	33.5
Patient report missing doses of ULT		
Yes	55	31.8
No	117	68.2

Recent serum uric acid level determination at least 6 months after the initiation of ULT was found only for 62% of the studied patients and of those who have their level determined less than 30% had achieved a target uric acid level of less than 6mg/dl. Acute gout flare is documented in 60% percent of patients while on treatment of whom 43.6% had one gout flare and more than 56% had two or more flare during the study period. It took more than 6 months for the 20% of the patients until they were able to achieve a target serum UA level of less than 6mg/dl after initiating ULT.

Table 5. Treatment Outcome of patients with Gout

Variable	Frequency	Percentage
Patient had recently determined UA		
Yes	145	62.2
No	88	37.8
Patients most recent uric acid level		
<6mg/dl	43	29.6
≥6mg/dl	102	70.4
Patient had flare as reported by the patient or documented by a physician		
Yes	140	60.1
No	93	39.9
Number of flare Patient had (n=140)		
1	61	43.6
1-3	54	38.6
>3	25	17.9
Time in months to achieve UA below 6mg/dl		
<6	31	77.5
6-12	8	20
>6	1	2.5

6.5. Predictors of treatment outcomes of Patients

Patient's age and use of anti-inflammatory medications are found to increase the odds of achieving a target serum UA level of less than 6mg/dl by multivariate logistic regression. Specifically, those patient in the age group of 61-75 year has AOR of 4.4 (95%CI=1.31, 14.59)) to achieve UA below 6mg/dl as compared to those whose age is between 30-45 years. In addition, those patients who were given anti-inflammatory medication/s has AOR of 2.2 (95%CI=1.80, 5.87) to achieve a target serum UA of less than 6mg/dl as opposed to those who were not concomitantly started on them with taking ULT. On the other hand, involvement of 5 or more joint by the disease decreased the odds of achieving the recommended target serum UA of less than 6mg/dl by 67% (95% CI= (0.11, 0.93).

Polyarticular GA and being older than 75 years of age predicted increased risk of disease relapse at least 6 months after initiation of ULT. The odds of patients aged >75 years to have disease relapse is 1.5 times higher than those in the age between 30-45 years (AOR=1.5, 95%CI=1.23, 10.42). And having >4 joint involvements by the disease increase the odds of disease relapse by 2.1 times when compared to those with mono-articular gout (AOR=2.1, 95%CI=1.58, 7.86).

Table 6. Association between UA level below 6mg/dl and independent variables

Variable	P-value	AOR with 95%CI
Sex		
Female	0.367	1.9(0.47, 7.79)
Male	1	
Age in years		
30-45	1	
46-60	0.213	2.1(0.66, 6.54)
61-75	0.017	**4.4(1.31, 14.59)**
>75	0.087	1.6(0.28, 9.22)
Number of joint Involved joint		
1-2	1	
3-4	0.357	0.61(0.21, 1.74)
>4	0.037	**0.33(0.11, 0.93)**
MTP joint involvement		
Yes	0.058	2.7(0.11, 6.35)
No	1	
Received anti-inflammatory therapy		
Yes	0.026	**2.2(1.80, 5.87)**
No	1	

Table 7. Association between flare after 6month of treatment and independent variable

Variable	GA Flare after 6 Months		P-value	AOR with 95%CI
	Yes	No		
Age in years				
30-45	37	27	1	
46-60	59	35	0.978	0.98(0.21, 4.67)
61-75	33	27	0.683	0.72(0.15, 3.40)
>75	11	4	0.043	**1.5(1.23, 10.42)**
CKD				
No	47	36	1	
Yes	15	6	0.215	2.1(0.64, 7.08)
Involved joint				
1	31	34	1	
2-4	46	30	0.253	2.1(0.64, 7.08)
>4	63	29	0.023	**2.1(1.58, 7.86)**
Joint deformity				
Yes	17	8	0.273	2.3(0.52, 9.93)
No	123	85	1	
Patient is on ULT				
Yes	110	62	0.391	1.8(0.47, 6.71)
No	30	31	1	

7. Discussion

The mean age of our patients who were having follow-up with the diagnosis of GA in our study was 55.1 years. This finding is higher than what is reported from studies done in Zimbabwe and Togo where the mean age was found to in the early and mid-forties.[40, 41] A recent scoping review of studies done on gouty arthritis in the Sub-Saharan Africa region which included studies only from west African countries has reported a mean age of 53.55 years which is comparable to our finding.[37] However, our patients mean age is lower than that of the finding of studies done in Europe and USA; as their patients were found to be consistently above 60 years of age.[38,39] The median age of the patients at diagnosis of gout in our study was 53 years.

As we have expected, this disease is diagnosed more often in male patients than female patients with M: F ratio of 12.7:1 in our study which is comparable to most of the studies done in Africa; with the exception of a study which was done in Mali where a male to female ratio of 2:1 is reported.[37,42] Many studies have reported M: F ratio to be between 3-4:1 in the western setting unlike that of the finding of the African studies.[1,7] The reason why the male to female ratio of the disease is higher in the African studies is not completely understood and is not studied well in the region but we think multiple factors including social factors like better health care access for males, hormonal factors and environmental factors are likely to act in concert or it might be that females with polyarticular GA are misdiagnosed with other rheumatic disease like RA since auto-immune arthritis are more common in females. But we believe further studies are required to confirm this claim.

Alcohol utilization is one of the risk factors for development of first gout attack and recurrent flare of GA.[44,45] In our study, nearly 53% of the patients admitted to utilization of variable amount of alcohol before the first attack of gout. Among these patients who were drinking alcohol before the first attack, 21.9% of them continued to do so even after diagnosis. This finding is lower than what has been reported from studies done in western setting which documented the prevalence of alcohol use in GA patient to be more than 90% before and at the time of diagnosis and more than 40% the patients will continue to drink after diagnosis of gout.[43,45]

The interaction between GA and cardio-metabolic-renal disease is bidirectional as GA is more common in patients with comorbid cardio-metabolic-renal disease conditions like hypertension, DM, IHD, HF, CKD and its diagnosis predicts higher likelihood of developing one or more of these cardio-metabolic-renal disease.[6,7] Among the 233 patient included in our study nearly 45% of them were found to have comorbid medical condition/s. Among the comorbidities identified HTN is the most common as it was found in 77.9% of those patients with comorbidity followed by DM in 38.5% and CKD in 20.8%. The prevalence of

comorbid cardio-metabolic-renal disease is higher in studies done in the west and the Indian sub-continent. Unlike to that of our finding, the reported prevalence of comorbid cardio-metabolic disease ranges between 67 to 80% in these patient population and HTN, CKD and DM are the most commonly identified comorbidities.[46,47]

Studies have shown genetic basis to the disease with heritability estimates in the range of 45% to 73%. This finding is supported by epidemiologic studies which documented family of GA in 20% of the patients.[48] Similarly, our study has confirmed the presence of family history of gout in 22% of our patients.

When we stratified our patients based on the number of joint/s involved by the disease, the arthritis was mono-articular, oligo-articular and poly-articular in 27.9%, 32.6% and 39.5% respectively. Our finding is different from the findings of studies done in Nigeria and the developed world which reported less percentage of polyarticular GA.[49,50] This difference might be because of late presentation of our patient to seek health care or misdiagnosis or not starting ULT at the earlier stage of the disease before it becomes polyarticular. The First MTP joint was found to be affected by symptomatic crystal deposition in 58.8% of the patients; which is lower than the finding of a systematic review of 11 studies, which found 73% involvement by the disease. Physically palpable subcutaneous tophaceous gout was found among 40% of our patients. This finding is twice the finding of other studies done in Nigeria and Asia.[50,51] Again this is probably related to late presentation of our patient to seek health care or misdiagnosis or not starting ULT at the earlier stage of the disease. We also found joint deformity in 10.7% of the studied patients. Although, we were not able to find studies which directly assessed prevalence of visible joint deformity in gouty arthritis patient, taking imaging finding as surrogate the prevalence can reach upward of 40%.[50] But given how common gout is and the impact it can impose we feel more studies are required to assess this issue.

Of the 211 patients who had determination of serum UA at the initial visit while they were having acute attack of gout; the serum uric acid level was found to be < 6mg/dl for 18.9% of patients and was between 6 and 10mg/dl and above 10mg/dl in little more than 70% and 10.4% of the patients respectively. This finding of UA level of < 6mg/dl is within the range reported by other studies.[53] Of those 44.6% of patients who had X-ray image of involved joint; imaging changes characteristics of GA was seen in 41.3% of the patients. This finding is comparable with reported x-ray abnormality percentage of around 44% in those patient who had the disease for 7-10 years.[52] The fact that our patients had x-ray changes of gout upward of 41% suggest that majority of our patients likely had long standing disease before diagnosis. U/S scanning of involved joint was performed for 37% of the patients; 71.1% the scanned patients had sonographic findings which are highly suggestive of gouty arthritis[54] and this finding is similar to other literature reports and may be in setting like that of ours, where polarized light microscopy is not available the use of this

imaging modality likely improve diagnostic certainty of GA if these typical changes are appreciated at the time of scanning.

Looking at the treatment profile of the 233 patients involved in this study, ULT therapy was prescribed for a little less than 74% of the patients. The percentage of patient who were on ULT in our study is very high when compared to other study finding of 30 to 40%.[55] This might be because of the fact that majority of the patients were evaluated by rheumatologist and were being treated in tertiary hospital.

Among these 172 patients for whom ULT was prescribed; most of them are put on Allopurinol as it is prescribed for 65.1% the patients and Febuxostat is the second most commonly used ULT as it was used to lower the serum uric acid level in 34.9% of the patients. The use of Febuxostat is higher in our study as compared to other studies, as its use is reported to be limited to only 4-14% of patients.[37,56,57] We strongly believe that the higher prevalence of CKD in our patients likely contributed for its higher rate of use.

The dose of ULT used was 100mg or less for Allopurinol and 40mg or less for Febuxostat in 48% and 78.3% of patients respectively. 5.4% of the patients were taking Allopurinol at dose of ≥300mg per day. The daily dose of Febuxostat prescribed was between 40 and 80mg in 21.7% of the patients. This practice of use of lower dose of ULT is better here when compared with other studies[56] but still require a lot of improvement. Concomitant anti-inflammatory therapy as a prophylaxis of flare was given for 06 months for 82% of the patients which is much higher than from what has been reported by other studies mainly done in the primary care setting which reported use of prophylactic anti-inflammatory medications only in 9.4%-42%.[58,59] Colchicine is the most commonly used medication for this purpose followed by Prednisolone and its analog as they were given for 68.1% and 33.5% respectively. NSAIDs were used in 25.5% of the patients. The use of colchicine as a preferred prophylaxis medication is consistent with what has been published from Korean study.[59,60] 31.8% of the patients who were put on ULT therapy admitted missing variable doses of the medication prescribed for them to take. This level of non-compliance to ULT in our patients is lower than what was reported by a 2016 systematic review which documented non-persistence in 54-87% of patients.[61] This finding when combined with higher rate of recurrent attack should make an astute physician to take his/her time during counseling regarding the importance of adherence on treatment outcome.

Recent serum uric acid level determination at least 6 months after the initiation of ULT was done only for 62% of the studied patients and of those who have their level determined less than 30% had achieved a target uric acid level of less than 6mg/dl. This finding is slightly lower than what is reported by other studies.[62,63] Acute gout flare is documented in 60% percent of patients while on treatment of whom 43.6% had one gout flare and more than 56% had two or more flare during the study period. A number of studies

had documented the occurrence of flare in 6%-61% of patients depending on their initial uric acid level.[64,65] It took more than 6 months for the 20% of patients until they were able to achieve a target serum UA level of less than 6mg/dl after initiating ULT which is higher than the finding of study done in Korea.[66]

Looking at factors affecting treatment outcomes of patients with GA using the recommended target serum UA of < 6mg/dl as treatment endpoint, there was a notable significant correlation by multivariate logistic regression between older age and use of anti-inflammatory medications in increasing the odds of achieving a target serum UA level of less than 6mg/dl. Specifically, those patient in the age group of 61-75 year had AOR of 4.4 (95%CI=1.31, 14.59)) to achieve UA below 6mg/dl as compared to those whose age is between 30-45 years. Other studies had also found positive correlation of older age with achievement of a target serum UA level below 6mg/dl with odds ratio ranging from 1.02 to 2.59.[67, 68] This might be because of better adherence of older patients to ULT. In addition, those patients who were given anti-inflammatory medication/s had AOR of 2.2 (95%CI=1.80, 5.87) to achieve a target serum UA of below 6mg/dl as opposed to those who were not taking them with the ULT. We were unable to find prior study with similar finding but this finding could be a result of better adherence to ULT as it help prevent disease flare and in turn encouraging patients to be more adherent to ULT. On the other hand, involvement of 5 or more joint by the disease decreased the odds of achieving the recommended target serum UA of less than 6mg/dl by 67% (95% CI=(0.11, 0.93). Although we were again unable to find a study which tried to correlate the involved joint number as a predictor of achievement of target UA level of less than 6mg/dl; it is kind of intuitive to think that patients with polyarticular gout will likely have higher total body uric acid burden and likely will have lower chance of achieving UA below the recommended target of <6mg/dl.

Polyarticular GA and being older than 75 years of age predicted increased risk of disease flare 6 months after initiation of ULT. Those patients aged >75 years were found to have 1.5 times higher odds of having gout flare when compared with those in the age range of 30-45 years (AOR=1.5, 95%CI=1.23, 10.42). In addition, having polyarticular gout increased the odds of disease flare by 2.1 times when compared to those who had single joint disease (AOR=2.1, 95%CI=1.58, 7.86). Unfortunately, we could not find studies which assessed this factors as a predictor of recurrent gout flare, we believe that it might be related to higher tissue burden of uric acid crystal in the case of polyarticular gout and longer duration of disease might be the reason for those who have age >75 years as both are shown to predict recurrent disease flare.[69,70]

8. Conclusion

Gout Arthritis is among the common joint disease patients present with to TASH and Lancet General hospital. The socio-demographic characteristics of our patients with GA is more or less similar with what is seen in other setting except increased M: F ratio. Our patients with GA tend to have more of polyarticular disease, higher likelihood to have tophi and joint deformity. We were also able to know that patients here had higher percentage of x-ray changes of gout in the involved joints and U/S can be used as an adjunct tool to make diagnosis GA with fairly good sensitivity. The use of ULT therapy is higher than what other studies had documented but the dose used is similarly low to that of other studies. Similar to studies done in other area target UA is achieved in only less than a third of patients and nearly two-third of the patient had gout flare after 6 months of therapy. Age in the range of 61-75, use of anti-inflammatory medication prophylaxis increased the odds of achieving target UA of < 6 mg/dl whereas polyarticular disease reduces the odds of achieving this goal. Age > 75 years and Polyarticular GA were found to increase the odds of recurrent gout flare.

9. Recommendations

Gouty Arthritis is the most common inflammatory arthritis that affect adults. It is currently considered as a systemic disease as it can affect multiple organ systems and its diagnosis confers significant morbidity to the patient and predicts higher chance of developing acute CVD events in the three months to come. It is a chronic relapsing and remitting disease, and making accurate diagnosis and treating patients to target determine the outcome of patient as whole.

According to our finding, many of our patients are diagnosed late in the disease course after incurring irreversible damage to the joints. Therefore, we urge health care workers to be vigilant not to misdiagnose and treat gout as other arthritis specially in those patients presenting with polyarticular subtype of gout. Because U/S is readily available, non-invasive and has good sensitivity, working together with a MSK sonographer to make diagnosis of gout might be helpful specially in difficult cases. The other thing we identified which requires improvement is to solve the lack of a very important diagnostic modality; polarized light microscopy, which poses a major limitation for ascertaining the diagnosis of GA among the different types of inflammatory arthritides. Hence, we recommend concerned bodies such as the FMoH, Tikur Anbessa Hospital, Private Hospitals, NGOs and health professionals to work together on acquiring such investigational modalities at least at one center in the country which will have a major impact in improving the care of GA patients.

In terms of treatment of these patients, there still remains significantly lower rate of utilization of ULT, concomitant use of anti-inflammatory medication prophylaxis and using lower dose of ULT even without achieving target UA level, failure to properly address comorbidities and failure to prevent recurrent gout flare and its attending complications. So physicians caring for these group of patients should take in to account the complexities of these patient and should be able to provide care that meets the minimum standard with clear and achievable goals.

The other major finding of our study is a high rate of non-compliance to treatment regimen particularly to ULT. Therefore, we recommend that the treating team should emphasize on the chronic nature of the disease and why each of the medications should be taken even in the absence of acute gout symptoms during each patient encounter.

10. Strength and Limitation

The strength of this study is that it is the first of its kind to be done in Ethiopia on the topics of gouty arthritis. The other strength of the study is that it only included clearly defined patients who fulfilled the ACR/EULAR gout classification criteria. It has also included relatively larger number of patients and it tried to gather detailed information regarding all aspects of the disease including both clinical profile as well as treatment outcome and factors affecting treatment outcome over what might be considered a fairly adequate study period of three years. And the study was also able to acquire complete data for majority of the included patients regarding the studied variables. Even though it was not the main objective of the study, it also tried to assess major limitation in diagnostic modalities

However, the major limitation of our study is the retrospective nature of the study with some missing or incomplete data. This might have affected the depth and quality of the study. The other limitation is that all of the patients included in the study did not have the gold standard diagnostic test for gout which is identification of MSU crystal under polarized light. Even though the finding of the study is similar with studies done elsewhere, it might be difficult to generalize the finding of this study to the general population as this is hospital based study.

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12. Annexes

Annex-1:

Data collection questionnaire for the retrospective study of patients with Gout at the TASH and Lancet General Hospital

(DD/MM/YYYY) _____/_____/_____.

Section 1: Sociodemographic factors. Put a ■ on the choice that applies to the patient.

1.1 Sex: ☐ Male ☐ Female

1.2 Age (in full years): _____.

1.3 Family history of gout:

Yes ☐ No ☐

I do not know ☐

1.4. Did the patient have history of alcohol intake when you had the first attack?

Yes ☐ No ☐

1.5. Does the patient report ongoing use of Alcohol?

Yes ☐ No ☐

1.6. Does the patient have any of the following comorbidities?

DM ☐ HTN ☐ Obesity ☐ IHD ☐ PAD ☐ CHF ☐

CKD ☐

Others: _____.

Section 2: Questions to assess Clinical characteristics of Patients with Gout.

2.2. Number of joint/s involved:

2.2.1. Is the 1st MTP joint involved?

☐ Yes ☐ No

2.3. Tophi present?

☐ Yes ☐ No

2.4. Did the patient reported or the physician documented any joint deformity?

☐ Yes ☐ No

2.5. Was synovial fluid aspiration done for the patient?

☐ Yes ☐ No

Section 3: Questions to assess Radio-Biochemical Characteristics of Patients with Gout.

3.1. Uric acid level at the diagnosis of gouty arthritis

☐ Less than 6 mg/dl ☐ 6 mg/dl or more

3.2. Uric acid level 6 month from diagnosis

☐ Less than 6 mg/dl ☐ 6 mg/dl or more

3.3. Was Joint X-ray ever been done?

☐ Yes ☐ No

3.4. Typical X-ray changes present?

☐ Yes ☐ No

3.5. Was Joint U/S ever been done?

☐ Yes ☐ No

3.6. Typical sonographic change present?

☐ Yes ☐ No

Section 4: Questions to Assess Treatment Profile of patients with Gout.

4.1. Is the patient on any form of Urate lowering therapy?

☐ Yes ☐ No

4.1.1. If yes, what is it? ☐ Allopurinol ☐ Febuxostat

☐ Other

4.2. Was the patient given additional anti-inflammatory medication?

☐ Yes ☐ No

4.3. What was it?

. ☐ NSAIDs ☐ Colchicine ☐ Prednisolone

4.4. If on allopurinol, Dose of Allopurinol currently taking.

. ☐ 100 or less ☐ 100-300 ☐ more than 300

4.5. If on Febuxostat, Dose of Febuxostat currently taking.

. ☐ 40 or less ☐ 40-80 ☐ 80-120

4.6. Did the patient report missing any dose of ULT?

Yes ☐ No ☐

4.7. Does the patient use thiazide diuretics?

Yes ☐ No ☐

Section 5: Questions to Assess Treatment Outcome of patients with Gout

5.1. Current Uric acid level

☐ Less than 6 mg/dl ☐ 6 mg/dl or more

5.2. Patient reported or the physician documented any relapse of symptoms(flare) of gouty arthritis in the past 06 months after initiation of Treatment?

☐ Yes ☐ No

5.3. If yes, how many attack did you have?

☐ 1 ☐ 2-3 ☐ more than 3

5.4. How many months did it take for the patient to achieve Uric acid below 6mg/dl

☐ 6 or less ☐ 6-12 ☐ more than 12

Annex-2: 2015 ACR/EULAR Gout Classification Criteria

Step 1: Entry criterion (only apply criteria below to those meeting this entry criterion)	At least 1 episode of swelling, pain, or tenderness in a peripheral joint or bursa	
Step 2: Sufficient criterion (if met, can classify as gout without applying criteria below)	Presence of MSU crystals in a symptomatic joint or bursa (ie, in synovial fluid) or tophus	
Step 3: Criteria (to be used if sufficient criterion not met)		
Clinical		
Pattern of joint/bursa involvement during symptomatic episode(s) ever	Ankle *or* mid-foot (as part of monoarticular or oligoarticular episode without involvement of the first metatarsophalangeal joint	1
	Involvement of the first metatarsophalangeal joint (as part of monoarticular or oligoarticular episode)	2
Characteristics of symptomatic episode(s) ever		
▶ Erythema overlying affected joint (patient-reported or physician-observed)	One characteristic	1
▶ Can't bear touch or pressure to affected joint	Two characteristics	2
▶ Great difficulty with walking or inability to use affected joint	Three characteristics	3
Time course of episode(s) ever		
Presence (ever) of ≥2, irrespective of anti-inflammatory treatment:		
▶ Time to maximal pain <24 h	One typical episode	1
▶ Resolution of symptoms in ≤14 days	Recurrent typical episodes	2
▶ Complete resolution (to baseline level) between symptomatic episodes		
Clinical evidence of tophus		
Draining or chalk-like subcutaneous nodule under transparent skin, often with overlying vascularity, located in typical locations: joints, ears, olecranon bursae, finger pads, tendons (eg, Achilles)	Present	4
Laboratory		
Serum urate: Measured by the uricase method. Ideally should be scored at a time when the patient was not receiving urate-lowering treatment and it was >4 weeks from the start of an episode (ie, during the intercritical period); *if* practicable, retest under those conditions. The highest value irrespective of timing should be scored	<4 mg/dL (<0.24 mmol/L)†	−4
	6–<8 mg/dL (0.36–<0.48 mmol/L)	2
	8–<10 mg/dL (0.48–<0.60 mmol/L)	3
	≥10 mg/dL (≥0.60 mmol/L)	4
Synovial fluid analysis of a symptomatic (ever) joint or bursa (should be assessed by a trained observer)‡	MSU negative	−2
Imaging§		
Imaging evidence of urate deposition in symptomatic (ever) joint or bursa: ultrasound evidence of double-contour sign¶ *or* DECT demonstrating urate deposition**	Present (either modality)	4
Imaging evidence of gout-related joint damage: conventional radiography of the hands and/or feet demonstrates at least 1 erosion††	Present	4

NB: A threshold score of ≥8 classifies an individual as having gout