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## Sonographic Evaluation of the Relationship between Rheumatoid Arthritis and Renal Stones

**Background/Objectives:** Considering the different renal manifestations of rheumatoid arthritis (RA), we carried out this study to investigate the prevalence of renal stones in patients with RA compared to general population.

**Patients and Methods:** From January 2000 to March 2001, 74 patients with RA and 58 healthy individuals as the control group were evaluated for kidney stones with sonography. All patients were diagnosed on the basis of 1987 criteria of American College of Rheumatology (ACR).<sup>1</sup>

**Results:** In the group of patients with RA, 6 out of 74 subjects (8.1%) had renal stones. The prevalence of renal stones in the control group was 8.6% (5 out of 58 persons). The difference in the incidence of renal stones in the two groups was not statistically significant. The size of renal stones in the two groups was not significantly different. We did not find any relationship between the duration of RA or its various symptoms and the incidence of renal stones.

**Conclusion:** Although RA involves kidneys and in previous studies it was mentioned that the incidence of renal stones in the patients with RA is higher than general population, we did not find any significant statistical correlation between RA and the incidence of renal stones in our study.

**Keywords:** rheumatoid arthritis, renal stone, kidney, ultrasound

### Introduction

Rheumatoid arthritis (RA) is a common autoimmune disease with different clinical aspects and a wide range of debilitating complications. This disease is a common cause of chronic disability.<sup>1</sup> The cornerstone of treatment is adjusting the immune responses. An important aspect in treatment of such patients, however, is the symptomatic relief, which requires understanding of different etiopathologies and complications of this disease. Therefore, it is obvious that a good knowledge of the complications of RA has a major impact over the treatment outcome.<sup>1</sup>

Kidney involvement in RA is common due to longterm use of NSAIDs. This complication worsens the clinical course of the disease and increases patient mortality in the long run.<sup>2, 3</sup> Reviewing previous articles on renal complications in RA, we found out that the relationship between the disease process and the incidence of renal stones was still unclear; so, we aimed to estimate the incidence of renal stones in such patients, to probe the possibility of a statistically significant relationship between RA and renal stones. Proving this hypothesis is crucial for clinicians, since it can affect the management of patients with RA.

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## Patients and Methods

In order to evaluate the relationship between RA and renal stones we carried out a historical cohort study. Since no reliable information was available on the prevalence of RA in our country, a pilot study was conducted in the summer of 1999. Using the results of our pilot study and a Japanese study,<sup>4</sup> a sample size of 70 patients was reached. We also performed a case-control study on patients with RA and renal stones to evaluate the known risk factors for renal stones in these patients. We studied 74 patients with rheumatoid arthritis as our cases and 58 healthy individuals as the control group. Rheumatoid arthritis was diagnosed according to the 1987 criteria of American College of Rheumatology (ACR).<sup>1</sup> These patients did not give any personal or family history of renal stone. The control group was selected from the patients who referred to Emam Reza Hospital specialty clinics other than rheumatology and urology. The control group had neither signs and symptoms of RA, nor personal or family history of renal stones.

The duration of disease was between 4-10 years in our patients. Treatment protocols were combination therapy with NSAIDs, chloroquine, MTX, and prednisone as a disease modifying anti-rheumatic drug (DMARD) in association with calcium-vitamin D3 replacement therapy. Patients were referred from Emam Reza Rheumatology Department to Radiology Department for kidney ultrasonography. Sonography was performed with a 3.5MHz convex probe of a Hitachi EUB-525 apparatus (Japan) for renal stone detection. Data from each patient was gathered in a specific database designed for the project. In order to avoid bias, the sonologist was masked to the patient's group (RA or the control group) and all patients were visited by a single radiologist for the ultrasound examination. The sonographic criteria for diagnosing renal stones were the presence of any echogenic foci larger than 4mm in diameter in the pyelocaliceal system of kidneys with a distal acoustic shadow.

## Results

Eighty-four percent of subjects in the RA group and 80% of subjects in the control group were female (P=0.544). There was not any statistically significant

difference between the mean age of patients of both groups. The mean age of individuals in the RA group was 66.47 years, and 66.38 years in the controls (P=0.362).

Regarding the relationship between RA and the incidence of renal stones, in the RA patients group, 6 out of 74 subjects (8.1%) had renal stones, and in the control group, 5 out of 58 subjects (8.6%) had renal stones. The different prevalences of renal stones between the two groups were not statistically significant (Fisher's exact P-value was 0.58) (Table 1). Relative risk for stone formation in RA patients in comparison to controls was 0.935 (95% confidence interval: 0.271-3.23)

The size of renal stones in RA patients was not significantly different from the control group's (P=0.387). There was no statistically significant difference between the prevalence of renal stones in disease durations of 4 years or less, and longer disease durations (up to 10 years) (P=0.711).

In this study, we also looked for the association between different symptoms of RA and the presence of renal stones. There was no statistically significant association between RA criteria of morning stiffness, arthritis in 3 or more joints, hand arthritis, symmetrical arthritis, and rheumatoid nodules with the presence of renal stones (Table 2).

## Discussion

Rheumatoid arthritis is a chronic autoimmune inflammatory disease which presents as a progressive destruction of the synovial joints.<sup>2,3</sup> It is accompanied by various extraarticular manifestations such as pleuropericarditis, eye involvement.<sup>2,6</sup> It is a multisystem disease which damages target organs including: heart, lungs, eyes, nervous system, as well as the kidneys.<sup>2</sup> Urinary tract involvement occurs in 1-5 % of RA patients and is a clinically important issue due to long term mortality and morbidity.<sup>2,6</sup>

Involvement of the kidneys in RA can present in different ways such as interstitial nephritis with he-

**Table 1.** Prevalence of renal stones in RA and control groups

Renal stone	Case	Control
Absent	68(91.9%)	53(91.7%)
Present	6(8.1%)	5(8.6%)

**Table 2.** Relationship between RA symptoms and renal stones

Symptom	Stone Present	Stone Absent	P value
Morning stiffness	3(50%)	43(63.2%)	0.33
Arthritis of $\geq 3$ joints	4(66.6%)	44(66.1%)	0.99
Hand arthritis	3(50%)	42(61.7%)	0.75
Symmetrical arthritis	3(50%)	46(67.6%)	0.50
Rheumatoid nodule	1(16.6%)	9(13.2%)	0.31

maturia, proteinuria and micro-albuminuria.<sup>6-8</sup> Iatrogenic nephropathy due to NSAIDs, the most common medication used in RA patients for a long period of time, is another form of kidney involvement in RA.<sup>10, 11</sup> In addition to NSAIDs, using different types of drugs such as cytotoxins, gold, D-penicillamine, and cyclosporins could be the other cause of renal problems in RA patients.<sup>10-15</sup> Amyloidosis, rarely vasculitis and chronic renal failure are other pictures of renal involvement in RA.<sup>16</sup>

In one study on 110 patients with RA who underwent renal biopsy, mesenchymal glomerulonephritis was the most common finding (n=40).<sup>15</sup> Nephrotic syndrome is one manifestation of kidney involvement and the most common finding in patients with nephrotic syndrome in this study was amyloidosis (n=33).<sup>16</sup>

Microscopic hematuria in RA patients has different etiologies. In a study by Roy et al. it was shown that hypercalciuria is more common in children with painless hematuria.<sup>17</sup> They also reported that anticalciuric treatment could eliminate hematuria in children. It was then concluded that hematuria in children and adults with RA is a sign of renal stones. They also showed that the incidence of renal stones in patients with RA is higher than the general population.<sup>17, 18</sup>

Another study by Ito et al. was conducted in Japan on 224 patients with RA (42 male and 182 female). Renal stones were found in 37 patients with RA and only in 3 subjects from the control group. This study showed a significantly higher incidence of renal stones in patients with RA that is in contrast to our results. Hyperechoic foci without distal shadow were found in 50 of 224 patients with RA, but only 4 of 64 controls.<sup>4</sup>

The difference between the results of Ito's study and ours may result from the variability between the patient selection methods and patient characteristics.

For example, all our RA and control cases were outpatients; in the mentioned study however, some of the RA patients were hospitalized while their control cases were selected from outpatients. It seems that this may have contributed to the higher prevalence of stones in the RA group. It thus would be more appropriate to select both groups from a similar population, i.e. from outpatients. Another point is that the control group of Ito's study had no history of renal colic but after excluding the patients with history of renal colic in the RA group, the prevalence of stones was still higher in the RA group in comparison to the control group.

Another difference between our study and Ito's study is that the mean duration of RA in Ito's study is higher than ours (the mean duration of RA in their study was 13.5 years while in our study, it was lower than 10 years). Despite this fact that we did not find any relation between the prevalence of renal stones and duration of RA (there was no statistically significant difference between the prevalence of renal stones in patients with disease duration of less than 4 years and patients suffering from RA for 4-10 years), we cannot explain the prevalence of renal stones in patients with longer durations of the disease. In fact, a longer duration of RA may be accompanied by a higher probability of urinary stone development.

Further evaluations and studies are needed to clarify the relationship between RA and renal stones. Thus the authors wish to make a few suggestions:

1- It is obvious that utilizing modalities like spiral CT scan will provide more reliable information about the presence of stones in the affected group.

2- The potentially confounding effects of different kinds of RA regimens should be considered in the future studies.

3- It would also be appropriate to follow RA patients for a longer period of time than that of previous studied articles in order to come up with better ideas.

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