ANALYSIS DONE TO ANSWER THE FOLLOWING QUESTIONS

1. Describe RA patients in terms of
    a. Age distribution
    b. Gender distribution
    c. DMARDs
    d. ESR
    e. CRP
    f. SJC
    g. TJC
    h. CDAI
    i. DAS28 ESR
    j. DAS28 CRP
2. What is the variation in levels of Uric acid in patients of RA?
3. Do Uric acid levels vary on the basis of
    a. Gender
    b. RF positivity
    c. Anti CCP positivity
    d. DMARD – Mtx vs Lef vs Mtx + Lef vs Others
    e. DMARD – Mtx vs Lef
4. Relationship between Uric acid and inflammatory markers
    a. Do Inflammatory markers vary between normouricemic and hyperuricemic subjects?
        i. ESR
        ii. CRP
    b. Is there a correlation between Uric acid levels and inflammatory markers?
        i. ESR
        ii. CRP
5. Does Uric acid levels vary with disease activity?
    a. Correlation between Uric acid levels and
        i. CDAI
        ii. DAS28 ESR
        iii. DAS28 CRP
    b. Do Uric acid levels vary in patients with High/Moderate disease activity VERSUS Remission/Low activity
        i. CDAI
        ii. DAS28 ESR
        iii. DAS28 CRP

STATISTICAL ANALYSIS

The data was entered in Microsoft Excel spreadsheet and analysis was done using Epi-Info, JASP and Statistical Package for Social Sciences (SPSS) version 23.0.

Continuous variables are represented as mean ± SD or medians with Inter-quartile range. Categorical variables are represented as number and percentage (%).
The variables were tested for normality with the Kolmogorov-Smirnov test for normality, Q-Q plots, visual inspection of the histograms and the z-scores for the degree of skewness and kurtosis. Spearman Rank correlation test was used to assess correlation between continuous quantitative variables. All tests of significance were two-tailed and statistical significance was defined as $P < 0.05$. Scatter diagrams were used to describe the relationship between two quantitative variables. Not all variables met the assumptions required for parametric; therefore, non-parametric tests (i.e., Mann-Whitney test, Spearman correlation) were used for all analyses for consistency. Appropriate graphs such as pie charts, bar diagrams and histograms have been constructed.

RESULTS AND OBSERVATIONS

A Prospective Observational study was conducted in Department of Medicine, PGIMER and DR. RML Hospital, New Delhi from 1st January 2021 to 31st May 2022. Patients attending the Rheumatology Clinic who fulfilled the ACR criteria for RA were interviewed. After application of appropriate inclusion and exclusion criteria, a total of 150 subjects were included in the study. They were evaluated by taking exhaustive history, general physical examination, systemic examination and blood investigations. Subjects with a serum uric acid level ≥7 mg/dL were classified as having hyperuricemia. Of the 150 subjects, 9 were classified as hyperuricemic while the rest were found to have a uric acid of < 7 mg/Dl (Normouricemic). The following observations were made:

AGE DISTRIBUTION

The vast majority (n = 98, 65.33%) of our subjects belonged to the age group 40 to 60 years. In the hyperuricemic group, 2 (22.22%) subjects belonged to the age group <40 years and the remaining 7 (77.77%) were in the age group 40-60 years. There were no subjects > 60 years in the hyperuricemic group.

In the normouricemic group, the majority of Subjects (n = 85, 60.3%) were between 40 and 60 years of age or below the age of 40 *n = 38, 27%). The remaining 18 (12.8%) of the subjects were above the age of 60 years.

Both the groups were compared using Fisher's Exact Test and found to be comparable in terms of age distribution (p value 0.689).

Subjects in the HyperUricemic group ranged from a minimum value of 32.0 to a maximum of 56.0. The Median (IQR) was 48.0 (10.0) and the Mean ± Standard Deviation was 46.56 ± 7.8.

On the other hand, the subjects in the NormoUricemic group ranged from a minimum value of 18.0 to a maximum of 72.0. The Median (IQR) was 46.0 (15.0) and the Mean ± Standard Deviation was 46.42 ± 11.05.

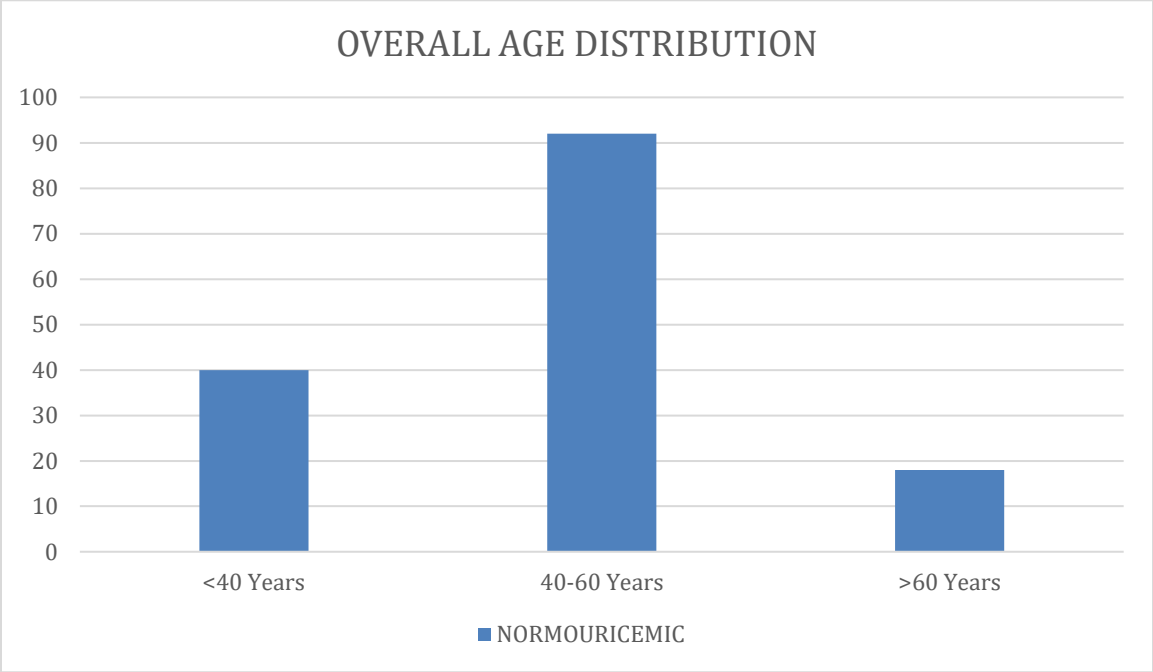
The Students T Test was used and no statistically significant difference was found between the groups (p Value 0.971).

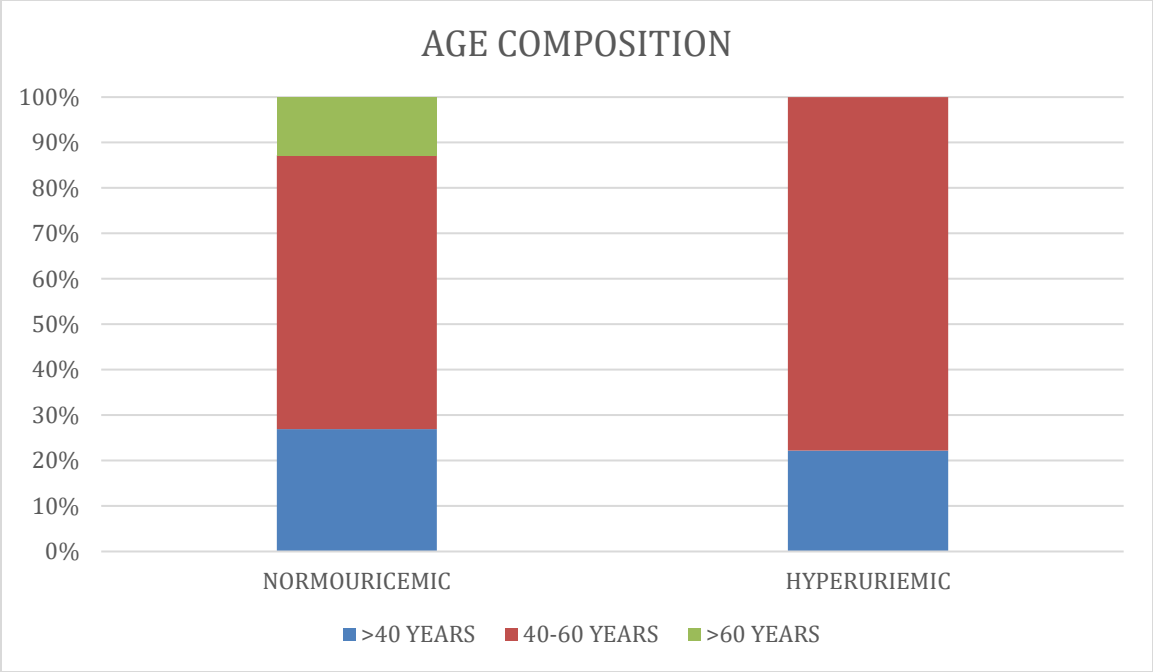
The same information is shown in the following table and figure.

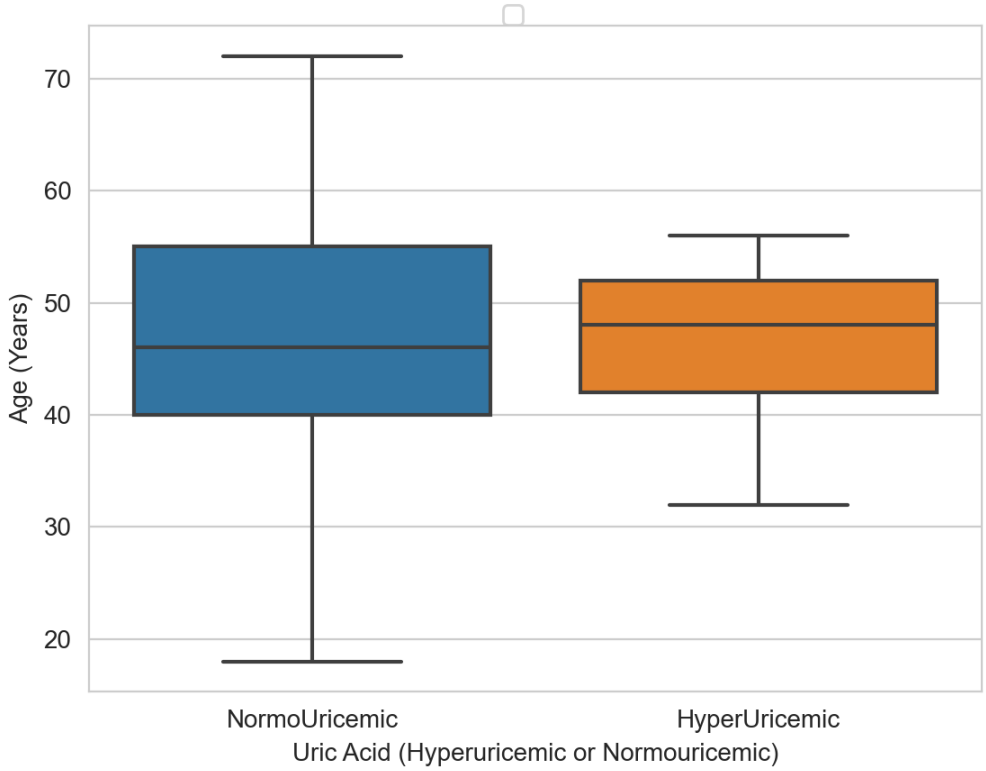
		Uric Acid		P VALUE	TEST APPLIED
		HyperUricemic	NormoUricemic		
Age (Years)	count	9.0	141.0	0.971	Students T Test
	mean	46.56	46.42		
	std	7.8	11.05		
	min	32.0	18.0		
	25%	42.0	40.0		
	50%	48.0	46.0		
	75%	52.0	55.0		
	max	56.0	72.0		

	URIC ACID GROUP	**P VALUE**	**TEST APPLIED**

		Normo-Uricemic	Hyper-Uricemic	TOTAL		
AGE GROUP	<40 YEARS	38	2	40	0.689	Fisher's Exact Test
	40-60 YEARS	85	7	92		
	>60 YEARS	18	0	18		




AGE COMPOSITION
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
NORMOURICEMIC
HYPERURIEMIC
>40 YEARS
40-60 YEARS
>60 YEARS


70
60
50
40
30
20
Age (Years)
NormoUricemic
HyperUricemic
Uric Acid (Hyperuricemic or Normouricemic)

GENDER DISTRIBUTION

The majority of our subjects were females (n =134, 89.33%) while male subjects were only 16 in number.

Of the 9 subjects in the group HyperUricemic, 7 (77.78%) belonged were Female while the remaining 2 (22.22%) were males.

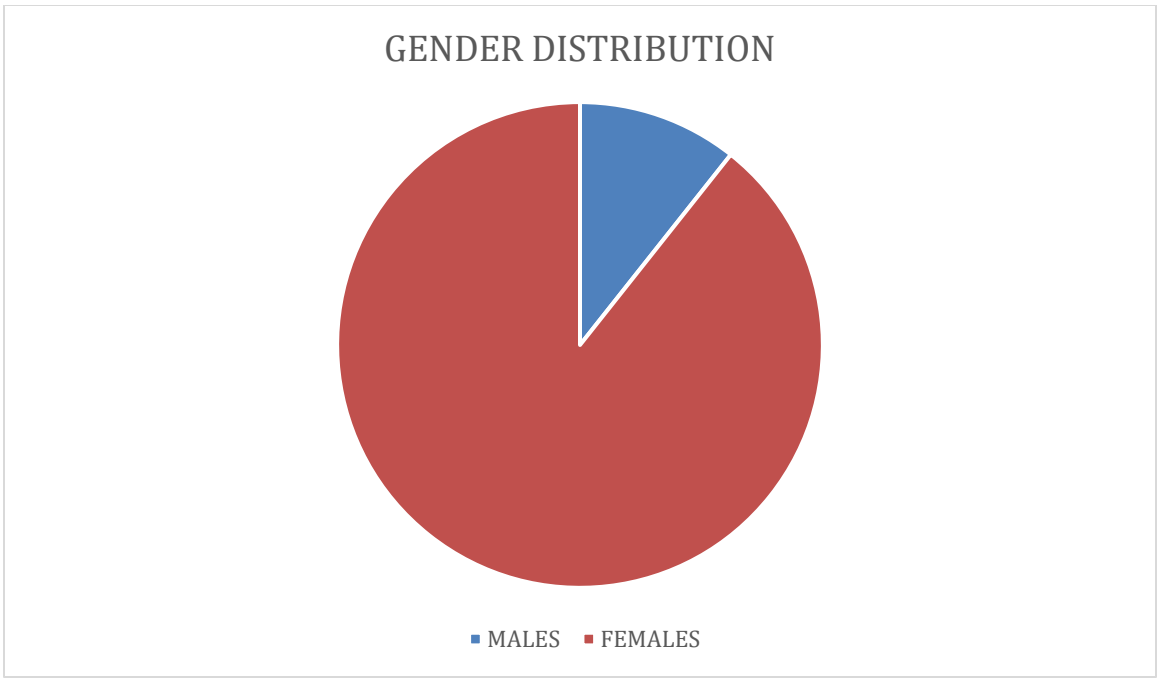
In the NormoUricemic subjects, 127 (90.07%) were females and the the remaining 14 (9.93%) subjects were males.

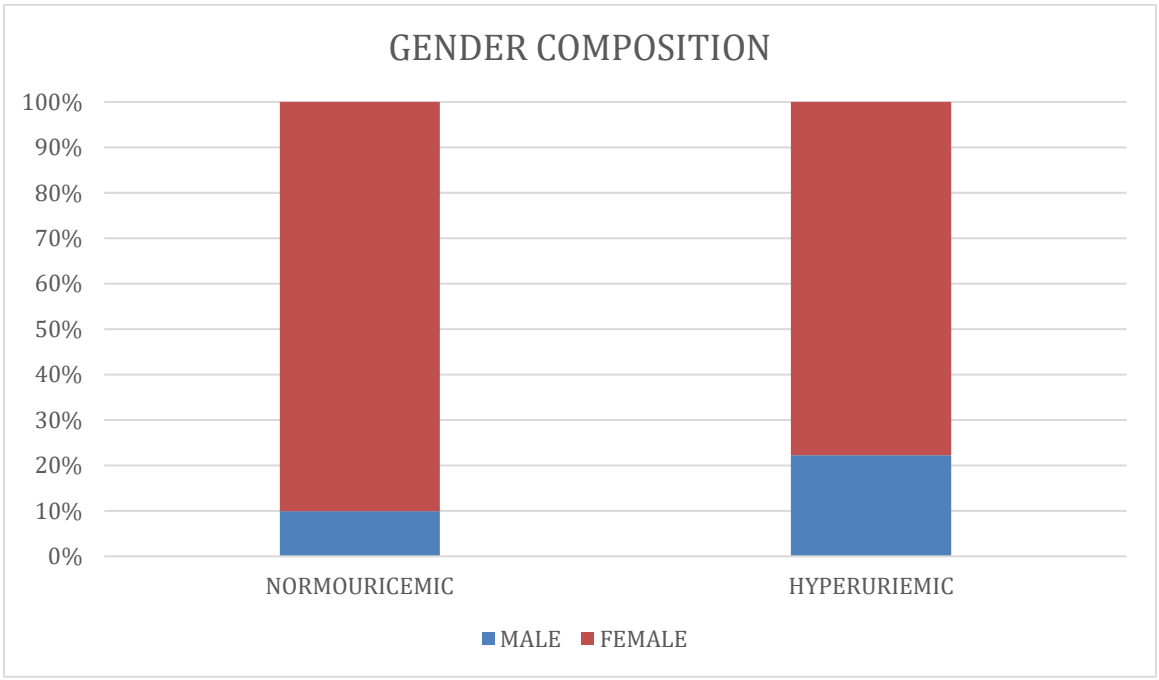
The Fisher Exact Test was used and no statistically significant difference was found between the groups (p Value 0.246).

Therefore, both the groups were similar in terms of gender distribution.

The same information is shown in the following table and figure.

		Gender			P VALUE	TEST APPLIED
		Female	Male	All		
Uric Acid	HyperUricemic	7	2	9	0.246	Fisher Exact Test
	NormoUricemic	127	14	141		
	All	134	16	150		


GENDER DISTRIBUTION
MALES
FEMALES


GENDER COMPOSITION
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
NORMOURICEMIC
HYPERURIEMIC
MALE
FEMALE

CURRENT DMARD

We studied the DMARD therapy being taken by the subjects.

The vast majority of our subjects (n = 119, 79.33%) were being treated with Methotrexate alone.

Of the 9 subjects in the HyperUricemic group, 7 (77.78%) were on methotrexate alone while the remaining 2 (22.22%) were taking methotrexate + leflunomide.

In the normouricemic group, 10 (7.09%) subjects each were being managed with Leflunomide alone and methotrexate + leflunomide. 9 subjects were taking other DMARDs such as Azathioprine, Hydroxychloroquine, Sulfasalazine etc. The remaining 112 were taking methotrexate alone (79.43%).

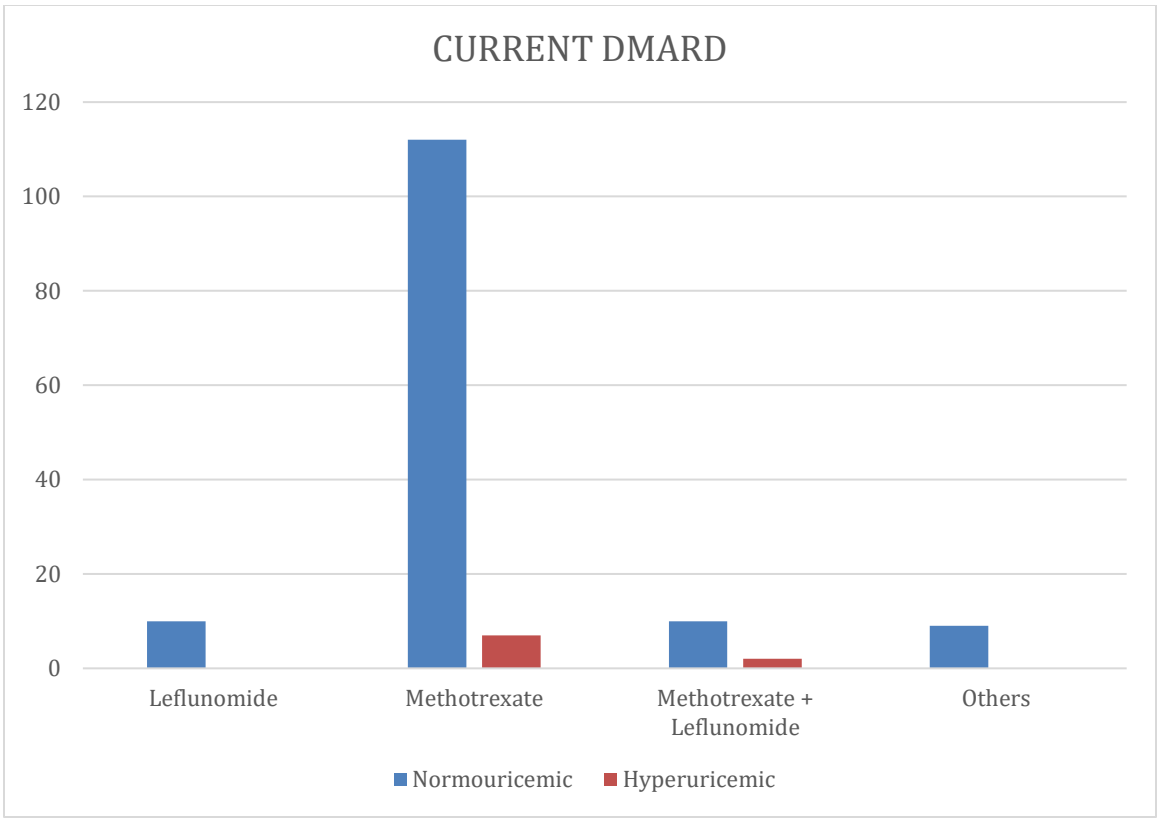
Only 2 subjects (1.33%) were being managed with bDMARDs – one each with Rituximab + Methotrexate and Golimumab + Methotrexate.

The Chi Square Test was used and no statistically significant difference was found between the groups (p Value 0.934).

Therefore, both the groups were comparable in terms of current DMARD.

The same information is shown in the following table and figure.

		DMARD					P VALUE	TEST APPLIED
		Leflunomide	Methotrexate	Methotrexate + Leflunomide	Others	All		
Uric Acid	HyperUricemic	0	7	2	0	9	0.934	Chi Square Test
	NormoUricemic	10	112	10	9	141		
	All	10	119	12	2	150		


CURRENT DMARD
120
100
80
60
40
20
0
Leflunomide
Methotrexate
Methotrexate + Leflunomide
Others
Normouricemic
Hyperuricemic

ESR (mm at the end of 1st hour)

We wanted to analyze the variation in ESR levels in normouricemic and hyperuricemic subjects.

Normouricemic subjects had comparatively lower levels of ESR ranging from a minimum value of 5 to a maximum of 100. The Median (IQR) was 40 (28) and the Mean ± Standard Deviation was 42.9 ± 19.6.

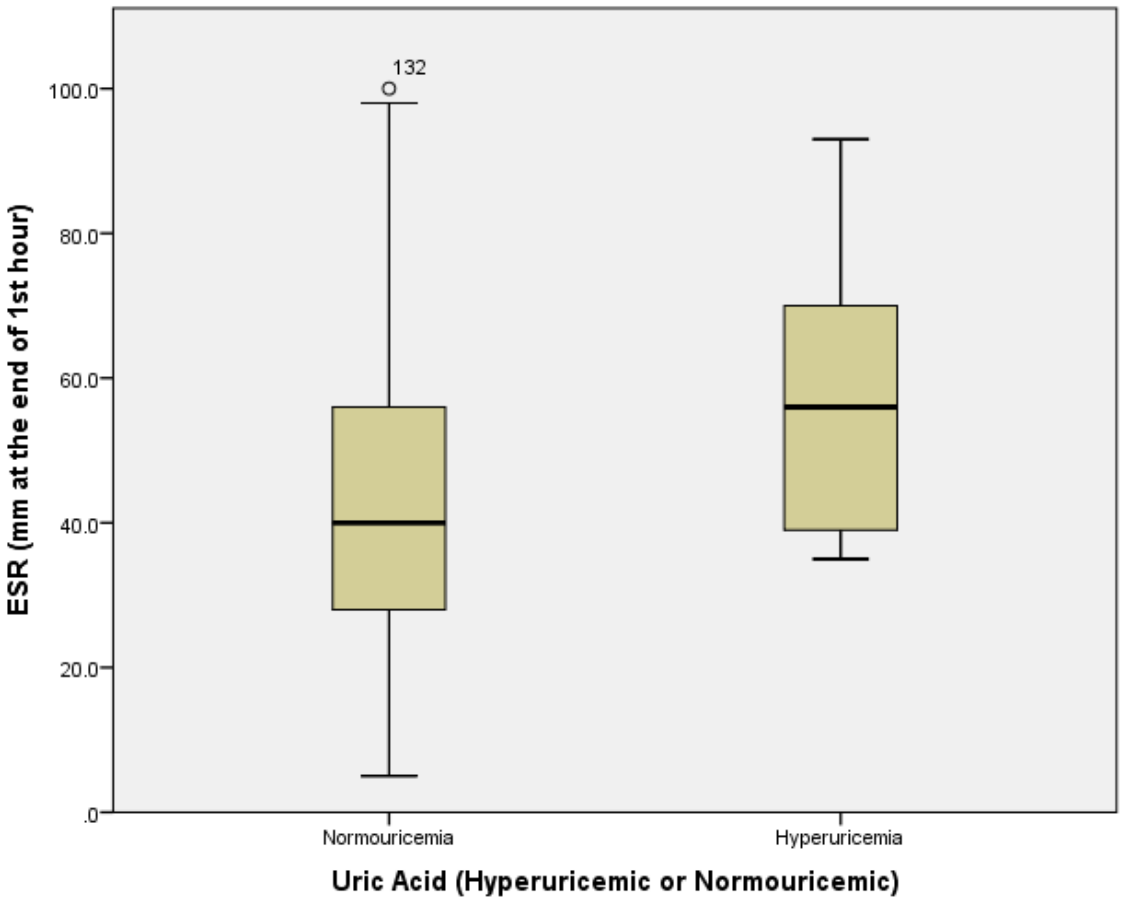
On the other hand, the levels in hyperuricemic subjects ranged from a minimum value of 35 to a maximum of 93. The Median (IQR) was 56 (31) and the Mean ± Standard Deviation was 56.7 ± 19.

The Mann Whitney Test was used and no statistically significant (p value 0.054) difference was found between the groups.

Thus, even though hyperuricemic subjects had comparatively higher ESR levels (56.7 ± 19 versus 42.9 ± 19.6), the difference was not significant (p value 0.054).

The same information is shown in the following table and figure.

		Uric Acid		**P VALUE**	**TEST APPLIED**
		Normouricemic	Hyperuricemic		
ESR	count	141	9	0.054	Mann Whitney Test
	mean	42.9	56.7		
	std	19.6	19		
	min	5	35		
	25%	28	39		
	50%	40	56		
	75%	56	70		
	max	100	93		


132
100.0
80.0
60.0
40.0
20.0
.0
ESR (mm at the end of 1st hour)
Normouricemia
Hyperuricemia
Uric Acid (Hyperuricemic or Normouricemic)

QUANTITATIVE CRP (mg/dL)

We also wanted to analyze the CRP levels in normouricemic and hyperuricemic subjects.

Normouricemic subjects had comparatively lower levels of CRP ranging from a minimum value of 0.1 to a maximum of 16.75. The Median (IQR) was 1.1 (3.7) and the Mean ± Standard Deviation was 2.8 ± 3.14.

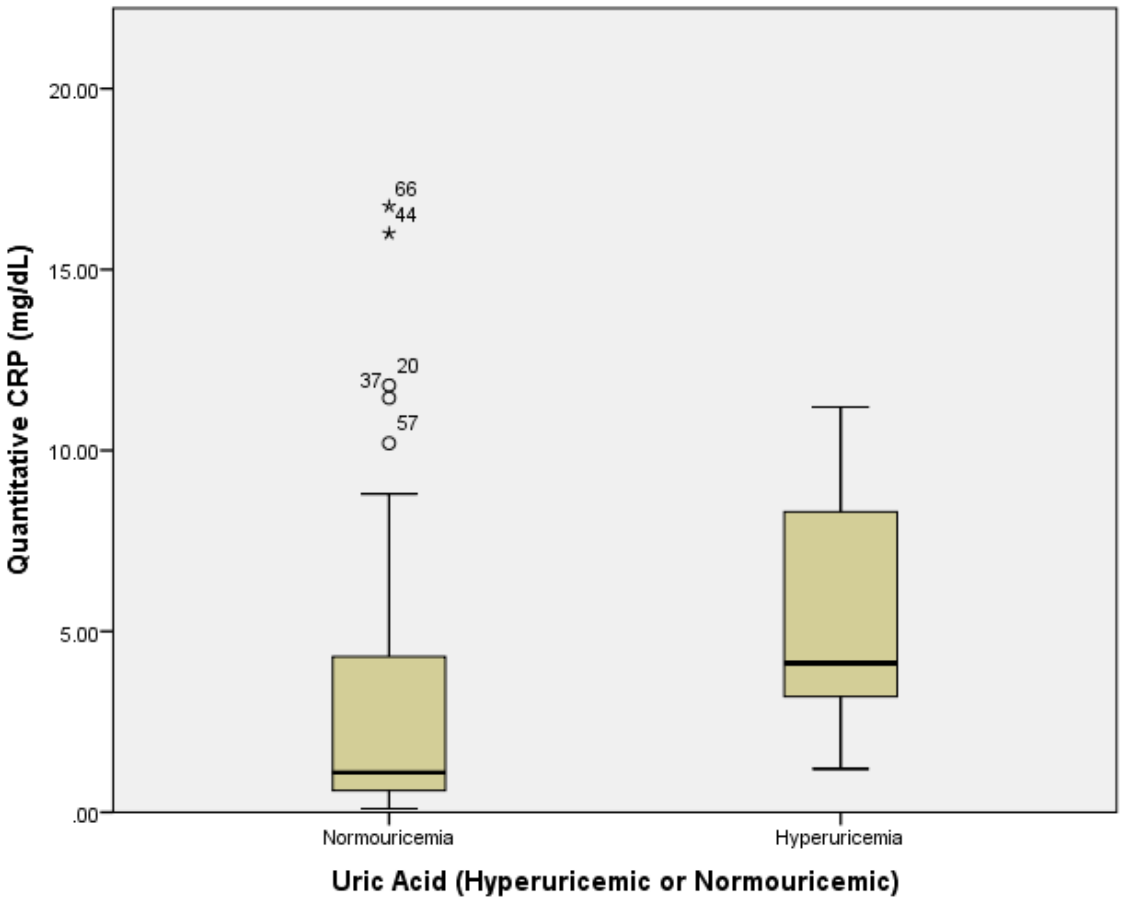
On the other hand, the levels in hyperuricemic subjects ranged from a minimum value of 1.2 to a maximum of 11.2. The Median (IQR) was 4.12 (4.9) and the Mean ± Standard Deviation was 5.52 ± 3.68.

The Mann Whitney Test was used and a statistically significant (p value 0.008) difference was found between the groups.

Thus, hyperuricemic subjects had significantly (p value 0.008) higher CRP levels (5.52 ± 3.68), as compared to normouricemic subjects (2.8 ± 3.14).

The same information is shown in the following table and figure.

		URIC ACID GROUP		P VALUE	TEST APPLIED
		NORMOURICEMIC	HYPERURICEMIC		
CRP	count	141	9	0.008	Mann Whitney Test
	mean	2.8	5.52		
	std	3.14	3.68		
	min	0.1	1.2		
	25%	0.6	3.2		
	50%	1.1	4.12		
	75%	4.3	8.3		
	max	16.75	11.2		


20.00
15.00
10.00
5.00
.00
Quantitative CRP (mg/dL)
66
44
37
20
57
Normouricemia
Hyperuricemia
Uric Acid (Hyperuricemic or Normouricemic)

Tender Joint Count

The hyperuricemic subjects had TJC ranging from from a minimum value of 0.0 to a maximum of 14.0. The Median (IQR) was 7.0 (10.0) and the Mean ± Standard Deviation was 7.22 ± 5.65.

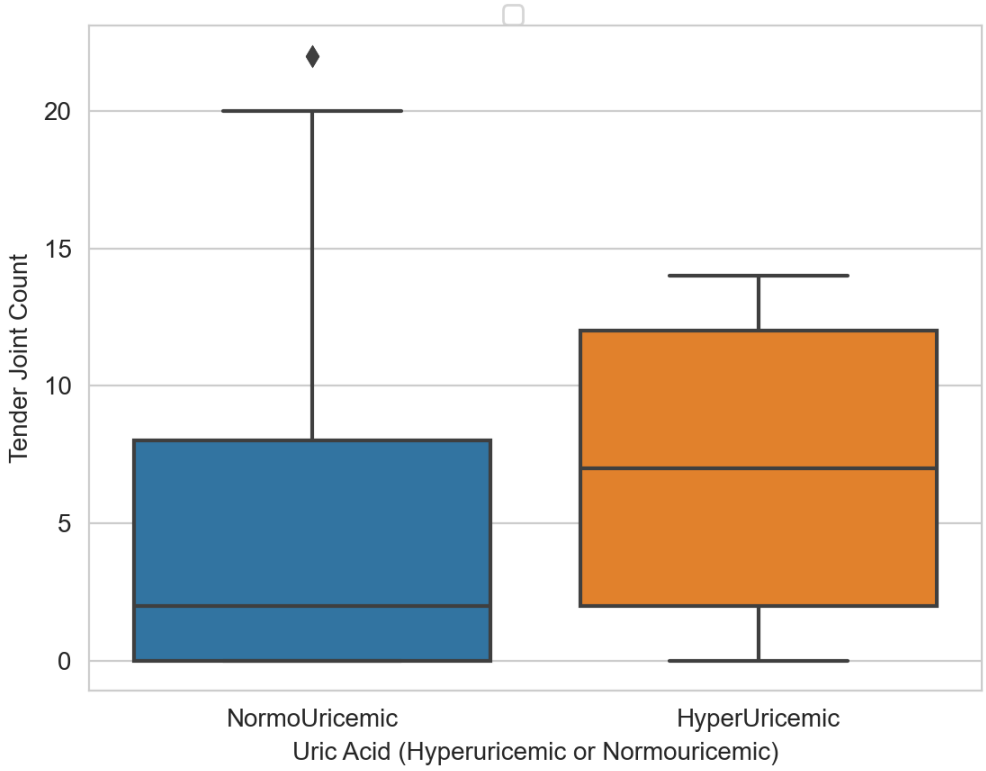
On the other hand, in the normouricemic group, TJC ranged from a minimum value of 0.0 to a maximum of 22.0. The Median (IQR) was 2.0 (8.0) and the Mean ± Standard Deviation was 4.95 ± 6.46.

The Mann Whitney Test was used and no statistically significant difference was found between the groups (p Value 0.163).

Thus, even though the hyperuricemic group had a higher (7.22± 5.65) TJC as compared to the normouricemic group (4.95 ± 6.46), the difference was not significant (p value 0.163).

The same information is shown in the following table and figure.

		Uric Acid		P VALUE	TEST APPLIED
		HyperUricemic	NormoUricemic		
Tender Joint Count	count	9.0	141.0	0.163	Mann Whitney Test
	mean	7.22	4.95		
	std	5.65	6.46		
	min	0.0	0.0		
	25%	2.0	0.0		
	50%	7.0	2.0		
	75%	12.0	8.0		
	max	14.0	22.0		


20
15
10
5
0
Tender Joint Count
NormoUricemic
HyperUricemic
Uric Acid (Hyperuricemic or Normouricemic)

Swollen Joint Count

The HyperUricemic group had swollen joints ranging from a minimum value of 0.0 to a maximum of 8.0. The Median (IQR) was 4.0 (2.0) and the Mean ± Standard Deviation was 3.33 ± 2.65.

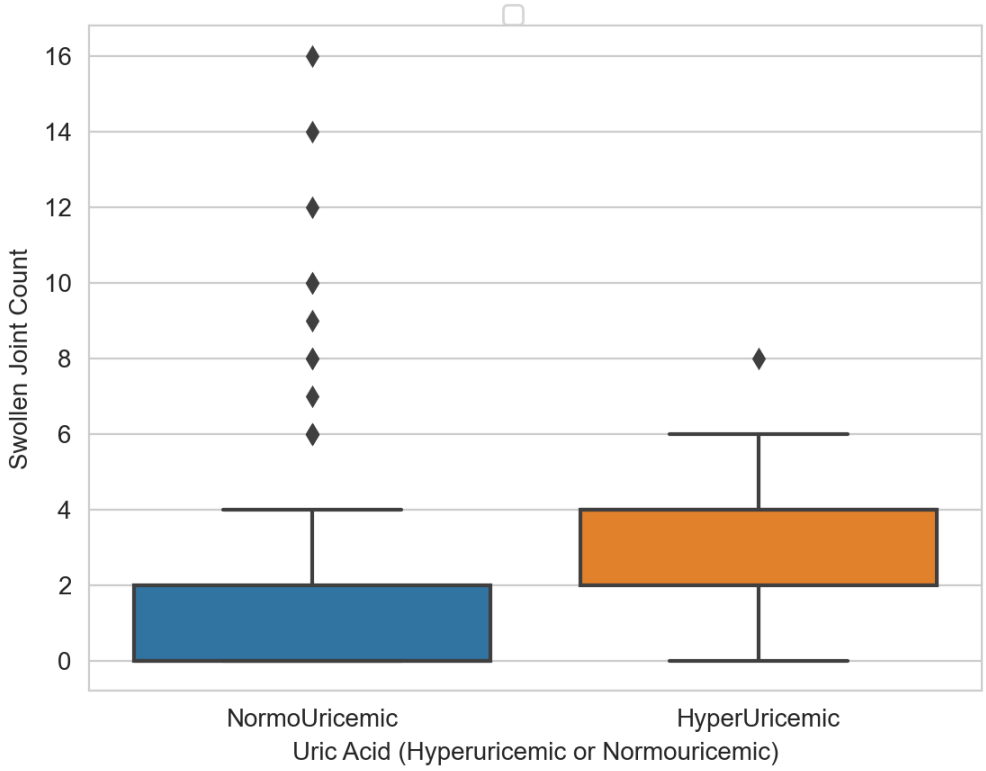
In the normouricemic group, it ranged from a minimum value of 0.0 to a maximum of 16.0. The Median (IQR) was 0.0 (2.0) and the Mean ± Standard Deviation was 1.61 ± 2.87.

The Mann Whitney Test was used and a statistically significant difference was found between the groups (p Value 0.014).

Thus, the hyperuricemic group had a significantly (p value 0.014) higher swollen joints (3.33 ± 2.65) as compared to the normouricemic group (1.61 ± 2.87).

The same information is shown in the following table and figure.

		Uric Acid		P VALUE	TEST APPLIED
		HyperUricemic	NormoUricemic		
Swollen Joint Count	count	9.0	141.0	0.014	Mann Whitney Test
	mean	3.33	1.61		
	std	2.65	2.87		
	min	0.0	0.0		
	25%	2.0	0.0		
	50%	4.0	0.0		
	75%	4.0	2.0		
	max	8.0	16.0		


16
14
12
10
8
6
4
2
0
Swollen Joint Count
NormoUricemic
HyperUricemic
Uric Acid (Hyperuricemic or Normouricemic)

Patient Global Disease Activity

The Patient Global Disease Activity in the HyperUricemic subjects ranged from a minimum value of 0.0 to a maximum of 8.0. The Median (IQR) was 5.0 (3.0) and the Mean ± Standard Deviation was 5.0 ± 2.69.

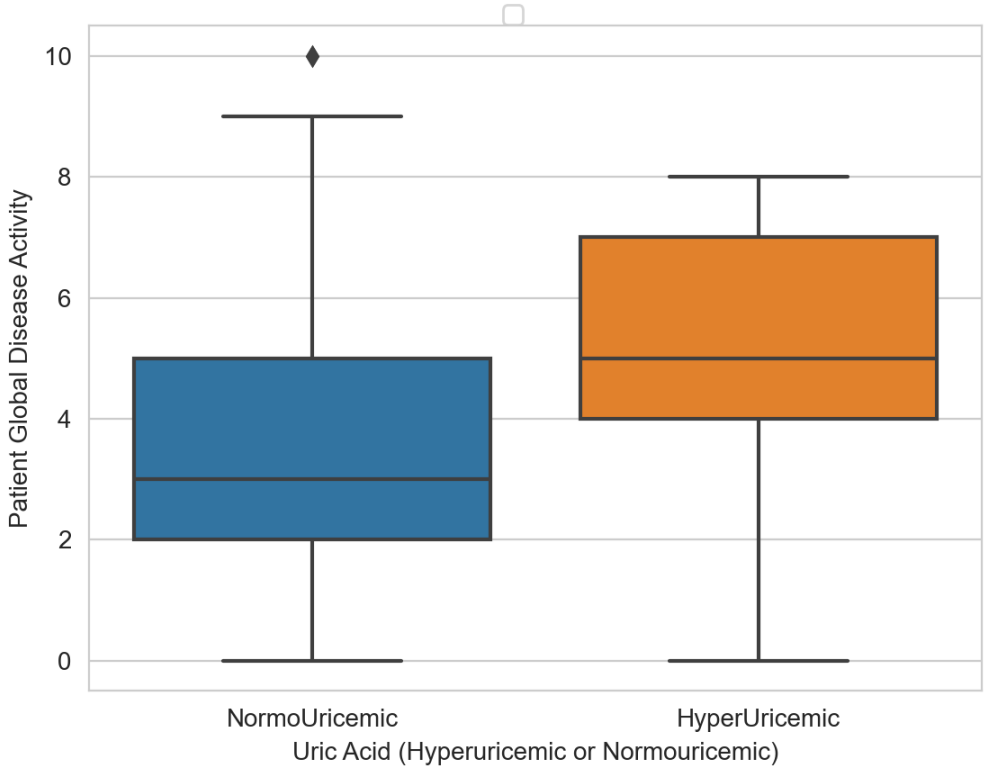
In the NormoUricemic subjects, it ranged from a minimum value of 0.0 to a maximum of 10.0. The Median (IQR) was 3.0 (3.0) and the Mean ± Standard Deviation was 3.81 ± 2.33.

The Mann Whitney Test was used and no statistically significant difference was found between the groups (p Value 0.135).

Thus, even though the hyperuricemic group had a higher PGDA (3.81 ± 2.33) as compared to the normouricemic group (5.0 ± 2.69), the difference was not significant (p value 0.135).

The same information is shown in the following table and figure.

		Uric Acid		P VALUE	TEST APPLIED
		HyperUricemic	NormoUricemic		
Patient Global Disease Activity	count	9.0	141.0	0.135	Mann Whitney Test
	mean	5.0	3.81		
	std	2.69	2.33		
	min	0.0	0.0		
	25%	4.0	2.0		
	50%	5.0	3.0		
	75%	7.0	5.0		
	max	8.0	10.0		


10
8
6
4
2
0
Patient Global Disease Activity
NormoUricemic
HyperUricemic
Uric Acid (Hyperuricemic or Normouricemic)

Evaluator Global disease Activity

The HyperUricemic subjects had an EGDA ranging from 0.0 to 6.0. The Median (IQR) was 3.0 (2.0) and the Mean ± Standard Deviation was 3.44 ± 2.01.

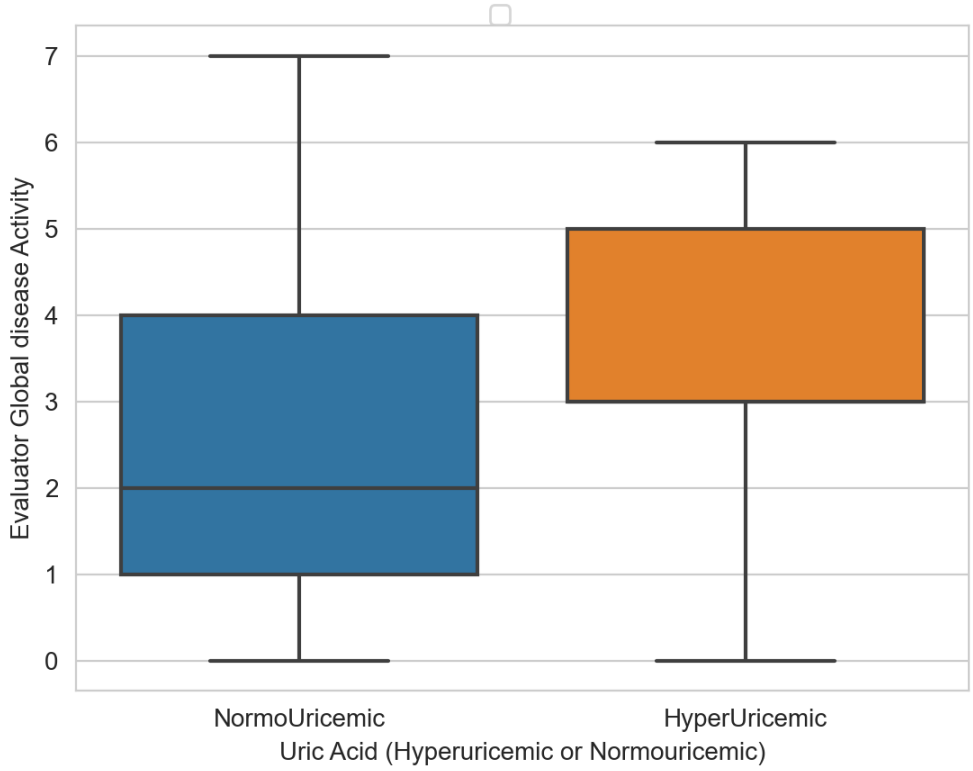
On the other hand, the normouricemic subjects had an EGDA ranging from a minimum value of 0.0 to a maximum of 7.0. The Median (IQR) was 2.0 (3.0) and the Mean ± Standard Deviation was 2.19 ± 1.82.

The Mann Whitney Test was used and no statistically significant difference was found between the groups (p Value 0.063).

Thus, even though the hyperuricemic group had a higher (3.44 ± 2.01) EGDA as compared to the normouricemic group (2.19 ± 1.82), the difference was not significant (p value 0.063).

The same information is shown in the following table and figure.

		Uric Acid		P VALUE	TEST APPLIED
		HyperUricemic	NormoUricemic		
Evaluator Global disease Activity	count	9.0	141.0	0.063	Mann Whitney Test
	mean	3.44	2.19		
	std	2.01	1.82		
	min	0.0	0.0		
	25%	3.0	1.0		
	50%	3.0	2.0		
	75%	5.0	4.0		
	max	6.0	7.0		


Evaluator Global disease Activity
7
6
5
4
3
2
1
0
NormoUricemic
HyperUricemic
Uric Acid (Hyperuricemic or Normouricemic)

CDAI

In order to study the clinical disease activity, we analyzed the CDAI of our subjects.

The CDAI in the HyperUricemic group ranged from a minimum value of 0.0 to a maximum of 31.0. The Median (IQR) was 23.0 (9.0) and the Mean ± Standard Deviation was 19.0 ± 10.91.

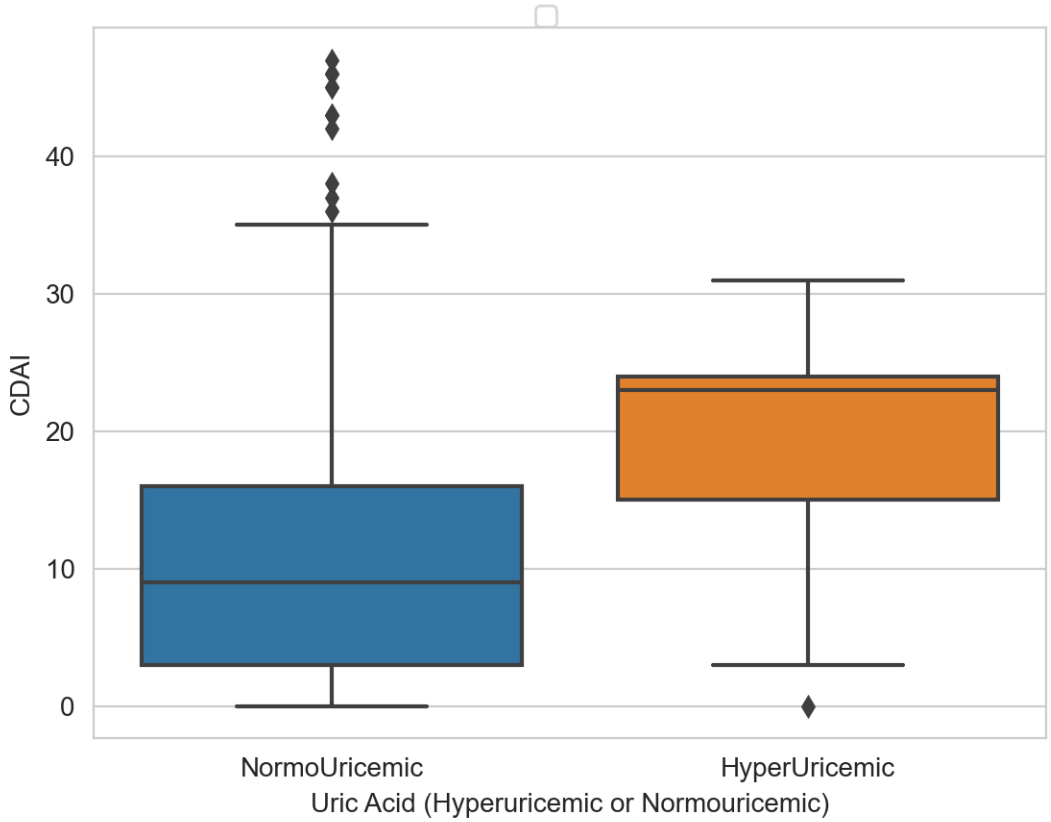
On the other hand, CDAI of NormoUricemic subjects ranged from a minimum value of 0.0 to a maximum of 47.0. The Median (IQR) was 9.0 (13.0) and the Mean ± Standard Deviation was 12.56 ± 12.1.

The Mann Whitney Test was used and no statistically significant difference was found between the groups (p Value 0.089).

Thus even though the CDAI was higher in the hyperuricemic group (19.0 ± 10.91) as compared to the normouricemic group (12.56 ± 12.1), the difference was not significant (p value 0.089).

The same information is shown in the following table and figure.

		Uric Acid		P VALUE	TEST APPLIED
		HyperUricemic	NormoUricemic		
CDAI	count	9.0	141.0	0.089	Mann Whitney Test
	mean	19.0	12.56		
	std	10.91	12.1		
	min	0.0	0.0		
	25%	15.0	3.0		
	50%	23.0	9.0		
	75%	24.0	16.0		
	max	31.0	47.0		


CDAI
40
30
20
10
0
NormoUricemic
HyperUricemic
Uric Acid (Hyperuricemic or Normouricemic)

DAS 28 ESR

We analyzed the disease activity in our subjects using DAS 28 ESR.

The DAS28-ESR score in the HyperUricemic group ranged from a minimum value of 2.5 to a maximum of 6.9. The Median (IQR) was 5.8 (1.0) and the Mean ± Standard Deviation was 5.19 ± 1.53.

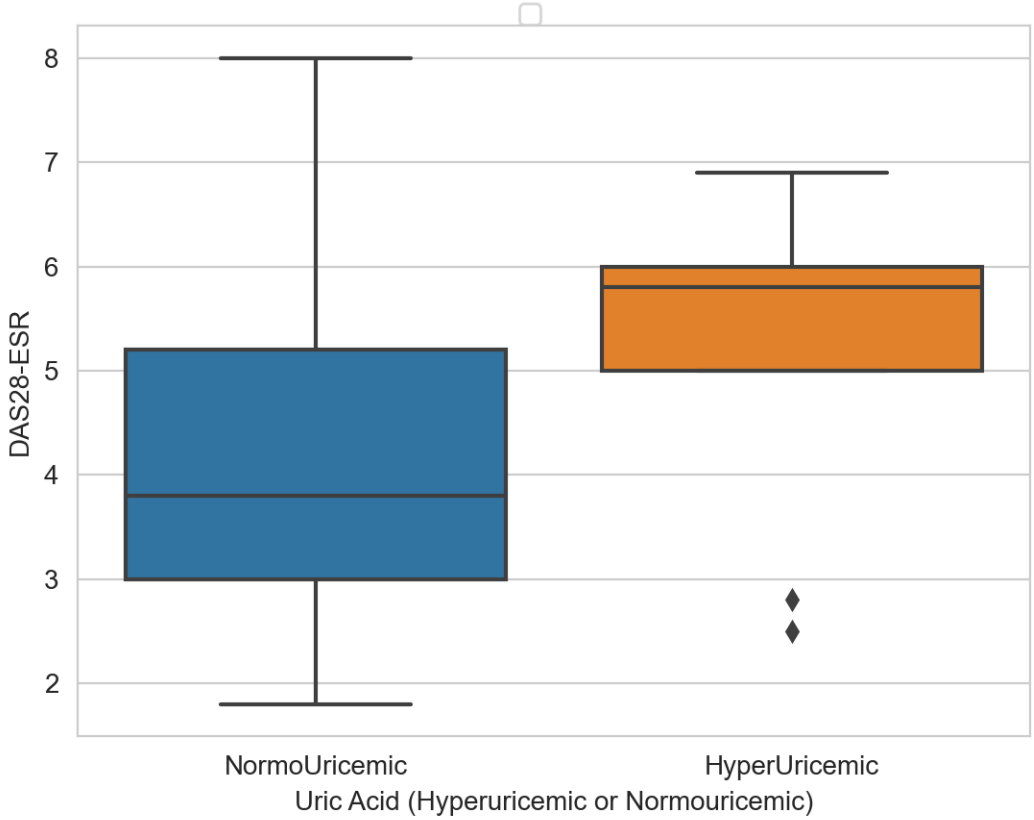
Iin the normouricemic group, the DAS28-ESR ranged from a minimum value of 1.8 to a maximum of 8.0. The Median (IQR) was 3.8 (2.2) and the Mean ± Standard Deviation was 4.19 ± 1.54.

The Mann Whitney Test was used and no statistically significant difference was found between the groups (p Value 0.08).

Thus, even though the DAS28 ESR score was higher for the hyperuricemic subjects (5.19 ± 1.53 versus 4.19 ± 1.54), the difference was not significant (p value 0.08).

The same information is shown in the following table and figure.

		Uric Acid		P VALUE	TEST APPLIED
		HyperUricemic	NormoUricemic		
DAS28-ESR	count	9.0	141.0	0.08	Mann Whitney Test
	mean	5.19	4.19		
	std	1.53	1.54		
	min	2.5	1.8		
	25%	5.0	3.0		
	50%	5.8	3.8		
	75%	6.0	5.2		
	max	6.9	8.0		


8
7
6
5
4
3
2
DAS28-ESR
NormoUricemic
HyperUricemic
Uric Acid (Hyperuricemic or Normouricemic)

DAS28 CRP

We analyzed the disease activity in our subjects using DAS 28 CRP.

The DAS28-CRP in the HyperUricemic group ranged from a minimum value of 2.31 to a maximum of 6.33. The Median (IQR) was 5.15 (0.99) and the Mean ± Standard Deviation was 4.76 ± 1.4.

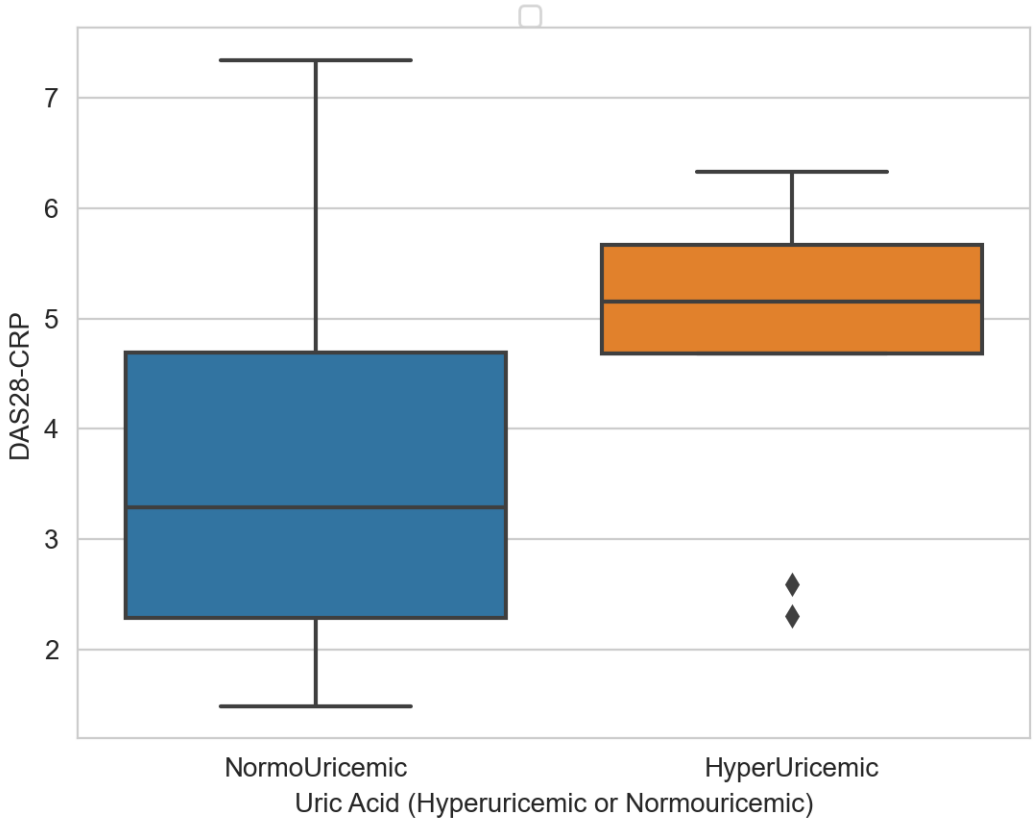
On the other hand, in the NormoUricemic group, it ranged from a minimum value of 1.49 to a maximum of 7.34. The Median (IQR) was 3.29 (2.40) and the Mean ± Standard Deviation was 3.61 ± 1.56.

The Mann Whitney Test was used and a statistically significant difference was found between the groups (p Value 0.028).

Thus, the hyperuricemic subjects (4.76 ± 1.4) had a significantly (p value 0.028) higher DAS28 CRP as compared to the normouricemic subjects (3.61 ± 1.56).

The same information is shown in the following table and figure.

		Uric Acid		P VALUE	TEST APPLIED
		HyperUricemic	NormoUricemic		
DAS28-CRP	count	9.0	141.0	0.028	Mann Whitney Test
	mean	4.76	3.61		
	std	1.4	1.56		
	min	2.31	1.49		
	25%	4.68	2.29		
	50%	5.15	3.29		
	75%	5.67	4.69		
	max	6.33	7.34		


7
6
5
4
3
2
DAS28-CRP
NormoUricemic
HyperUricemic
Uric Acid (Hyperuricemic or Normouricemic)

Uric Acid

The main objective of our study was to assess the levels of uric acid in RA patients.

In our study, an overwhelming majority (n = 141, 94%) had a uric acid level of <7 mg/dL and were classified as Normo-Uricemic while the remaining 9 (6%) of the subjects had uric acid levels of > 7 mg/dL (Hyper-Uricemic).

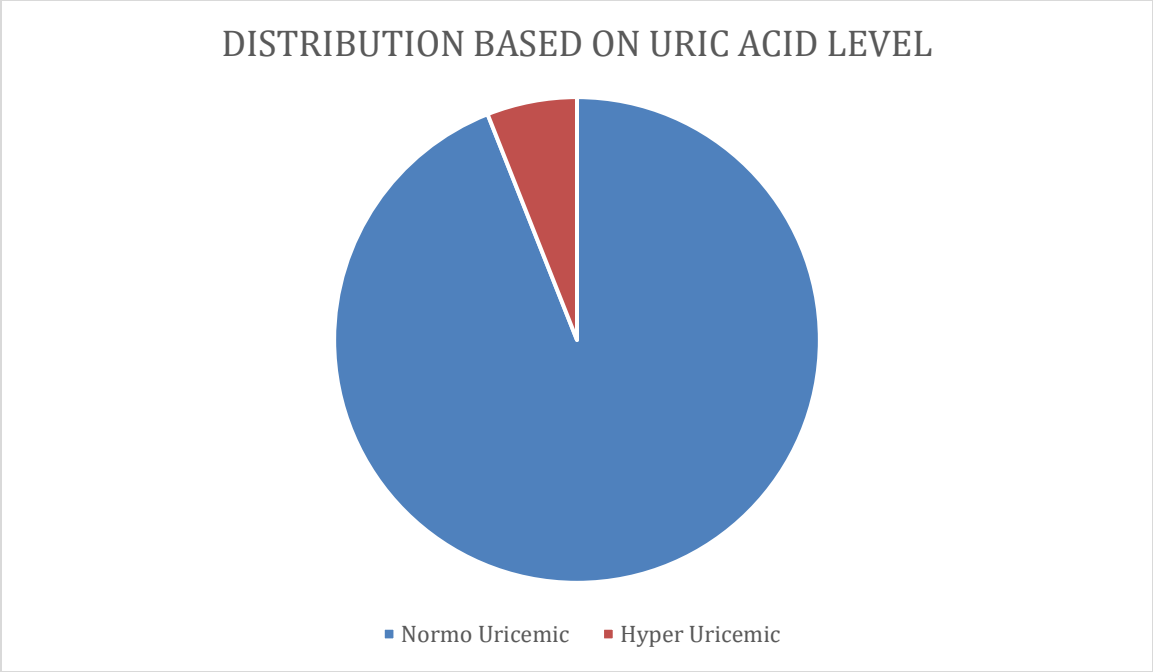
Normo-Uricemic subjects had lower levels of uric acid ranging from a minimum value of 2.1 to a maximum of 6.8. The Median (IQR) was 4.6 (1.75) and the Mean ± Standard Deviation was 4.61 ± 1.14.

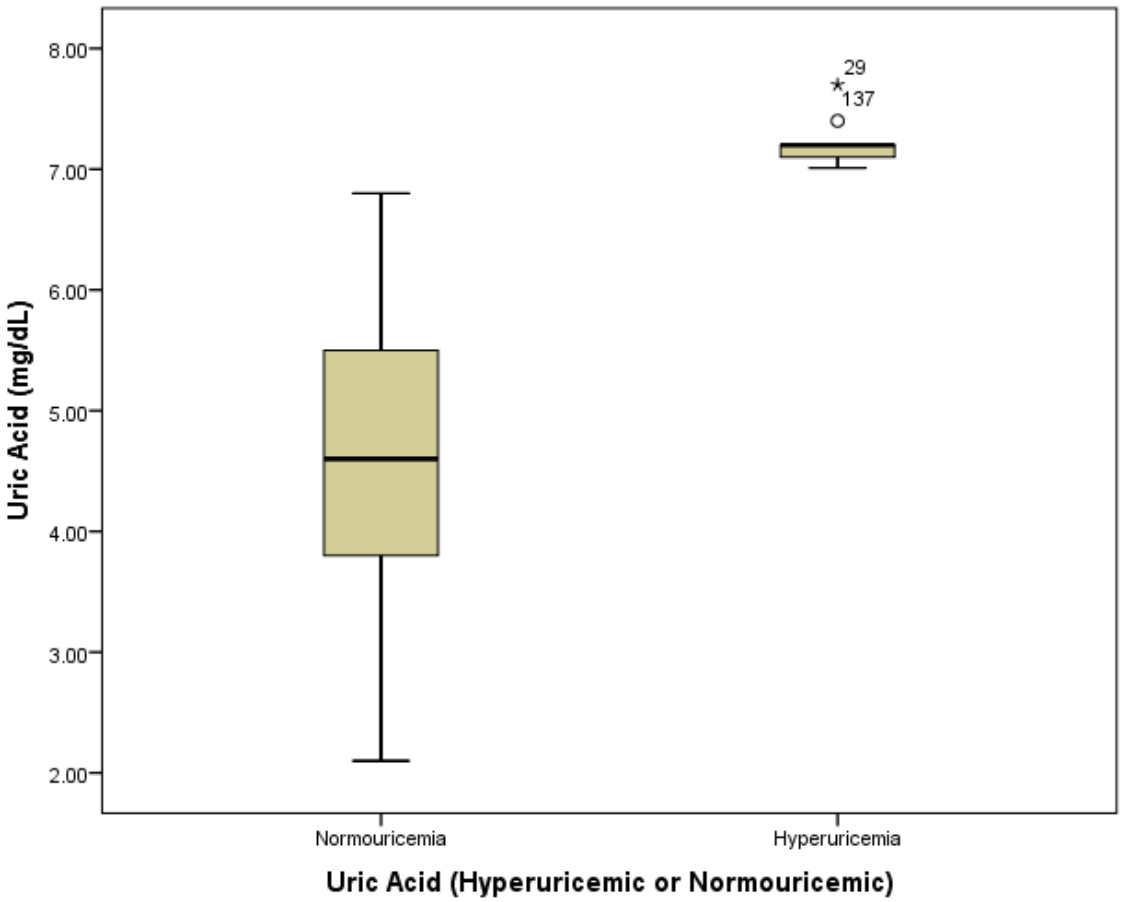
We had classified the subjects into 2 groups based on the levels of their serum uric acid. Therefore, as expected, the uric acid levels in hyperuricemic subjects were higher - ranging from a minimum value of 7.01 to a maximum of 7.7. The Median (IQR) was 7.2 (0.24) and the Mean ± Standard Deviation was 7.21 ± 0.22.

The Mann Whitney Test was used and (as expected) a statistically significant difference was found between the groups (p Value < 0.001).

The same information is showed in the following table and graph.

		URIC ACID GROUP		**P VALUE**	**TEST APPLIED**
		Normo-Uricemic	**Hyper-Uricemic**		
Uric Acid (mg/dL)	count	141	9	<0.001	Mann Whitney Test
	mean	4.61	7.21		
	std	1.14	0.22		
	min	2.1	7.01		
	25%	3.8	7.1		
	50%	4.6	7.2		
	75%	5.5	7.2		
	max	6.8	7.7		


DISTRIBUTION BASED ON URIC ACID LEVEL
Normo Uricemic
Hyper Uricemic


8.00
7.00
6.00
5.00
4.00
3.00
2.00
Uric Acid (mg/dL)
29
137
Normouricemia
Hyperuricemia
Uric Acid (Hyperuricemic or Normouricemic)

Gender VERSUS Uric Acid (mg/dL)

We wanted to analyze the variations in the levels of uric acid of RA patients based on gender.

Female subjects had comparatively lower levels ranging from a minimum value of 2.1 to a maximum of 7.7. The Median (IQR) was 4.6 (1.79) and the Mean ± Standard Deviation was 4.73 ± 1.24.

On the other hand, the levels in male subjects ranged from a minimum value of 2.3 to a maximum of 7.4. The Median (IQR) was 5.15 (2.10) and the Mean ± Standard Deviation was 5.08 ± 1.5.

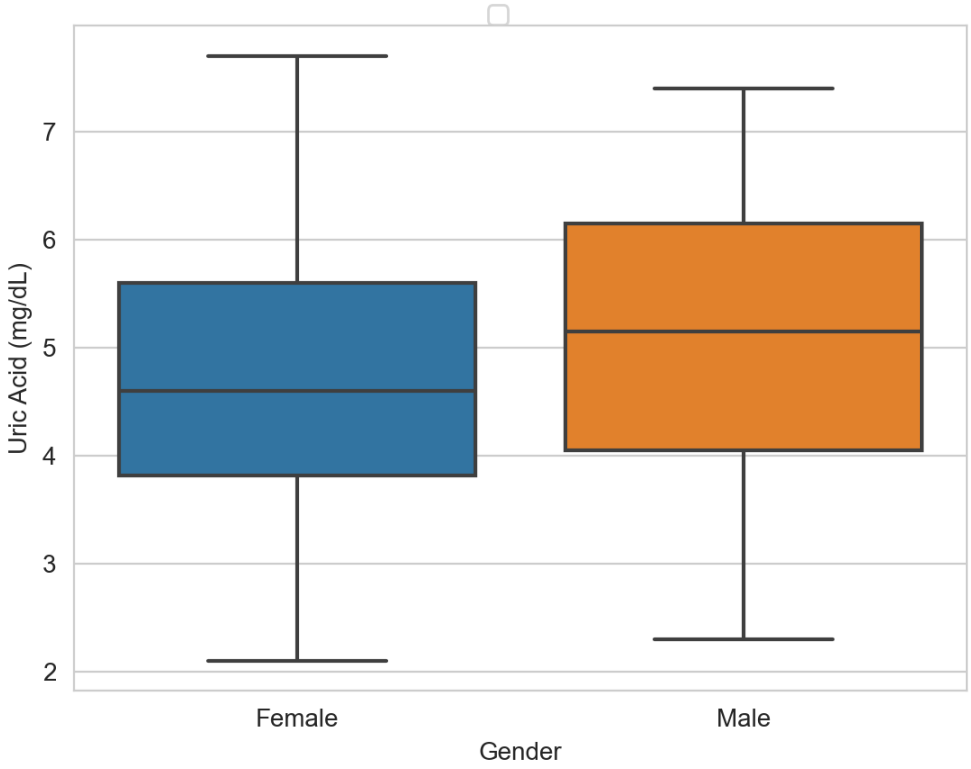
The Students T Test was used and no statistically significant difference was found between the groups (p Value 0.29).

Thus, even though males had a higher (5.08 ± 1.5) uric acid level as compared to females (4.73 ± 1.24), the difference was not significant (p value 0.29).

We also studied the distribution of males in the normouricemic and the hyperuricemic groups.

The same information is shown in the following table and figure.

		Gender		P VALUE	TEST APPLIED
		Female	Male		
Uric Acid (mg/dL)	count	134.0	16.0	0.29	Students T Test; Test Statistic - 1.127
	mean	4.73	5.08		
	std	1.24	1.5		
	min	2.1	2.3		
	25%	3.81	4.05		
	50%	4.6	5.15		
	75%	5.6	6.15		
	max	7.7	7.4		


Uric Acid (mg/dL)
7
6
5
4
3
2
Female
Male
Gender

Rheumatoid Factor VERSUS Uric Acid (mg/dL)

We wanted to analyze whether there is any difference in the levels of serum uric acid in patients who have detectable Rheumatoid Factor versus those who do not.

In the subjects who had no detectable levels of Rheumatoid Factor, the Uric Acid (mg/dL) ranged from a minimum value of 2.3 to a maximum of 7.7. The Median (IQR) was 4.02 (1.26) and the Mean ± Standard Deviation was 4.22 ± 1.63.

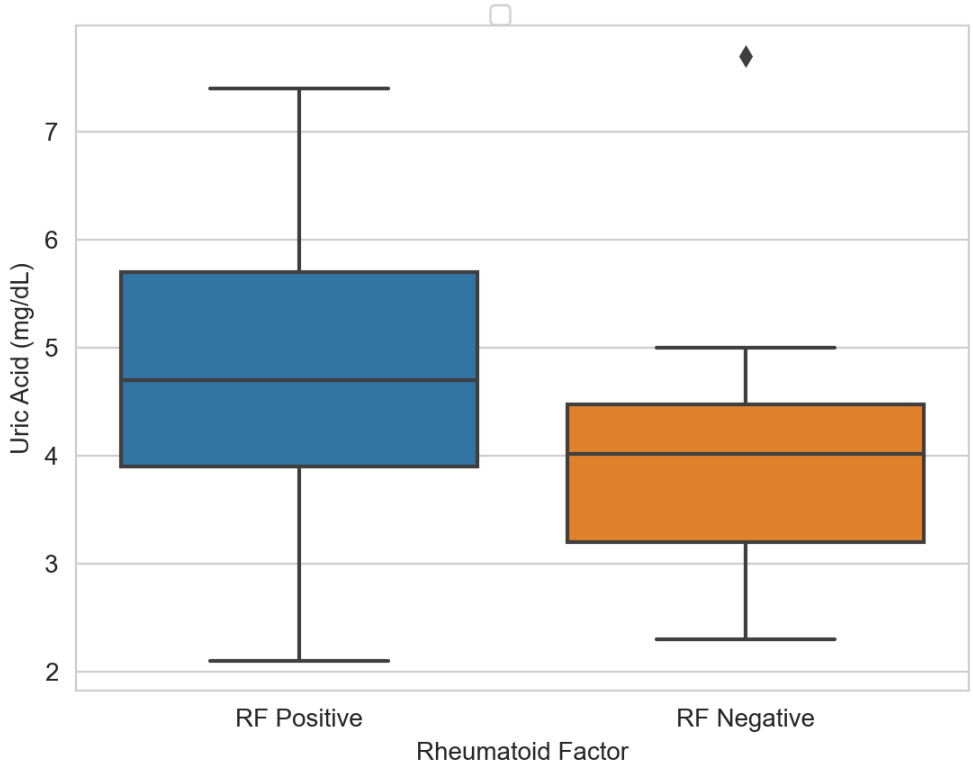
The uric acid levels were only marginally higher in the subjects who were found to have detectable Rheumatoid Factor. It Positive ranged from a minimum value of 2.1 to a maximum of 7.4. The Median (IQR) was 4.7 (1.80) and the Mean ± Standard Deviation was 4.79 ± 1.24.

The Student's T Test was used and no statistically significant difference was found between the groups (p Value 0.211).

Therefore, there was no significant (p value 0.211) difference between the uric acid level of subjects with detectable levels of RF (4.79 ± 1.24) and those without detectable RF (4.22 ± 1.63).

The same information is shown in the following table and figure.

		Rheumatoid Factor		**P VALUE**	**TEST APPLIED**
		RF Negative	**RF Positive**		
Uric Acid (mg/dL)	count	8.0	142.0	0.211	Students T Test; Test Statistic - 1.58
	mean	4.22	4.79		
	std	1.63	1.24		
	min	2.3	2.1		
	25%	3.2	3.9		
	50%	4.02	4.7		
	75%	4.47	5.7		
	max	7.7	7.4		


Uric Acid (mg/dL)
7
6
5
4
3
2
RF Positive
RF Negative
Rheumatoid Factor

Anti CCP VERSUS Uric Acid (mg/dL)

We wanted to analyze whether there is any difference in the levels of serum uric acid in patients who have detectable antibodies to CCP versus those who do not.

In the subjects who had no detectable levels of Anti CCP, the Uric Acid (mg/dL) ranged from a minimum value of 2.1 to a maximum of 7.7. The Median (IQR) was 4.75 (1.68) and the Mean ± Standard Deviation was 4.77 ± 1.18.

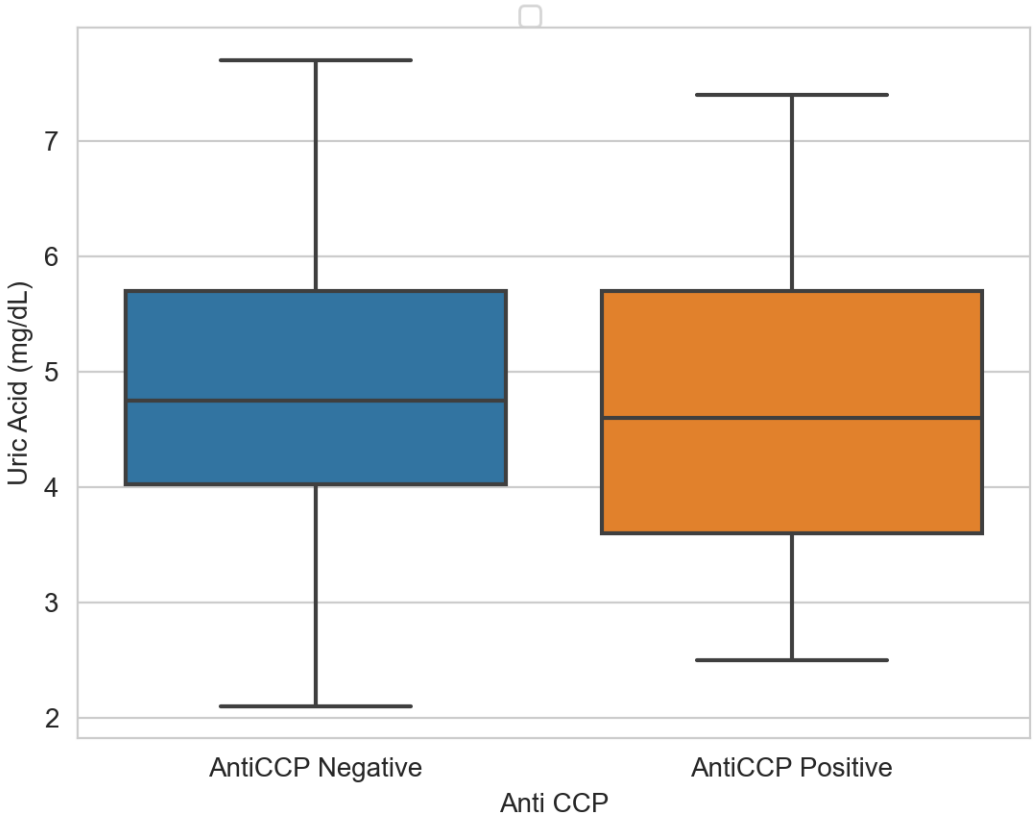
The uric acid levels were only marginally higher in the subjects who were found to have detectable Anti CCP antibodies. It ranged from a minimum value of 2.5 to a maximum of 7.4. The Median (IQR) was 4.6 (2.1) and the Mean ± Standard Deviation was 4.78 ± 1.37.

The Mann Whitney Test was used and no statistically significant difference was found between the groups (p Value 0.789).

Thus, there was no significant (p value 0.789) difference between the uric acid level of subjects with detectable levels of Anti CCP (4.78 ± 1.37) and those without (4.77 ± 1.18).

The same information is shown in the following table and figure.

		Anti CCP		**P VALUE**	**TEST APPLIED**
		AntiCCP Negative	**AntiCCP Positive**		
Uric Acid (mg/dL)	count	84.0	65.0	0.789	Mann Whitney Test; Test Statistic - 0.072
	mean	4.77	4.78		
	std	1.18	1.37		
	min	2.1	2.5		
	25%	4.02	3.6		
	50%	4.75	4.6		
	75%	5.7	5.7		
	max	7.7	7.4		


Uric Acid (mg/dL)
7
6
5
4
3
2
AntiCCP Negative
AntiCCP Positive
Anti CCP

DMARD - Methotrexate OR Methotrexate + Leflunomide OR Other VERSUS Uric Acid (mg/dL)

We classified the subjects into 3 groups based on the DMARDs – Methotrexate alone, Leflunomide alone, combined methotrexate + leflunomide and others.

In the Leflunomide group, uric acid ranged from a minimum value of 2.4 to a maximum of 6.2. The Median (IQR) was 3.88 (1.21) and the Mean ± Standard Deviation was 4.08 ± 1.3.

The subjects who were on Methotrexate alone had uric acid which ranged from a minimum value of 2.1 to a maximum of 7.7. The Median (IQR) was 4.7 (1.65) and the Mean ± Standard Deviation was 4.76 ± 1.23.

The levels were comparatively higher in the subjects who were on combination of methotrexate and leflunomide with levels ranging from a minimum value of 2.3 to a maximum of 7.1. The Median (IQR) was 6.05 (2.43) and the Mean ± Standard Deviation was 5.28 ± 1.67.

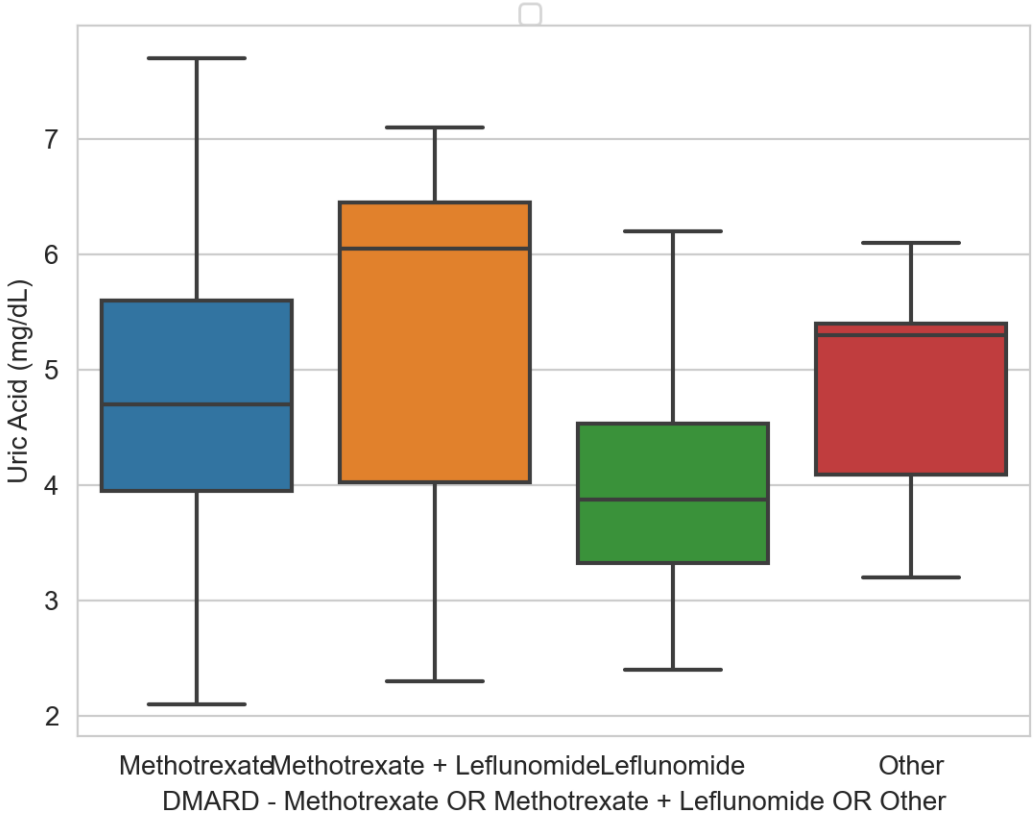
Only 9 subjects were taking other DMARDs and had a Mean ± Standard Deviation of 4.83 ± 0.93.

The Kruskall Wallis Test was used and no statistically significant difference was found between the groups (p Value 0.176).

Therefore, no significant difference in the uric acid levels were found between the groups taking various DMARDs.

The same information is shown in the following table and figure.

		DMARD				P VALUE	TEST APPLIED
		Leflunomide	Methotrexate	Methotrexate + Leflunomide	Other		
Uric Acid (mg/dL)	count	10.0	119.0	12.0	9.0	0.176	Kruskall Wallis Test
	mean	4.08	4.76	5.28	4.83		
	std	1.3	1.23	1.67	0.93		
	min	2.4	2.1	2.3	3.2		
	25%	3.32	3.94	4.02	4.09		
	50%	3.88	4.7	6.05	5.3		
	75%	4.53	5.6	6.45	5.4		
	max	6.2	7.7	7.1	6.1		


Uric Acid (mg/dL)
7
6
5
4
3
2
Methotrexate
Methotrexate + Leflunomide
Leflunomide
Other
DMARD - Methotrexate OR Methotrexate + Leflunomide OR Other

DMARD - Methotrexate OR Leflunomide VERSUS Uric Acid (mg/dL)

We studied the uric acid levels of those taking methotrexate (either alone or in combination with other DMARDs except leflunomide) and those on leflunomide (either alone or in combination with others DMARDs except methotrexate).

In the Leflunomide group, uric acid ranged from a minimum value of 2.3 to a maximum of 7.1. The Median (IQR) was 4.1 (2.7) and the Mean ± Standard Deviation was 4.67 ± 1.6.

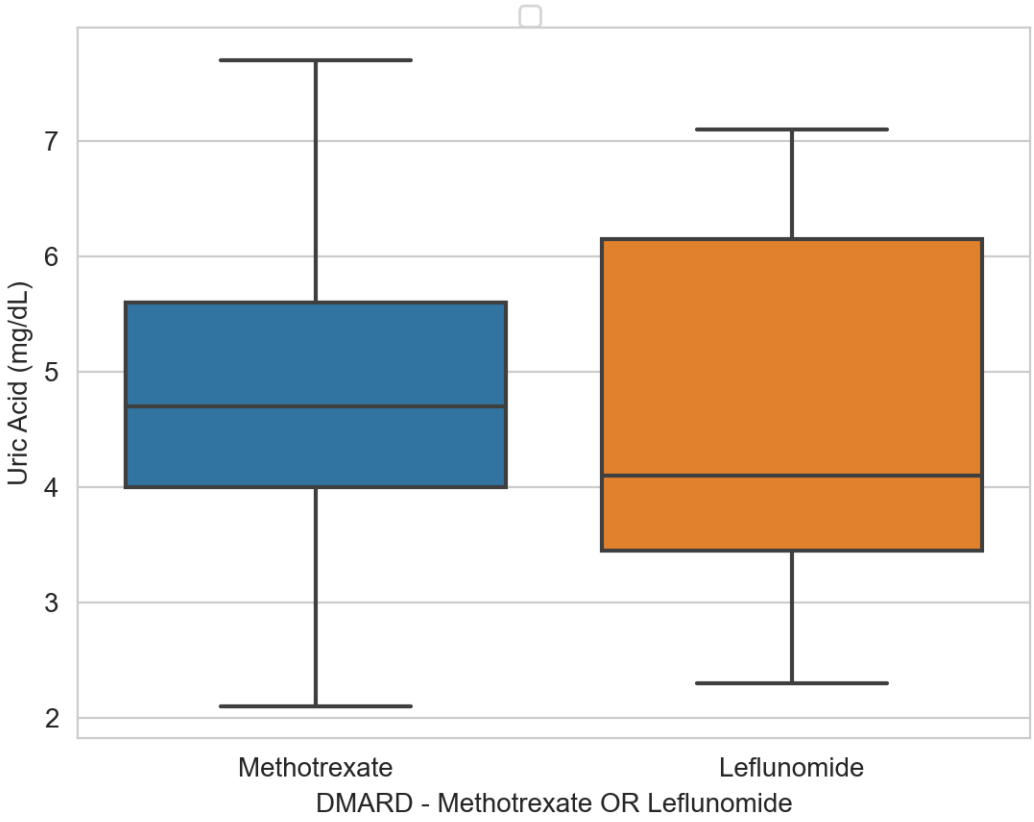
The subjects who were on Methotrexate had uric acid levels which ranged from a minimum value of 2.1 to a maximum of 7.7. The Median (IQR) was 4.7 (1.59) and the Mean ± Standard Deviation was 4.77 ± 1.22.

The Mann Whitney Test was used and no statistically significant difference was found between the groups (p Value 0.703).

Therefore, no significant difference (p value 0.703) in the uric acid levels were found between the groups taking either methotrexate (4.77 ± 1.22) or leflunomide (4.67 ± 1.6).

The same information is shown in the following table and figure.

		DMARD		P VALUE	TEST APPLIED
		Leflunomide	Methotrexate		
Uric Acid (mg/dL)	count	23.0	123.0	0.703	Mann Whitney Test; Test Statistic - 0.146
	mean	4.67	4.77		
	std	1.6	1.22		
	min	2.3	2.1		
	25%	3.45	4.0		
	50%	4.1	4.7		
	75%	6.15	5.6		
	max	7.1	7.7		


Uric Acid (mg/dL)
7
6
5
4
3
2
Methotrexate
Leflunomide
DMARD - Methotrexate OR Leflunomide

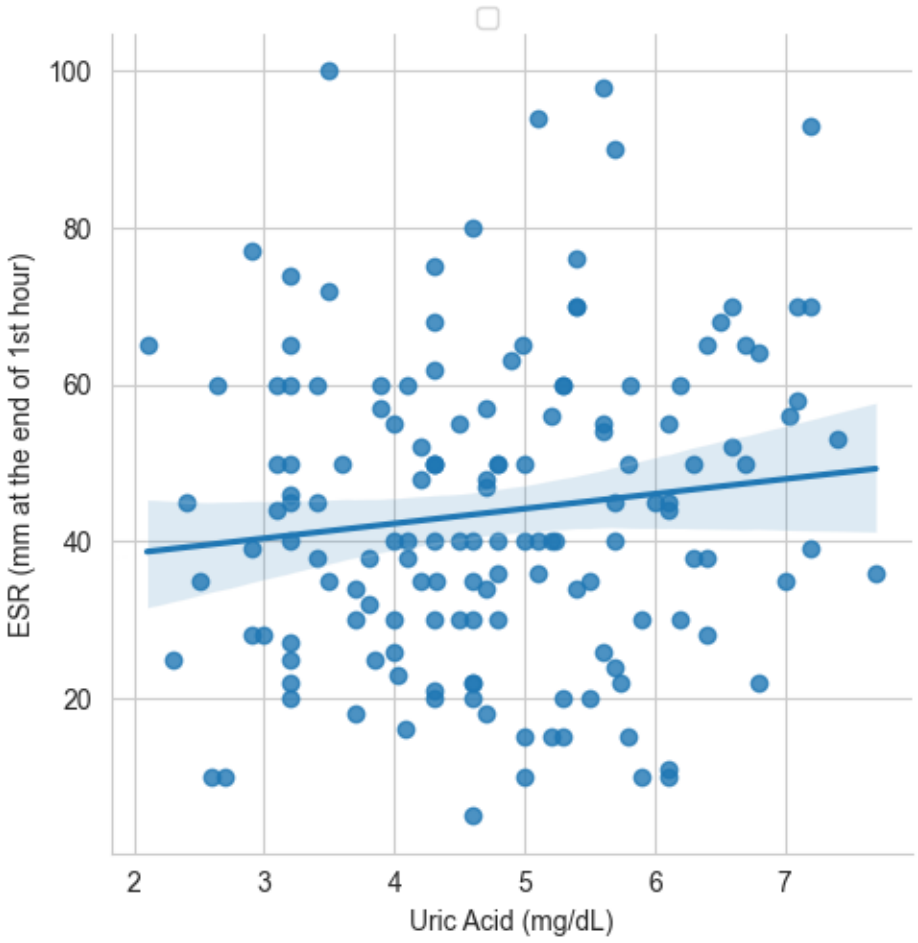
Uric Acid (mg/dL) VERSUS ESR (mm at the end of 1st hour)

A Spearman's rank-order correlation was run to determine the relationship between Uric acid and ESR. There was a positive correlation between the 2 variables which was not statistically significant (r = 0.111, p value 0.176).

Therefore, there was no significant correlation between the levels of uric acid and ESR in our subjects.

The same information is shown in the following table and figure.

	Uric Acid (mg/dL)	**ESR (mm at the end of 1st hour)**	**P VALUE**	**TEST APPLIED**
count	150.0	150.0	0.176	Spearman Rank Correlation; Test Statistic - 0.111
mean	4.76	43.73		
std	1.27	19.75		
min	2.1	5.0		
25%	3.86	30.0		
50%	4.7	40.0		
75%	5.7	57.0		
max	7.7	100.0		


ESR (mm at the end of 1st hour)
100
80
60
40
20
2
3
4
5
6
7
Uric Acid (mg/dL)

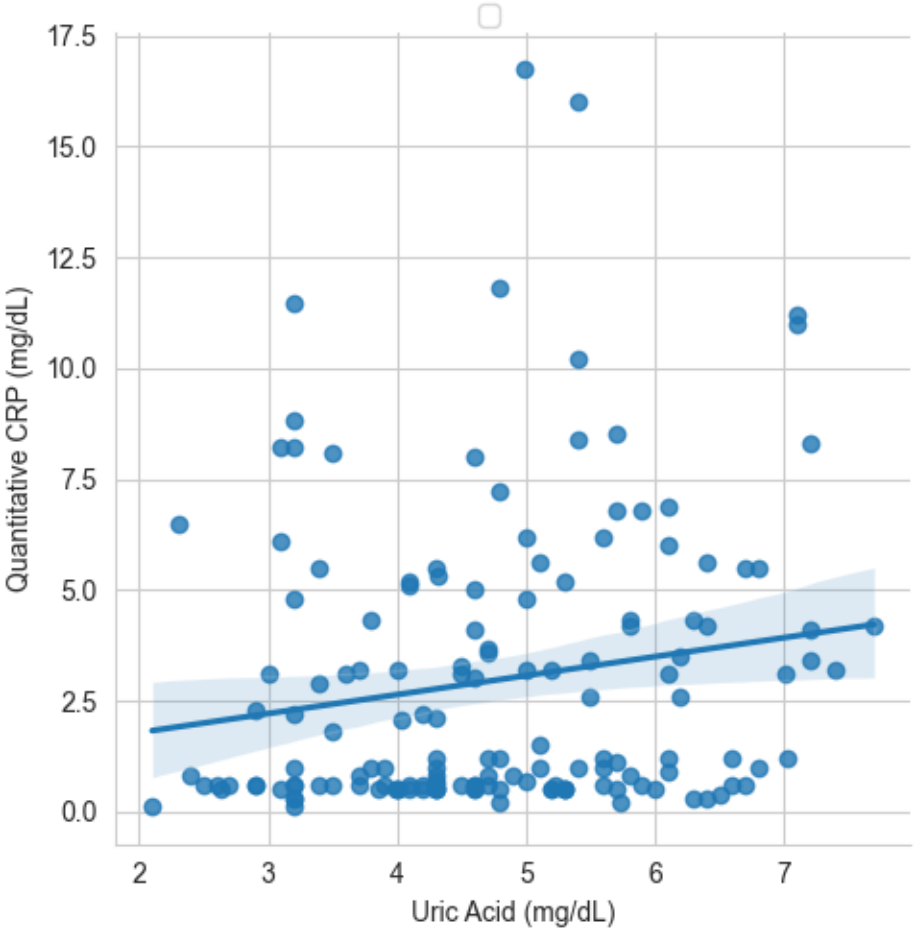
Uric Acid (mg/dL) VERSUS Quantitative CRP (mg/dL)

A Spearman's rank-order correlation was run to determine the relationship between Uric acid and CRP. There was a positive correlation between the 2 variables which was statistically significant (r = 0.203, p value 0.013).

Thus, as the qCRP levels increase, the uric acid levels also increase.

The same information is shown in the following table and figure.

	Uric Acid (mg/dL)	Quantitative CRP (mg/dL)	P VALUE	TEST APPLIED
count	150.0	150.0	0.013	Spearman Rank Correlation; Test Statistic - 0.203
mean	4.76	2.96		
std	1.27	3.23		
min	2.1	0.1		
25%	3.86	0.6		
50%	4.7	1.2		
75%	5.7	4.32		
max	7.7	16.75		


Quantitative CRP (mg/dL)
17.5
15.0
12.5
10.0
7.5
5.0
2.5
0.0
2
3
4
5
6
7
Uric Acid (mg/dL)

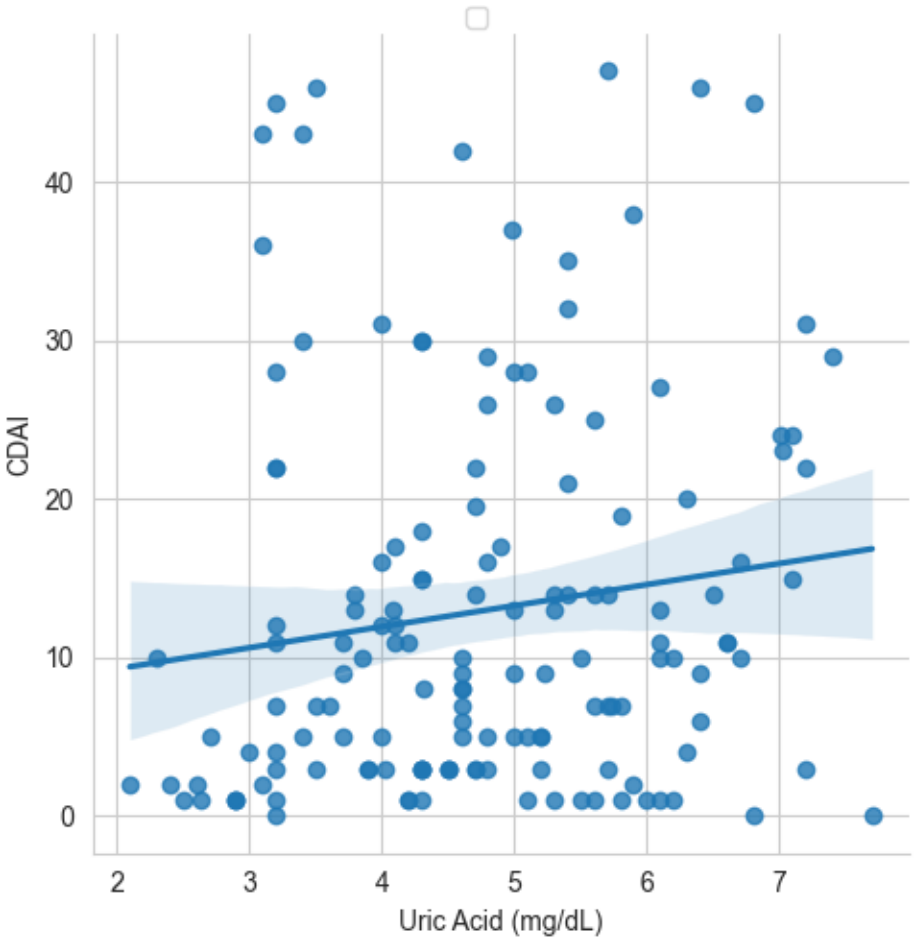
Uric Acid (mg/dL) VERSUS CDAI

A Spearman's rank-order correlation was run to determine the relationship between Uric acid and CDAI. There was a positive correlation between the 2 variables which was statistically significant (r = 0.177, p = 0.031).

Thus, as the clinical disease activity (as measured by CDAI) increases, the uric acid levels also increase.

The same information is shown in the following table and figure.

	Uric Acid (mg/dL)	**CDAI**	**P VALUE**	**TEST APPLIED**
count	150.0	150.0	0.031	Spearman Rank Correlation; Test Statistic - 0.177
mean	4.76	12.95		
std	1.27	12.1		
min	2.1	0.0		
25%	3.86	3.0		
50%	4.7	10.0		
75%	5.7	18.75		
max	7.7	47.0		


CDAI
40
30
20
10
0
2
3
4
5
6
7
Uric Acid (mg/dL)

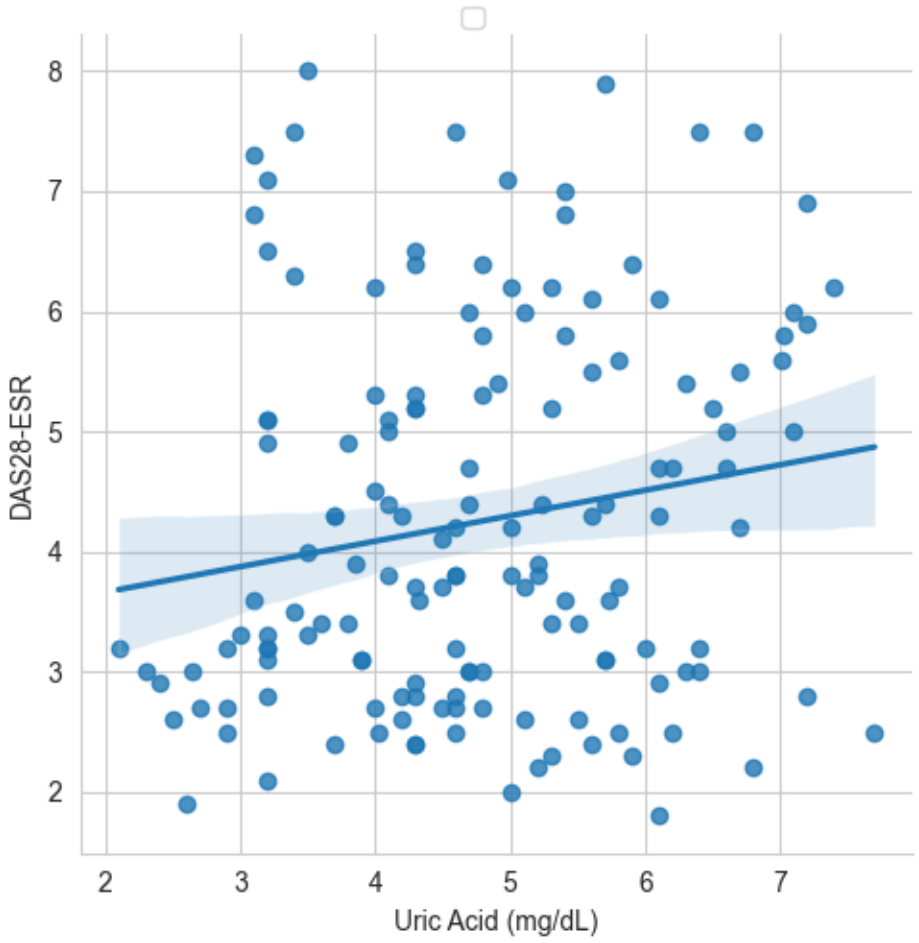
Uric Acid (mg/dL) VERSUS DAS28-ESR

A Spearman's rank-order correlation was run to determine the relationship between Uric acid and DAS28 ESR. There was a positive correlation between the 2 variables which was not statistically significant (r = 0.157, p value 0.055).

Thus, there is no significant change in the disease activity (as measured by DAS28 ESR) with uric acid levels.

The same information is shown in the following table and figure.

	Uric Acid (mg/dL)	DAS28-ESR	P VALUE	TEST APPLIED
count	150.0	150.0	0.055	Spearman Rank Correlation; Test Statistic - 0.157
mean	4.76	4.25		
std	1.27	1.56		
min	2.1	1.8		
25%	3.86	3.0		
50%	4.7	3.8		
75%	5.7	5.38		
max	7.7	8.0		


DAS28-ESR
Uric Acid (mg/dL)
8
7
6
5
4
3
2
2
3
4
5
6
7

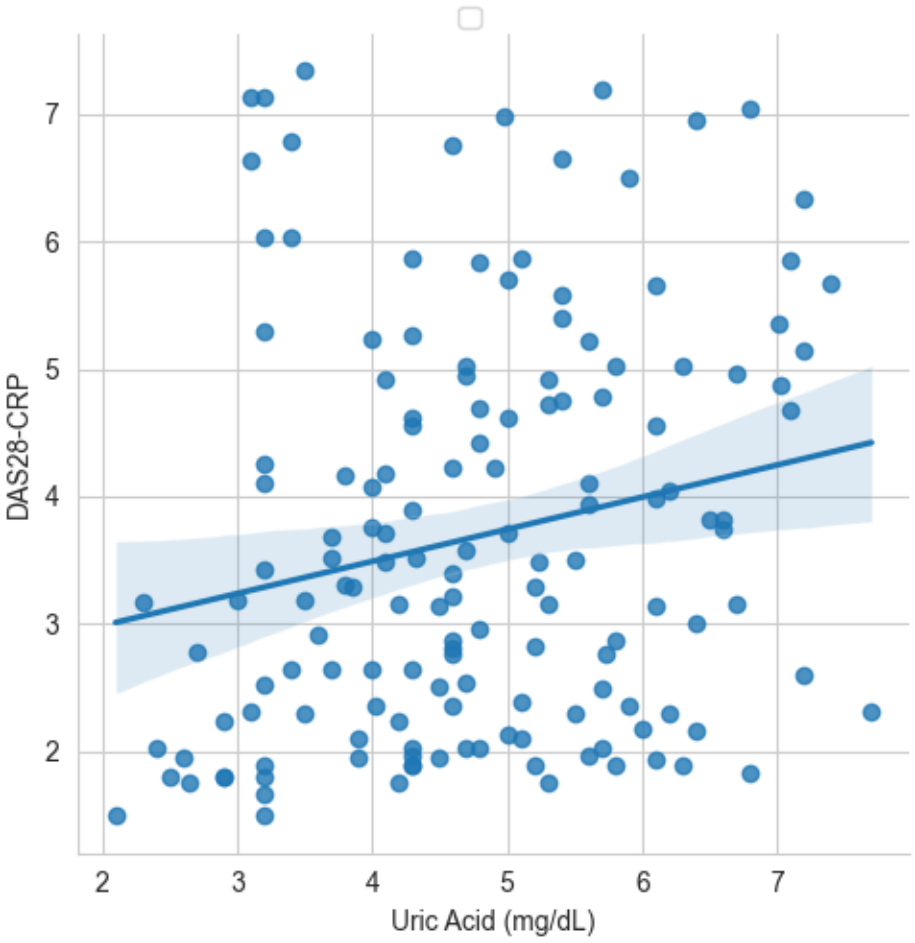
Uric Acid (mg/dL) VERSUS DAS28-CRP

A Spearman's rank-order correlation was run to determine the relationship between Uric acid and DAS28 CRP. There was a positive correlation between the 2 variables which was statistically significant (r = 0.221, p value 0.007).

Thus, as the disease activity (as measured by DAS28 CRP) increases, the uric acid levels also increase.

The same information is shown in the following table and figure.

	Uric Acid (mg/dL)	DAS28-CRP	P VALUE	TEST APPLIED
count	150.0	150.0	0.007	Spearman Rank Correlation; Test Statistic - 0.221
mean	4.76	3.68		
std	1.27	1.58		
min	2.1	1.49		
25%	3.86	2.3		
50%	4.7	3.35		
75%	5.7	4.86		
max	7.7	7.34		


DAS28-CRP
Uric Acid (mg/dL)
2
3
4
5
6
7

CDAI CLASS - Remission/Low Activity VS Moderate/High Activity VERSUS Uric Acid (mg/dL)

We wanted to study if there were any differences in the uric acid levels in subjects who had moderate or higher disease activity (CDAI) versus those in remission or low disease activity.

In the Moderate/High Disease Activity subjects, uric acid ranged from a minimum value of 3.1 to a maximum of 7.4. The Median (IQR) was 4.9 (1.81) and the Mean ± Standard Deviation was 5.0 ± 1.25.

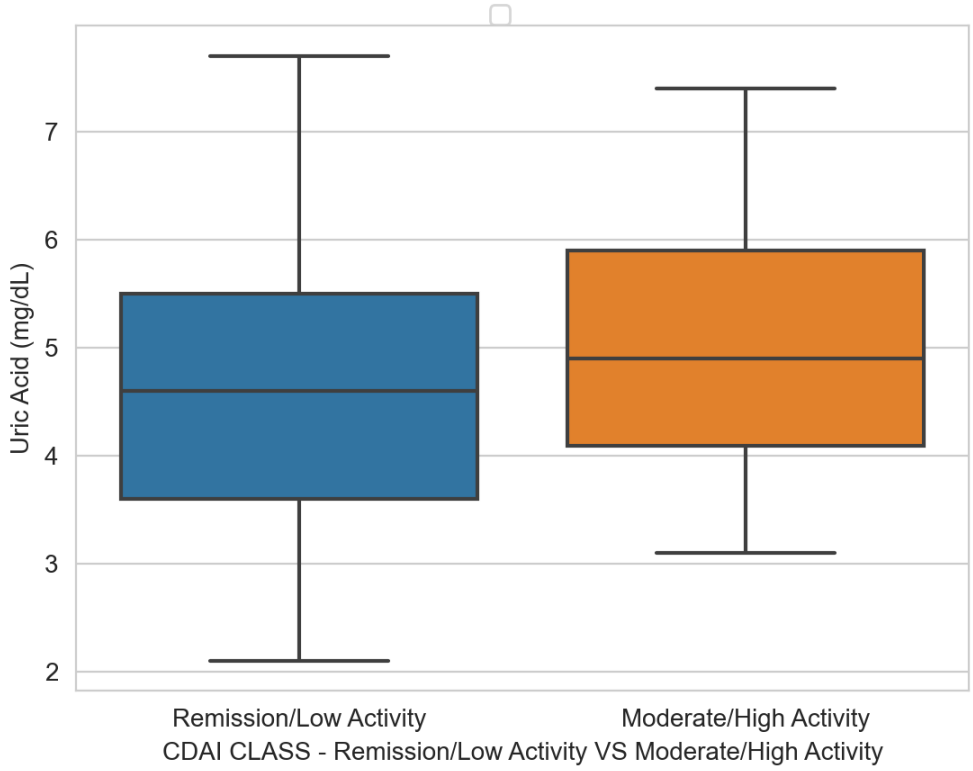
The subjects in Remission/Low Activity had comparatively lower uric acid levels ranging from a minimum value of 2.1 to a maximum of 7.7. The Median (IQR) was 4.6 (1.9) and the Mean ± Standard Deviation was 4.56 ± 1.26.

The Mann Whitney Test was used and no statistically significant difference was found between the groups (p Value 0.054).

Thus, there was no difference between uric acid levels of subjects who were in remission or low disease activity and those who had a moderate or high disease activity.

The same information is shown in the following table and figure.

		CDAI CLASS - Remission/Low Activity VS Moderate/High Activity		**P VALUE**	**TEST APPLIED**
		Moderate/High Activity	**Remission/Low Activity**		
Uric Acid (mg/dL)	count	69.0	81.0	0.054	Mann Whitney Test
	mean	5.0	4.56		
	std	1.25	1.26		
	min	3.1	2.1		
	25%	4.09	3.6		
	50%	4.9	4.6		
	75%	5.9	5.5		
	max	7.4	7.7		


Uric Acid (mg/dL)
7
6
5
4
3
2
Remission/Low Activity
Moderate/High Activity
CDAI CLASS - Remission/Low Activity VS Moderate/High Activity

DAS 28 ESR CLASS - Remission/Low Activity VS Moderate/High Activity VERSUS Uric Acid (mg/dL)

We calculated the DAS 28 ESR score for all our subjects. We wanted to study if there were any differences in the uric acid levels in subjects who had moderate or higher disease activity versus those in remission or low disease activity.

In the Moderate/High Disease Activity subjects, uric acid ranged from a minimum value of 3.0 to a maximum of 7.4. The Median (IQR) was 4.8 (1.70) and the Mean ± Standard Deviation was 4.9 ± 1.19.

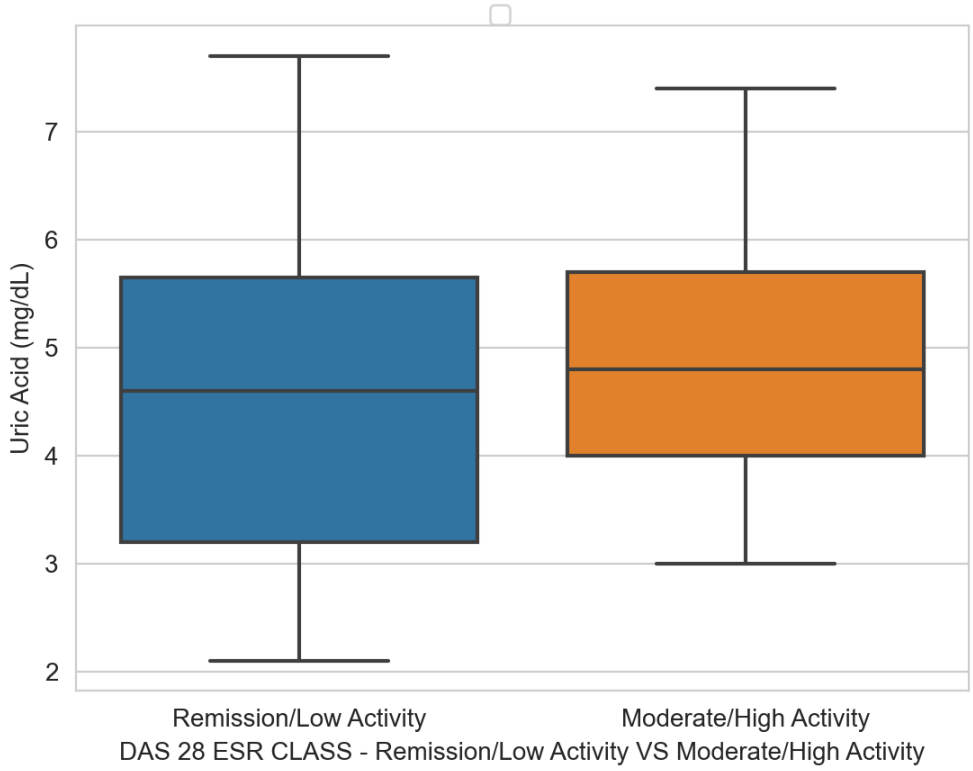
The subjects in Remission/Low Activity had comparatively lower uric acid levels ranging from a minimum value of 2.1 to a maximum of 7.7. The Median (IQR) was 4.6 (2.45) and the Mean ± Standard Deviation was 4.53 ± 1.37.

The Mann Whitney Test was used and no statistically significant difference was found between the groups (p Value 0.111).

Thus, there was no significant difference (p value 0.111) between uric acid levels of subjects who were in remission or low disease activity (4.53 ± 1.37) and those who had a moderate or high disease activity (4.9 ± 1.19.).

The same information is shown in the following table and figure.

		DAS 28 ESR CLASS - Remission/Low Activity VS Moderate/High Activity		**P VALUE**	**TEST APPLIED**
		Moderate/High Activity	**Remission/Low Activity**		
Uric Acid (mg/dL)	count	95.0	55.0	0.111	Mann Whitney Test
	mean	4.9	4.53		
	std	1.19	1.37		
	min	3.0	2.1		
	25%	4.0	3.2		
	50%	4.8	4.6		
	75%	5.7	5.65		
	max	7.4	7.7		


Uric Acid (mg/dL)
7
6
5
4
3
2
Remission/Low Activity
Moderate/High Activity
DAS 28 ESR CLASS - Remission/Low Activity VS Moderate/High Activity

DAS 28 CRP CLASS - - Remission/Low Activity VS Moderate/High Activity VERSUS Uric Acid (mg/dL)

We calculated the DAS 28 CRP score for all our subjects. We wanted to study if there were any differences in the uric acid levels in subjects who had moderate or higher disease activity versus those in remission or low disease activity.

In the Moderate/High Disease Activity subjects, uric acid ranged from a minimum value of 3.1 to a maximum of 7.4. The Median (IQR) was 4.9 (1.66) and the Mean ± Standard Deviation was 4.99 ± 1.19.

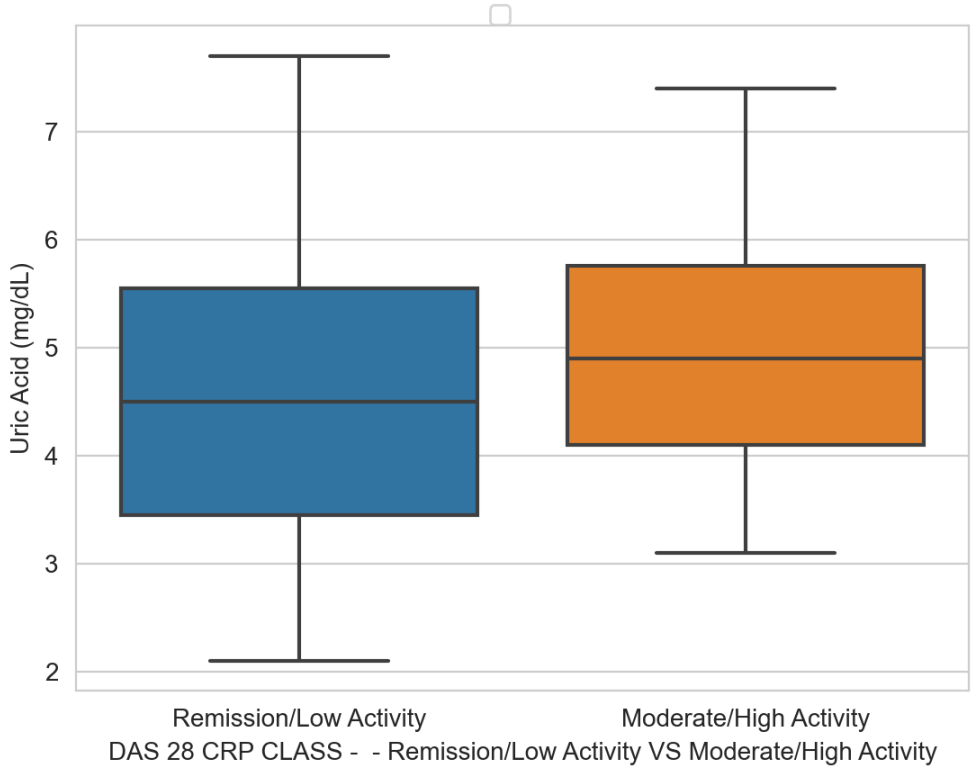
The subjects in Remission/Low Activity had comparatively lower uric acid levels ranging from a minimum value of 2.1 to a maximum of 7.7. The Median (IQR) was 4.5 (2.09) and the Mean ± Standard Deviation was 4.51 ± 1.31.

The Mann Whitney Test was used and a statistically significant difference was found between the groups (p Value 0.029).

Thus, the subjects who were having a moderate or high disease activity had significantly higher levels of uric acid as compared to subjects who were in remission or low disease activity.

The same information is shown in the following table and figure.

		DAS 28 CRP CLASS - - Remission/Low Activity VS Moderate/High Activity		**P VALUE**	**TEST APPLIED**
		Moderate/High Activity	**Remission/Low Activity**		
Uric Acid (mg/dL)	count	79.0	71.0	0.029	Mann Whitney Test
	mean	4.99	4.51		
	std	1.19	1.31		
	min	3.1	2.1		
	25%	4.1	3.45		
	50%	4.9	4.5		
	75%	5.76	5.55		
	max	7.4	7.7		


Uric Acid (mg/dL)
7
6
5
4
3
2
Remission/Low Activity
Moderate/High Activity
DAS 28 CRP CLASS - - Remission/Low Activity VS Moderate/High Activity