Systemic lupus erythematosus is a common autoimmune disorder with unknown etiology (1). It is associated with variety of multiple immunologic phenotypes representing chronic immunologic activation. SLE involves predominantly women between 15-40 years. With multiple organ affection, renal involvement is the most serious complication in the course of disease (2). Renal involvement becomes clinically apparent in approximately 50 percent of patients and significantly increases mortality and morbidity (3). Despite standard conventional treatment, five years survival in lupus patients with nephritis will decrease significantly (4). However, it is obvious that early diagnosis and treatment of lupus may be able to improve kidney function and life span relatively (5). Hence, it would be very beneficial if presence of nephritis presence of nephritis could be detected in the early stage of disease(5). Uric acid is an end product of purine nucleotide metabolism. Emerging evidence suggest that hyperuricemia are risk factors for cardiovascular disease, hypertension, diabetes mellitus particularly insulin resistant type and metabolic syndrome (9, 10). Hyperuricemia is observed in 20% lupus patients, but gout manifestation is reported rarely(10). On the other hand, a few patients have simultaneously involved with lupus and got arthritis associated with nephropathy, but the correlation between hyperuricemia and development of lupus nephritis has still remained unclear(11,12). In animal model, researchers have shown that induced hyperuricemia has correlation with kidney involvement manifestation. Moreover, in human being with diabetic nephropathy, hyperuricemia has been related to in isolate and progression of kidney involvement. (13,14).

Nevertheless, a few studies have been reported about correlation between hyperuricemia and frequency of lupus nephritis so far. (15, 16)

Table 1: Comparison between LN and non-LN patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>LN</th>
<th>Non-LN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum uric acid</td>
<td>6.5 ± 1.2 mg/dL</td>
<td>4.2 ± 0.8 mg/dL</td>
</tr>
<tr>
<td>SLEDAI score</td>
<td>12 ± 3</td>
<td>6 ± 2</td>
</tr>
</tbody>
</table>

Results:

In this cross-sectional prospective study, we evaluated one hundred lupus patients referred to Rheumatologic Clinic at Imam Reza Hospital. All patients in this study All patients were diagnosed according to American College of Rheumatology (ACR) 1997 criteria for lupus (SLE). Patients are assessed using standard protocol includes complete history, physical examination and laboratory evaluation by two rheumatologist. Written informed consent is obtained from patients at the time of enrollment into this study at the Rheumatologic clinic. A 6-page data collection sheet consist of required parameters was designed. All data included socioeconomic and ethical variables (e.g. age, gender, disease duration (calculated from the time patients first fulfilled the ARA criteria), laboratory findings, disease activity (assessed by the SLEDAI-2K), were obtained by reviewing of hospital clinical records in a clinic visit.

Blood samples were obtained for determination of the uric acid levels, Anti- dsDNA, C3, C4. Disease activity was measured by SLEDAI-2K, a valid measure of disease activity in SLE. SLEDAI-2K was modeled on clinician’s global judgment to standardize and measure disease severity. SLEDAI-2K based on the presence of 12 descriptors in 19 organ system in patients within past ten days. The total score of SLEDAI-2K fall between 0-106 with higher scores representing increased disease severity.

Patients were divided into two groups, including lupus patients with and without lupus nephritis. Active lupus nephritis was defined by persistent protein in urine more than 500 mg during 24 hours, or active urine sediment or lupus nephritis in biopsy. Descriptive data was expressed by mean ± SD. Serum uric acid (SUA) level were measured and compared in two groups of lupus patients with and without nephritis by Student t-Test exam.

For assessment of correlation between SLEDAI-2k and other variables with serum uric acid (SUA), Spearman’s correlation test was used in two study groups. Sensitivity and specificity of serum uric acid was represented by receiver operating characteristic curve (ROC). Data analysis was done by SPSS 19.0 version statistical software. P-value less than 0.05 considered significant.

Conclusions:

In this study, the average of serum uric acid in LN patients was significantly higher than that in non LN patients. There is a direct and significant correlation between levels of serum uric acid with ANA, Anti ds DNA, SLEDAI; however Serum uric acid level had significant indirect relation with C3, C4 levels.

In 2011, Yang and his colleagues study revealed there is a correlation between serum uric acid and lupus nephritis. In LN patients, SLEDAI score, serum uric acid levels and Anti dsDNA were higher than in non LN patients. In contrast, in LN patients, C3 levels were lower than non LN patients. Positivity of anti dsDNA was more (1). In another research, Yang and et al. showed a positive correlation between serum uric, creatinine, uric acid with activity of lupus patients from both aspects of clinical and laboratory view of lupus patients. (2)

In this study, median serum uric acid (sUA) in MicroMoled, in LN and non LN patients were 416 µmol/l (338-561) and 279 µmol/l (217-329), respectively. There have also been demonstrated that uric acid was an independent risk factor for lupus nephropathy with 78.1% sensitivity, 75.4% specificity. The area under curve (AUC) was 0.803±0.039 (95% CI 0.727-0.878) with a cut-off 385µmol/L. Other studies have also revealed the role of serum uric acid in renal diseases like primary systemic patients and diabetic nephropathy. (16)

In our study, we showed the valuable role of serum uric acid for diagnosis of lupus nephritis with significant statistically sensitivity and specificity, authenticating previous study, with highest level of ‘under ROC curve area’ in our study compare with Yang study. Recent advanced researches have showed uric acid is able to activate inflammation NLRP3, which gives a noteworthy character in many inflammatory responses like gout and nephritis. Therefore it may have prominent role in evolving of lupus nephritis. Hyperuricemia triggers endothelial dysfunction, renin angiotensin system (RAS) activation, oxidative stress and proliferative and proinflammatory process. (17)

Sympson J. et al. and Shin J. et al. studied, hyperuricemia is an independent risk factor in IgA nephropathy progression. (18, 19). Iftikhar K. et al. studied, serum uric acid has a significant positive correlation in developing high serum creatinine in Japanese population (20). Moreover, the result of this study showed a significant positive correlation of renal failure prognosis with renal function (21). Interestingly, uric acid not only exacerbates kidney damage through RAS activation, which increases systemic and glomerular pressure, but also increases through direct fibrogenic effects upon both renal and vascular cells. (21)

The study results showed uric acid level could be useful for lupus nephritis diagnosis alongside urinalysis, serum creatinine and kidney biopsy. Accordingly, considering implementing alloplurin in treatment lupus nephritis may be merit in renal function recovery. Further researches and clinical trials should be performed in future.

References:


Poster presented at: On J-Poster