A Comparative Study of Serum and Synovial Fluid Levels of Uric Acid between Patients with Gout and Other Arthritides

Suparaporn Wangkaew MD*, Nuntana Kasitanon MD*,
Sith Hongsongkiat MD*, Chaiyut Tanasombat BSc**,
Waraporn Sukittawut BSc*, Worawit Louthrenoo MD*

** Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand*
*** Division of Clinical Chemistry Laboratory, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand*

Background: *The urate levels and the correlations of urate levels between the serum and synovial fluid (SF) of many arthritic diseases have not been well described.*
Objective: *Compare urate levels in the serum and SF of gouty arthritis, calcium pyrophosphate dihydrate deposition disease (CPPD), rheumatoid arthritis (RA), septic arthritis, ankylosing spondylitis (AS), and osteoarthritis (OA) patients.*
Material and Method: *Paired samples of serum and SF from 95 patients comprised of 33 patients with gout, 22 with CPPD, 18 with RA, nine with septic arthritis, three with AS, and 10 with OA were collected simultaneously for urate measurement by photometric test.*
Results: *Ninety-five patients, including 53 males, with mean (SD) age of 64.1(15.3) years were recruited. In gout, serum and SF urate levels were significantly higher than those of CPPD, RA, septic arthritis, AS, and OA ($p<0.01$). In all the study population, the serum/SF ratios of urate levels of gout were not different across all groups. However, after excluding 24 patients with creatinine >1.5 mg/dl, the serum/SF ratios of urate were significantly lower in gout compared with the others ($p = 0.02$). There were strongly positive correlations between serum and SF urate levels in gout similar to CPPD, RA, septic arthritis, AS, and OA ($r = 0.81$-0.91, $p<0.01$).*
Conclusion: *Despite the highest level of serum and SF urate across all groups, the serum/SF urate ratio in gout patients was the lowest, which suggests that SF urate levels are uniquely higher than their serum. In addition, the levels of serum urate of the entire groups strongly reflect their SF levels.*

Keywords: *Synovial fluid, Urate, Uric acid*

J Med Assoc Thai 2014; 97 (7): 679-85
Full text. e-Journal: *http://www.jmatonline.com*

The synovial membrane permits urate and other small molecules to pass freely through the double barrier of endothelium and interstitium into the synovial fluid (SF)[1-4], which, as a result, can be considered as a dialysate of blood plasma[1]. The concentration of small molecules in the SF is dependent on many factors, including the synovial permeability, coexistence of other substances, intrasynovial volume, and lymphatic or tissue clearance[3-7].

To date, previous studies on serum and SF urate levels in gout and other arthritis diseases have not yet been settled. Beutler et al[8], for instance, reported that SF urate levels tend to reflect serum levels in gout and non-inflammatory arthropathies but not in inflammatory joint disease; in other studies, Rozin et al[9] found a negative serum-synovial gradient (SSG) of urate in normouricemic patients with a history of gout. Simkin et al[10] reported that rheumatoid synovium is less permeable to uric acid than in the normal knee joint. The relationship of uric acid concentrations in SF and serum have been reported in patients with RA, juvenile RA and psoriatic arthritis[11].

As the data comprised of urate levels and the correlations of urate levels between the serum and SF of many arthritic diseases, to our knowledge, have not been well described. The present study aims to compare the levels of urate in six groups of patients with different joint disorders (gout, CPPD, RA, septic arthritis, AS and OA), to determine their serum/SF ratio

Correspondence to:
Wangkaew S, Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand.
Phone: 053-946-449, Fax: 053-357-959
E-mail: suparaporn.w@cmu.ac.th

of urate, and to evaluate the correlations of their urate levels in paired serum and SF.

Material and Method

The present prospective cross-sectional study was conducted at the Division of Rheumatology, Chiang Mai University Hospital between September 2010 and January 2012. The study recruited all patients developing arthritis with available joint effusion for arthrocentesis, diagnosed with either of the following definitions: 1) gouty arthritis is defined as presence of monosodium urate crystal in SF determined by compensated polarized light (PL) microscopy with negative SF culture and negative chondrocalcinosis on X-ray; 2) calcium pyrophosphate dihydrate (CPPD) deposition disease, as presence of CPPD crystal in SF determined by PL microscopy with negative SF culture and positive chondrocalcinosis on X-ray; 3) septic arthritis, as having positive SF Gram staining or SF culture; 4) osteoarthritis (OA), as having degenerative changes of the knee joint and negative chondrocalcinosis on X-ray; 5) rheumatoid arthritis (RA) is defined according to the 1987 ACR classification criteria for RA[12]; and 6) ankylosing spondylitis (AS), according to the 1984 modified New York classification criteria for AS[13].

All participants were older than 18 years and able to provide informed consent. Patients developing more than one joint disease (such as combined gouty arthritis with CPPD), or receiving an intra-articular corticosteroid injection during the past three months prior to the study were excluded. Paired serum and SF samples of the study patients were simultaneously collected for urate measurement.

The present study was conducted according to the principles of the Declaration of Helsinki and all the participants gave written informed consent. The study received ethics approval from the Research Ethics Committee of the Faculty of Medicine, Chiang Mai University.

Synovial fluid and serum samples

Blood samples were collected from the patients in EDTA tubes, and then centrifuged. Hitachi-917 automated analyzer (Tokyo, Japan) was used to determine urate levels in the serum by using standard photometric methods.

As the easiest aspirated site, arthrocentesis was also performed at the markedly swelling and the SF samples were collected in heparinized tubes, to examine automated leukocyte count and perform crystal identification by using PL microscopy. After centrifuged at 3,000 rpm for ten minutes, the supernatant was used for urate determination by the photometric method using Hitachi-917 automated analyzer. Both blood samples and their simultaneous SF were analyzed within four hours after obtaining specimens from each patient.

Statistical analysis

Statistical analysis was performed by SPSS software (version 16.0; Chicago, Illinois). Data were expressed as percentage, mean (SD), or median (IQR), where appropriate. Categorical variables and continuous variables in the six groups of patients were compared using the Fisher's exact test and Kruskal-Wallis test, respectively. Spearman's rank correlation coefficient (r value) was used to obtain the correlations of serum with SF levels of urate in each group of the arthropathies. All tests were 2-tailed, and p-values <0.05 were considered significant.

Results

Patients' characteristics

The present study included 95 arthritic patients, consisting of 33 patients with gouty arthritis, 22 patients with CPPD arthritis, 18 patients with RA, nine patients with septic arthritis [two *Salmonella* spp., two *Staphylococcus aureus*, one *Streptococcus agalactiae*, one *Klebsiella pneumonia*, one *Escherichia coli*, one *Penicillium marneffei*, one *Mycobacterium tuberculosis*], three patients with AS, and 10 patients with OA. The 95 SF samples were obtained from 87 (91.5%) knees, five (5.3%) ankles, two (2.1%) elbows, and one (1.1%) shoulder joint.

Demographic and clinical characteristics of the study population were shown in Table 1. The median (interquartile rage: IQR [Q1, Q3]) disease duration of patients with RA, AS, and OA were 3.3 (1.0, 6.5), 5.0 (0.0, 13.0), and 3.0 (2.0, 10.0) years, respectively. All patients with gout and CPPD were firstly diagnosed by the presence of crystal in SF at the date of study entry. There were significant differences of data including demographic data, NSAIDS used, and albumin levels across all the groups ($p<0.01$). Patients with gout had the highest proportion of chronic renal failure. Therefore, serum creatinine (cr) levels in gout patients were significantly higher than CPPD, RA, septic arthritis, AS and OA patients ($p<0.01$). Synovial fluid-leukocytes in non-inflammatory joint diseases (OA) was significantly

Table 1. Characteristics of 95 patients with different joint disorders

	Gout (n = 33)	CPPD (n = 22)	RA (n = 18)	Septic (n = 9)	AS (n = 3)	OA (n = 10)
Demographic						
Age[a], years	65.4 (14.8)	77.0 (7.2)	56.5 (8.6)	48.9 (18.9)	39.7 (4.5)	66.1 (10.5)
Male[b], n (%)	29 (87.9)	6 (27.3)	5 (27.8)	4 (44.4)	3 (100)	6 (60.0)
Arthritic duration before arthrocentesis[a], days	2.0 (1.0, 5.0)	3.0 (1.0, 10.0)	25.0 (7.0, 96.5)	6.0 (3.0, 15.0)	7.0 (7.0, 151.0)	31.0 (9.0, 33.7)
Comorbid disease, n (%)						
Hypertension	11 (33.3)	12 (54.5)	5 (27.8)	3 (33.3)	0	4 (40.0)
Dyslipidemia	6 (18.2)	5 (22.7)	2 (11.1)	3 (33.3)	0	4 (40.0)
Diabetes mellitus	6 (18.2)	5 (22.7)	0	2 (22.2)	0	1 (10.0)
Chronic renal failure[b]	13 (39.4)	4 (18.2)	0	0	1 (11.1)	0
Current medications, n (%)						
Aspirin	8 (24.2)	7 (31.8)	1 (5.6)	0	0	1 (10.0)
Diuretic	10 (30.3)	2 (9.1)	1 (5.6)	0	0	0
NSAIDs[b]	1 (3.0)	22 (100)	13 (72.2)	2 (22.2)	3 (100)	4 (40.0)
Allopurinol	5 (15.2)	0	0	0	0	0
Lab						
Hemoglobin, g/dl	10.5 (2.3)	10.7 (1.4)	10.9 (1.5)	9.4 (1.4)	11.9 (1.0)	11.4 (1.8)
Creatinine[a], mg/dl	3.1 (3.9)	1.2 (0.5)	0.8 (0.2)	0.9 (0.6)	0.9 (0.1)	1.2 (0.7)
Albumin[a], g/dl	2.8 (0.6)	2.8 (0.7)	3.3 (0.7)	2.2 (0.5)	2.5 (0.6)	3.5 (0.8)
AST, U/L	34.7 (20.8)	40.0 (30.0)	25.1 (13.4)	34.1 (16.2)	34.0 (9.5)	23.0 (10.9)
ALT, U/L	32.7 (33.5)	22.8 (20.2)	18.7 (8.7)	33.7 (29.9)	69.3 (24.1)	26.5 (23.3)
SF wbc[a]/mm^3	16,620 (5,441.2, 47,360)	21,340 (4,640, 37,480)	24,925 (4,472, 49,200)	58,700 (25,560, 111,545)	15,220 (14,920, 50,250)	105 (75, 625)

CPPD = calcium pyrophosphate dihydrate deposition disease; RA = rheumatoid arthritis; Septic = septic arthritis; AS = ankylosing spondylitis; OA = osteoarthritis; NSAIDs = nonsteroidal anti-inflammatory drugs; AST = aspartate aminotransferase; ALT = alanine aminotransferase; SF = synovial fluid; wbc = white blood cell
Continuous variables are mean (SD), median (IQR [Q1, Q3])
p-value from Kruskal-Wallis test: [a] $p<0.01$, *p*-value from Fisher's exact test: [b] $p<0.01$

lower than that of inflammatory joint diseases (gout, CPPD, RA, septic arthritis and AS) (p<0.01).

Serum and SF levels and serum/SF ratios of urate

The serum and SF fluid levels of urate and the serum/SF ratios of urate of the 95 participants were shown in Table 2. Obviously, the gout patients had the highest levels of urate in serum and SF compared with those of other groups (p<0.01). However, when compared with the serum/SF ratios of urate levels across all groups, the serum/SF ratios of urate levels of gout patients were not significantly different (p = 0.07).

To eliminate the influence of renal dysfunction resulted in developing high uric acid level, the study excluded 24 patients with serum creatinine >1.5 mg/dl, as shown in Table 3. Even when compared among the remaining patients (71 patients in total), both results of the serum and SF and the serum/SF ratios of urate of patients with gout remained the same, as in Table 2. However, the serum/SF ratio of urate of patients with gout showed significantly lower compared to the other joint disorders (p = 0.02).

Correlations between serum and SF levels of urate

Table 4 showed strongly positive correlations of urate levels between paired samples of serum and SF across all groups (r = 0.81-0.91, p<0.01). Ankylosing spondylitis group was excluded due to small sample size.

Discussion

The present data demonstrated that the urate levels in serum and SF of gout patients were higher while their serum/SF ratios of urate were lower than those in patients with CPPD, RA, septic arthritis AS and OA. This was consistent with Rozin et al[9] who had studied serum-synovial gradient (SSG) of urate in six normouricemic patients with history of gout and found three patients with negative SSG, reflecting that gout patients had higher levels of urate in SF than serum. Similarly, Tiliakos et al[14] reported that SF urate concentration of acute gouty arthritis was higher than serum and gradually equalized to the serum when the arthritis subsided. They also reported that total joint fluid urate was associated with gouty activity. This may explain our finding that all 33 gouty arthritis

Table 2. Serum and synovial fluid (SF) levels of urate in all study population

	Gout (n = 33)	CPPD (n = 22)	RA (n = 18)	Septic (n = 9)	AS (n = 3)	OA (n = 10)	p-value
Serum UA, mg/dl	7.9 (2.1)	5.8 (2.2)	4.9 (0.8)	4.1 (2.4)	4.1 (0.6)	6.2 (1.7)	<0.01
SF UA, mg/dl	8.1 (2.1)	5.6 (2.3)	4.8 (0.8)	3.7 (2.4)	3.7 (0.5)	6.0 (1.7)	<0.01
Serum/SF ratio of UA	0.9 (0.1)	1.1 (0.3)	1.0 (0.1)	1.2 (0.3)	1.1 (0.1)	1.0 (0.1)	0.07

UA = uric acid
Values are mean (SD), p-value from Kruskal-Wallis test

Table 3. Serum and synovial fluid (SF) levels of urate in 71 study population (serum creatinine ≤1.5 mg/dl)

	Gout (n = 16)	CPPD (n = 17)	RA (n = 18)	Septic (n = 8)	AS (n = 3)	OA (n = 9)	p-value
Serum UA, mg/dl	6.7 (1.6)	5.4 (2.2)	4.9 (0.8)	3.4 (1.5)	4.1 (0.6)	6.1 (1.7)	<0.01
SF UA, mg/dl	7.1 (1.6)	5.2 (2.0)	4.8 (0.8)	3.0 (1.3)	3.7 (0.5)	5.9 (1.8)	<0.01
Serum/SF ratio of UA	0.9 (0.1)	1.1 (0.3)	1.0 (0.1)	1.2 (0.3)	1.1 (0.1)	1.0 (0.1)	0.02

UA = uric acid
Values are mean (SD), p-value from Kruskal-Wallis test

Table 4. Spearman's rank correlation coefficients between serum and SF concentrations of urate in the different joint diseases

Serum vs. SF levels	Correlation coefficients (r)				
	Gout (n = 33)	CPPD (n = 22)	RA (n = 18)	Septic (n = 9)	OA (n = 10)
Urate	0.90[a]	0.90[a]	0.82[a]	0.91[a]	0.81[a]

[a] p<0.01

patients with acute attack had the lowest serum/SF ratios of urate compared to the other arthritides. To our knowledge, the data regarding urate levels in serum and SF, as well as their serum/SF ratio of patients with CPPD, RA, septic arthritis, AS, and OA were limited.

Interestingly, we also found strongly positive correlations (r = 0.81-0.91, $p<0.01$) of urate levels between paired samples of serum and SF in all groups of our study patients. This was similar to GudbjÖrnsson et al[11] who had found a strong correlation (r = 0.76, $p<0.01$) of urate levels in serum and SF of inflammatory arthritis patients (12 RA, 4 psoriatic arthritis, 2 juvenile RA). The strong correlation of the paired samples of serum and SF levels of copper, magnesium, cesium, lithium, rubidium, and strontium have been reported in patients with OA[15]. However, to our knowledge, the data regarding the correlation of serum with SF urate levels in patients with OA are limited.

The strong correlations of the paired samples of serum and SF urate levels of the patients with both inflammatory and non-inflammatory arthritis in our study revealed no significant differences, reflecting that synovial membrane permits urate molecules to diffuse freely into synovial cavity and was largely not depended on the inflammation consistent with previous data[1-3]. This may support the previous data that SF can be considered as a dialysate of plasma urate[1].

Beutler et al[8] reported that SF urate levels tend to reflect serum levels in patients with gout and non-inflammatory arthropathies but not with inflammatory joint disorders. Such contradictory from our findings might be resulted from different study population and study design.

Regarding the higher cr level in gout patients than that of the other groups, which might result in higher serum urate levels, we excluded 24 patients with serum cr >1.5 mg/dl but also found that the serum and SF urate levels in gout patients were still significantly higher than those in other patients with CPPD, RA, septic arthritis, AS and OA patients. However, the serum/SF ratio of urate in gout patients became significantly lower ($p = 0.02$). Without patients having renal dysfunction, the urate level was lower across all groups, which may explain the change.

The limitation of the present study was small sample size in the septic arthritis and AS groups, with nine and three patients, respectively. In addition, many different factors across the groups including age, gender, comorbidities, and current medications could influence the levels of urate in serum and SF. Hence, further study comparing larger groups of different arthritic diseases matched for age, gender, comorbid disease, and current medications needs to be performed to confirm our findings.

However, the strength of the present study is that the authors provide the extensive data on urate levels in serum, SF levels, and the serum/SF ratios of urate as well as the correlations of their levels in paired samples of serum and SF of patients with inflammatory arthritis (33 gout, 22 CPPD, 18 RA, nine septic arthritis and three AS) and non-inflammatory arthritis (10 OA). The present study found that acute gouty arthritis patients had the lowest serum/SF ratios of urate compare to those of the other arthritis, reflecting higher urate accumulation in gouty SF, which should be deserved for further evaluation of its clinical implication.

Conclusion

We demonstrated that despite the highest level of serum and SF urate across all groups, the serum/SF urate ratio in gout patients alone was the lowest, which suggested that gouty SF urate levels were uniquely higher than their serum. In addition, the levels of urate of the entire group (gout, CPPD, RA, septic arthritis, AS, and OA) strongly reflect their SF levels.

What is already known in this topic?

SF can be considered as a dialysate of blood plasma because synovial membrane permits urate and other small molecules to pass freely through its endothelium and interstitium barrier into the SF[1-3]. However, the data of previous studies comprised of urate levels and the correlations of urate levels between the serum and SF of many arthritic diseases have not yet been well described.

What this study adds?

In patients with gout, serum and SF urate levels were significantly higher than that of CPPD, RA, septic arthritis, AS, and OA. The serum/SF urate ratio in gout patients alone was the lowest, which suggested that gouty SF urate levels were uniquely higher than their serum. Our finding that gout patients had the lowest serum/SF ratios of urate compare to those of the other arthritis, reflecting higher urate accumulation in gouty SF, should be deserved for further evaluation of its clinical implication.

Acknowledgement

The present study received the grant support from Faculty of Medicine, Chiang Mai University Endowment Fund.

Potential conflicts of interest

None.

References

1. Gatter RA, Schumacher HR. A practical handbook of joint fluid analysis. 2nd ed. Philadelphia: Lea & Febiger; 1991.
2. Seegmiller JE. Serum uric acid. In: Cohen AS, editor. Laboratory diagnostic procedures in the rheumatic diseases. Boston: Little, Brown and Company; 1975: 222.
3. Simkin PA, Pizzorno JE. Transynovial exchange of small molecules in normal human subjects. J Appl Physiol 1974; 36: 581-7.
4. Simkin PA. Synovial perfusion and synovial fluid solutes. Ann Rheum Dis 1995; 54: 424-8.
5. Harris R, Millard JB. Clearance of radioactive sodium from the knee joint. Clin Sci (Lond) 1956; 15: 9-15.
6. Levick JR. Permeability of rheumatoid and normal human synovium to specific plasma proteins. Arthritis Rheum 1981; 24: 1550-60.
7. Wallis WJ, Simkin PA, Nelp WB, Foster DM. Intraarticular volume and clearance in human synovial effusions. Arthritis Rheum 1985; 28: 441-9.
8. Beutler AM, Keenan GF, Soloway S, Norden D, Luchi M, Schumacher HR Jr. Soluble urate in sera and synovial fluids from patients with different joint disorders. Clin Exp Rheumatol 1996; 14: 249-54.
9. Rozin AP, Braun-Moscovici Y, Balbir-Gurman A. Serum-synovial gradient data of normouricemic patients with history of gout and acute knee effusion. Clin Rheumatol 2006; 25: 886-8.
10. Simkin PA. Synovial permeability in rheumatoid arthritis. Arthritis Rheum 1979; 22: 689-96.
11. Gudbjornsson B, Zak A, Niklasson F, Hallgren R. Hypoxanthine, xanthine, and urate in synovial fluid from patients with inflammatory arthritides. Ann Rheum Dis 1991; 50: 669-72.
12. Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988; 31: 315-24.
13. van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum 1984; 27: 361-8.
14. Tiliakos AN, Tiliakos NA. Total joint fluid urate in gout. J Clin Rheumatol 2004; 10: 250-1.
15. Krachler M, Domej W, Irgolic KJ. Concentrations of trace elements in osteoarthritic knee-joint effusions. Biol Trace Elem Res 2000; 75: 253-63.

การศึกษาเปรียบเทียบระดับกรดยูริกในซีรัมและในน้ำไขข้อระหว่างผู้ป่วยโรคเกาต์และโรคข้ออักเสบชนิดอื่น ๆ

ศุภราภรณ์ วังแก้ว, นันทนา กสิตานนท์, สิทธิ์ หงษ์ทรงเกียรติ, ชัยยุทธ ธนะสมบัติ, วราพร สุชิตาวุธ, วรวิทย์ เลาห์เรณู

ภูมิหลัง: ข้อมูลการศึกษาเรื่องระดับกรดยูริกและความสัมพันธ์ระหว่างระดับกรดยูริกในซีรัมและในน้ำไขข้อของโรคข้ออักเสบชนิดต่าง ๆ นั้นยังมีไม่มาก

วัสดุและวิธีการ: การศึกษานี้ได้ทำการเจาะตรวจระดับกรดยูริกในซีรัมและในน้ำไขข้อของผู้ป่วย 95 ราย ประกอบด้วย โรคเกาต์ 33 ราย โรคข้ออักเสบ CPPD 22 ราย โรคข้ออักเสบรูมาตอยด์ 18 ราย โรคข้ออักเสบติดเชื้อ 9 ราย โรคข้ออักเสบกระดูกสันหลังติดยึด 3 ราย และโรคข้อเข่าเสื่อม 10 ราย แล้วตรวจวัดระดับกรดยูริกวัดโดยวิธี photometric

ผลการศึกษา: มีผู้เข้าร่วมการศึกษาทั้งหมดจำนวน 95 ราย (เพศชาย 53 ราย) มีค่าอายุเฉลี่ย (ค่าเบี่ยงเบนมาตรฐาน) 64.1 (15.3) ปี พบว่าผู้ป่วยโรคเกาต์มีระดับกรดยูริกในซีรัมและในน้ำไขข้อสูงกว่าโรคข้ออักเสบอื่นอย่างมีนัยสำคัญทางสถิติ ($p<0.01$) สัดส่วน serum/SF ของกรดยูริกมีระดับไม่แตกต่างกันในผู้ป่วยทั้ง 95 ราย แต่เมื่อคัดผู้ป่วย 24 ราย ที่มีระดับ creatinine >1.5 mg/dl ออก พบค่าสัดส่วน serum/SF ของกรดยูริกในผู้ป่วยโรคเกาต์ต่ำกว่าผู้ป่วยโรคข้ออื่นอย่างมีนัยสำคัญทางสถิติ ($p = 0.02$) นอกจากนี้ พบว่าระดับกรดยูริกในซีรัมมีความสัมพันธ์เชิงบวกกับระดับกรดยูกริกในน้ำไขข้อสูงมาก ($r = 0.81$-0.91, $p<0.01$) คล้ายกันในทุกกลุ่มโรค

สรุป: ผู้ป่วยโรคเกาต์มีระดับกรดยูริกในซีรัมและในน้ำไขข้อสูงกว่าโรคข้ออักเสบกลุ่มอื่น แต่มีค่าสัดส่วน serum/SF ของกรดยูริกต่ำที่สุด ซึ่งบ่งชี้ว่าโรคเกาต์มีระดับกรดยูริกในน้ำไขข้อสูงกว่าในซีรัมแตกต่างจากโรคอื่น และพบว่าระดับกรดยูริกในซีรัมมีความสัมพันธ์กับระดับกรดยูริกในน้ำไขข้อสูงมากในทุกกลุ่มโรคข้อที่ศึกษา