

## Clinico-Radiological Profile of Joint Involvement in Hyperuricemia Patients

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### Abstract

**Introduction:** Hyperuricemia is a condition characterized by abnormally elevated levels of serum uric acid. Symptoms are those of gout and nephrolithiasis. The gold standard for diagnosis of gout is identification of monosodium urate crystals in the synovial fluid, that is painful and leads to complications like joint effusion. In recent years with advancement of ultrasonography and dual energy computed tomography (DECT) new clinical picture and staging has been identified. The present study had been designed to study the clinical profile of hyperuricemia patients with regards to joint involvement as assessed by DECT and USG and comorbidities.

**Aim:** To study the clinical profile of hyperuricemia patients with regards to joint involvement as assessed by DECT and USG and comorbidities.

**Material and Method:** This was a cross sectional study which was done in Era's Lucknow Medical College & Hospital, Lucknow. The study was carried out on diagnosed hyperuricemia patients attending the medicine OPD and indoor patients of Era's Lucknow Medical College & Hospital in the last 18 months were included in the study till the required sample size was achieved. The overall sample size consisted of 66 cases of hyperuricemia.

**Results:** The age of patients ranged from 36 to 87 years. Majority of the cases were aged more than 60 years. Further, majority of patients were females (56.1%). Only 19 (28.8%) patients were symptomatic with symptoms of pain, swelling and tenderness at joints were reported. Six patients had no comorbidities while rest 60 patients reported comorbidities. Diabetes alone (15.2%) was most common comorbidity. The radiological evidence of abnormalities which were indicative of involvement of joint by USG were DCS or HAG which were observed in 45.5% patients. MSU crystals were observed in 39.1% cases by DECT. So overall radiological evidence of joint involvement was found in 56.1% cases. No significant association of joint involvement was found with no of comorbidities, CAD, hypertension, T2DM and dyslipidemia. Significant association of S. uricemic acid was found only with joint involvement indicated by radiological findings.

**Conclusion:** On the basis of these findings, it can be inferred that that asymptomatic patients (especially females and older) of hyperuricemia are at risk of developing joint involvement who should be radiologically examined. The overall prevalence of joint involvement in

hyperuricemia patients was lying in the range (44.13 - 68.07) with 95% confidence. A confirmed relationship of Sr Uric Acid Levels (mg/dl) with Joint Involvement was found.

**Keywords:** Hyperuricemia, Gout, USG, DECT Comorbidities, Risk of Developing Joint Involvement.

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## Introduction

Hyperuricemia is a condition characterized by abnormally elevated levels of serum uric acid. It may occur because of decreased excretion, increased production or a combination of these two. Symptoms are those of gout and nephrolithiasis [1]. Normal uric acid levels based on UA solubility capacity for men and postmenopausal women is accepted as 3.5 to 7.0 mg/dl (208–416  $\mu\text{mol/l}$ ), and for premenopausal women as 2.6–5.7 mg/dl (155–339  $\mu\text{mol/l}$ ) [2]. High uric acid blood levels can involve uric acid crystals articular and extra-articular deposition. This process is often silent, although it favour progressive joint destruction, renal failure and cardiovascular risk. Consecutively [3]. Its clinical manifestations include warm, swollen, erythematous and tender joints in acute condition and presence of tophi over the helix or antihelix of the ear, olecranon bursa or along the ulnar surface of the forearm in chronic condition [4]. Gout represents a subset of individuals with symptomatic hyperuricemia [5].

The gold standard for diagnosis of gout is identification of monosodium urate crystals in the synovial fluid. However, it is not only an invasive procedure that is painful but could also lead to complications like cartilage injury & Tendon rupture [6]. In recent years with advancement of ultrasonography and dual energy computed tomography (DECT) new clinical picture and staging has been identified namely deposition of uric acid crystals in joint and soft tissues without symptoms and also restriction of joint movement without any pain. So imaging

offers a non-invasive method for diagnosis of gout [7]. Ultrasonography (USG) has emerged as a useful measure for detection of joint effusion and synovitis, differentiating between active and inactive synovitis, studying cartilage, describing bone contour for erosions and osteophytes, evaluation of tendons and evaluation of crystal deposition. It is also useful in carrying out guided diagnostic or therapeutic procedures in gout cases [8]. DECT is a useful non-invasive technique that helps in visualization of monosodium urate crystals, along with different soft tissue changes as well as other erosive pathologies at high resolution, much earlier than the conventional radiography could do [9]. In view of this the present study had been designed to study the clinical profile of hyperuricemia patients with regards to joint involvement as assessed by DECT and USG and comorbidities.

## Material and Method

This was a cross sectional study which was done in Era's Lucknow Medical College & Hospital, Lucknow. The study was carried out on diagnosed hyperuricemia patients attending the medicine OPD and indoor patients of Era's Lucknow Medical College & Hospital over 18 months were included in the study till the required sample size was achieved. The overall sample size consisted of 66 cases of hyperuricemia.

Sample size was calculated on the basis of variation in MSU crystal deposit volume and its mean among the hyperuricemia cases. Taking 0.14, the SD of MSU crystal deposit volume among the cases and 90%

power of study, at 95% level of significance it was calculated to be 66.

All the patients with hyperuricemia from OPD/indoors were included in the study after taking informed consent and explaining all the procedures involved. Patients were clinically examined and demographic details like (age, sex etc), anthropometric measurements (height, weight, BMI) addictions and dietary habits were recorded. All the patients were enquired regarding their complaints and comorbidities like diabetes mellitus, hypertension, dyslipidemia, coronary artery disease. During clinical examination patients were enquired about joint pain, tenderness and restriction of movements. All the participants were subjected to radiological evaluation (using USG and DECT evaluation) to assess the joint involvement.

DECT evaluation was done using a dual source 128-MDCT (multiple detector computed tomography) Scanner as per protocol defined by Strobl et al. Both intra-articular as well as extra-articular urate depositions will be assessed. Based on DECT findings a provisional DECT diagnosis was proposed.

USG evaluation was performed using High Resolution USG machine using variable frequency linear probes.

Pathological findings, including DCS (double contour sign), tophi and aggregates were recorded. A provisional USG diagnosis was made.

Results were analyzed using descriptive statistics and making comparisons among various groups. categorical data were summarized as proportions and percentages (%) and quantitative data as mean  $\pm$  SD. Chi sq test was used for checking associations while unpaired t test and one way ANOVA were used to compare means of quantitative variables between the groups.  $P < 0.05$  was taken as level of significance. MS-Excel and SPSS ver 23 softwares were used for statistical analysis.

### Results

Among 66 study cases, the age of patients ranged from 36 to 87 years. Majority of the cases were aged more than 60 years (48.5%) followed by those aged 46-60 years (33.3%) and <45 years (18.2%). Mean age of patients was  $59.71 \pm 12.47$  years. Further, majority of patients were females (56.1%). There were 43.9% males [Table – 1].

**Table 1: Distribution of Cases according to Age& Sex.**

Characteristic	No.	%
Age Groups		
Young ( $\leq 45$ years)	12	18.2
Middle (46-60 years)	22	33.3
Old ( $\geq 61$ years)	32	48.5
Mean Age $\pm$ SD (Range)	59.71 $\pm$ 12.47 (36-87)	
Gender		
Female	37	56.1
Male	29	43.9

Out of 66 hyperuricemic patients, only 19 (28.8%) patients were symptomatic with symptoms of pain, swelling and tenderness at joints were reported. However majority of patients (71.2%) were asymptomatic. Further 6 patients had no comorbidities while rest 60 patients reported comorbidities. Majority of them reported single comorbidity [Table – 2A].

**Table 2A: Distribution of Cases according to Clinical Characteristics.**

Characteristic	Category	No.	%
Symptom Status	Absent	47	71.2
	Present	19	28.8
Comorbidity	Absent	6	9.1
	Present	60	90.9
No of Comorbidity	No comorbidity	6	9.1
	Single Comorbidity	21	90.9
	Multiple comorbidities	39	59.1

Diabetes alone (15.2%) was most common comorbidity, followed by CAD alone (13.6%) while Hypertension alone was observed in 3% cases. Rest of the cases had multiple combinations of comorbidities [Table – 2B].

**Table 2B: Distribution of Comorbidities.**

Distribution of Comorbidities	No.	%
CAD alone	9	13.6
Diabetes alone	10	15.2
Hypertension alone	2	3
Multiple	39	59.1

The radiological evidence of abnormalities which were indicative of involvement of joint by USG were DCS or HAG which were observed in 45.5% patients. MSU crystals were observed in 39.1% cases by DECT. So overall radiological evidence of joint involvement was found in 56.1% cases. Further the overall prevalence of

joint involvement in hyperuricemia patients was lying in the range (44.13 - 68.07) with 95% confidence. Whereas the prevalence of DCS/HAG and MSU crystals were found to be lying in the range (33.49 - 57.51) and (27.61 - 51.19) respectively [Table – 3].

**Table 3: Distribution of Joint Involvement in hyperuricemia patients.**

Variable		No.	%	95% CI
Radiological evidence of Joint involvement	USG: (DCS or HAGs)	30	45.5	(33.49 - 57.51)
	DECT (MSU Crystals)	26	39.4	(27.61 - 51.19)
	Any abnormality (USG and/or DECT)	37	56.1	(44.13 - 68.07)
Number of Joints involved	Nil	29	43.9	(27.95 - 59.93)
	Only one joints	21	31.8	(16.81 - 46.83)
	Two joints	13	19.7	(6.88 - 32.51)
	Three joints	3	4.5	(0.00 - 11.26)

Further only one joint was involved in majority of the patients (31.8% : 95%CI 16.81- 46.83), two joints were involved in 19.7% ( 95%CI 6.88 – 32.51) patients and three joints were involved in 4.5% (95%CI 0.0 - 11.26) patients.[Table – 3].

Majority of the symptomatic patients had been diagnosed with crystal deposition

seen for joint involvement by both USG and DECT as well as combination of both the radiological modalities in comparison to asymptomatic patients. However no significant association of joint involvement was found with no of comorbidities, CAD, hypertension, T2DM and dyslipidemia ( $p>0.05$ ) [Table – 4].

**Table 4: Association of Joint Involvement with Clinical Profile in hyperuricemia patients.**

Radiological evidence of Joint involvement		USG (n=30)		DECT (n=26)		USG+DECT (n=37)	
		No.	%	No.	%	No.	%
Symptomatic	Asymptomatic (n=47)	13	27.7	10	21.3	18	38.3
	Symptomatic (n=19)	17	89.5	16	84.2	19	100
	Significance	$\chi^2 = 20.85, p<0.001$		$\chi^2 = 22.45, p<0.001$		$\chi^2 = 20.91, p<0.001$	
Comorbidity	No comorbidity (n=6)	3	50	4	66.7	4	66.7
	Comorbidity (n=60)	27	45	22	36.7	33	55
	Significance	$\chi^2 = 0.06, p=0.815$		$\chi^2 = 2.06, p=0.152$		$\chi^2 = 0.30, p=0.583$	
CAD	No CAD (n=38)	14	36.8	12	31.6	18	47.4
	CAD (n=28)	16	57.1	14	50	19	67.9
	Significance	$\chi^2 = 2.68, p=0.102$		$\chi^2 = 2.29, p=0.130$		$\chi^2 = 2.75, p=0.097$	
Hypertension	No HTN (n=41)	20	48.8	17	41.5	25	61
	HTN (n=25)	10	40	9	36	12	48
	Significance	$\chi^2 = 0.48, p=0.487$		$\chi^2 = 0.19, p=0.659$		$\chi^2 = 1.06, p=0.303$	
T2DM	Non-diabetic (n=23)	12	52.2	10	43.5	14	60.9
	T2DM (n=43)	18	41.9	16	37.2	23	53.5
	Significance	$\chi^2 = 0.64, p=0.423$		$\chi^2 = 0.25, p=0.619$		$\chi^2 = 0.33, p=0.565$	
Dyslipidemia	No Dyslipidemia (n=52)	25	48.1	21	40.4	29	55.8
	Dyslipidemia (n=14)	5	35.7	5	35.7	8	57.1
	Significance	$\chi^2 = 0.68, p=0.410$		$\chi^2 = 0.10, p=0.751$		$\chi^2 = 0.01, p=0.927$	

Significant association of S. uricemic acid was found only with joint involvement indicated by radiological findings ( $p=0.003$ ). S. uricemic acid of patients in whom joint was involved was found to be significantly higher than those in whom no joint was involved [Table 5].

**Table 5: Association of Sr Uric Acid Levels (mg/dl) with Joint Involvement and Clinical Profile in hyperuricemia patients.**

Variable	n	Mean	SD	Significance
Comorbidities				
No comorbidities	6	10.27	1.16	't'=0.052; p=0.959
Comorbidities	60	10.21	2.63	
CAD				
No CAD	38	10.07	2.42	't'=-0.576; p=0.567
CAD	28	10.43	2.7	
Hypertension				
Normotensive	41	10.33	2.12	't'=0.477; p=0.635
Hypertension	25	10.02	3.12	
Type 2 DM				

Non-diabetic	23	9.65	1.66	't'=-1.332; p=0.188
Diabetic	43	10.52	2.86	
Hypothyroidism				
No hypothyroid	59	10.2	2.51	't'=-0.187; p=0.852
Hypothyroid	7	10.39	2.87	
Dyslipidemia				
No dyslipidemia	52	10.34	2.64	't'=0.785; p=0.435
Dyslipidemia	14	9.74	2.08	
CVA				
No CVA	62	10.27	2.53	't'=0.703; p=0.484
CVA	4	9.35	2.7	
Symptoms				
Asymptomatic	47	9.84	2.28	't'=-1.945; p=0.056
Symptomatic	19	11.15	2.91	
Joint involvement (Radiological finding)				
No joint involved	29	9.19	2.24	't'=-3.117; p=0.003
Joints involved	37	11.02	2.47	
No. of joints involved (n=37)				
Only one	21	11.05	1.82	F=0.080; p=0.923
Two	13	11.11	2.96	
Three	3	10.47	4.86	

None of the tested laboratory parameters showed any significant difference among hyperuricemic cases with and without involvement of joints [Table 6].

**Table 6: Association of Joint Involvement with Laboratory Parameters in hyperuricemia patients.**

Laboratory parameters	No Jt. Inv. (n=29)		Jt. Inv. (n=37)		Student 't' test	
	Mean	SD	Mean	SD	't'	'p'
Hb	11.03	2.46	10.83	2.36	0.348	0.729
TLC	8972	2835	7989	2154	1.602	0.114
Neutrophils	77.69	10.74	74.19	12.51	1.199	0.235
Lymphocytes	17.52	9.46	19.49	10.91	-0.771	0.444
Monocytes	2.59	1.64	3.68	3.39	-1.589	0.117
Eosinophils	2.21	1.29	2.65	1.34	-1.351	0.181
Platelets	2.1	0.6	2.33	1.17	-0.988	0.327
Urea	36.03	16.76	38.65	21.61	-0.537	0.593
Creat	0.9	0.25	0.92	0.3	-0.263	0.793
HbA1c	8.45	2.82	9.48	2.9	-1.043	0.305

## Discussion

The present study was planned to study the clinico-radiological profile of hyperuricemia patients with a primary focus to assess the prevalence of gout (crystal depositions of monosodium urate) using USG, DECT and other comorbid conditions. Age of the patients ranged from 36 to 87 years (mean age

59.71±12.47). Majority of patients were females (56.1%). Compared to present study Younes et al [10], in their study reported included hyperuricemic patients aged 25 to 55 years of age with a mean age of 48.5 years, of these 75.5% were males. Zhang et al. [11] in a recent study from China reported the mean age of hyperuricemia and gout patients to be

52.07 and 52.17 years and proportion of males as 51.2% and 53.1% respectively. Compared to these patients, patients in the present study were relatively older and had a higher proportion of females as compared to the males. In the present study, a total of 47 (71.2%) patients were asymptomatic and 19 (28.8%) were symptomatic. Compared to the present study, Younes et al. [10] in their study had all asymptomatic patients. On the other hand, Bongartz et al. [12] in their study had all the symptomatic patients. In the study of Cao et al. [13] there were a total of 202 symptomatic and 43 asymptomatic hyperuricemic patients. Majority of patients having serum uric acid levels above the defined range remain asymptomatic without the need of any treatment. However, hyperuricemic patients are at a high risk of developing gout, still, nearly two-third of the hyperuricemic patients remain asymptomatic throughout. [4] In the present study, among different comorbidities, diabetes alone or in combination (50%) was the commonest comorbidity followed by CAD (>40%) and hypertension (>25%) were the most common comorbid conditions. In a recent study, Hypertension, type 2 diabetes, metabolic syndrome and cardiovascular disease were reported as the risk factors in 75.7%, 47.8%, 6.6% and 23.5% patients respectively in asymptomatic hyperuricemia patients [14].

In the present study, joint involvements on USG were seen in 30 (45.5%) and on DECT by 26 (39.4%) patients. Combined use of both modalities show abnormalities suggestive of gout to in 37 (56.1%). Thus prevalence of gout in the present study was 56.1%. Compared to the present study, Gruber et al. (2014) [15] in a clinically suspected patients with 37 involved joints diagnosed urate crystal deposition in 67.6% joints as compared to 64.9% for DECT and USG respectively. Bongartz et al. [12] reported DECT positivity in 53.1%. In the study of Cao et al. [13]

prevalence of gout was found to be 25.6% in patients with asymptomatic hyperuricemia and 76.2% in symptomatic patients. The present study included both asymptomatic as well as symptomatic patients and thus the prevalence of imaging diagnosed gout in the present study was in between these two.

In the present study, as almost all the hyperuricemic patients (90.9%) had comorbidity, hence we could not find a significant association of mere presence of comorbidity to be associated significantly with gout diagnosis either by USG or DECT or for combined assessment by USG+DECT. These findings suggested that clinical profile of the patient is insufficient to provide information regarding gout status and that is why imaging modalities or other confirmatory modalities are required. It also showed that a lot of asymptomatic patients could have the risk of gout development and progression. Compared to the present study, Kim et al. [16] in their study found too did not report association of any comorbid condition with prevalence of gout.

In the present study, we did not find a significant association of uric acid levels with different demographic and clinical parameters except with the imaging findings for joint involvement and showed that higher uric acid levels even among the hyperuricemic levels have a higher risk of gout development. [17]

One of the limitations of the present study was absence of a confirmatory diagnostic tests such as no synovial joint aspiration. However, within this limitation we could find that both DECT as well as USG are able to detect gout at subclinical level itself and combined use of two modalities enhances the sensitivity of two. Further studies on a larger sample size longitudinal design are recommended to assess the role of imaging diagnosis in clinical transformation of disease and subsequent conversion to symptomatic state.

## Conclusion

On the basis of these findings, it can be inferred that asymptomatic patients (especially females and older) of hyperuricemia are at risk of developing joint involvement who should be radiologically examined. The overall prevalence of joint involvement in hyperuricemia patients was lying in the range (44.13 - 68.07) with 95% confidence. A confirmed relationship of Sr Uric Acid Levels (mg/dl) with Joint Involvement was found. These findings thus indicated that diagnosed cases of hyperuricemia should be evaluated for gout and should be thoroughly followed up for the risk of gout. The radiological tools like USG and DECT are helpful in this.

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