COMPARISON OF SERUM URIC ACID BETWEEN LUPUS PATIENTS WITH AND WITHOUT LUPUS NEPHRITIS

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Objectives:

Systemic lupus erythematosus is a common autoimmune disorder with unknown etiology (1). It's associated with variety of multiple immunologic phenotype represents chronic immunologic activation. SLE involves predominantly women between 15-40 years with multiple target organs damage particularly kidney which 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 of disease(6) .Uric acid is an end product of purine nucleotide metabolism Emerging evidence suggest that hyperuricaemia are risk factors for cardiovascular disease, hypertension, diabetes mellitus particularly insulin resistant type and metabolic syndrome (8,9).

Hyperuricemia is observed in 29% lupus patients, but gout manifestation is reported rarely.(10) On the other hand , a few patients have simultaneously involved with lupus and gout arthritis associated with nephropathy; but the correlation between hyperuricemia and development of lupus nephritis has still remained unclear(11,12).

In animal model , researches have been showed that induced hyperuricemia has correlation with kidney involvement manifestation. Moreover, in human being with diabetic nephropathy, hyperuricemia has been related to initiate and progress 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)

Methods:

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 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 including Socio demographic status (sex, age), 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 same clinic visit.

Blood samples were obtained for determination of the uric acid levels, ANA, 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' global judgment to standardize and measure disease activity. SLEDAI-2K is based on the presence of 24 descriptors in 9 organ system in patients within past ten days. The total score of SLEDAI-2K falls between 0-105 with higher scores representing increased disease activity.

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 withserum 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 15.0 version statistical software. P-value less than 0.05 considered significant.

Table 1 Correlations between UA and other variables in LN or non-LN groups

Patient groups / variables	Non Lupus nephritis		Lupus nephritis		P. Value
	mean	*SD*	*mean*	*SD*	
Serum uric acid (mg/dl)	4.14	1.59	7.16	2.37	0.001[a]
Urine UA/Cr ratio (mg/g)	0.62	0.30	0.60	0.28	0.75
ANA (IU/ml)	65.19	27.77	105.50	105.82	0.008[a]
Anti ds DNA (IU/ml)	208.66	229.95	432.07	301.52	0.001[a]
C3 (mg/dl)	77.01	38.1	70.01	38.1	0.38
C4 (mg/dl)	39.03	24.32	21.10	19.24	0.001[a]
SLEDAI	7	4.52	12.95	7.36	0.001[a]

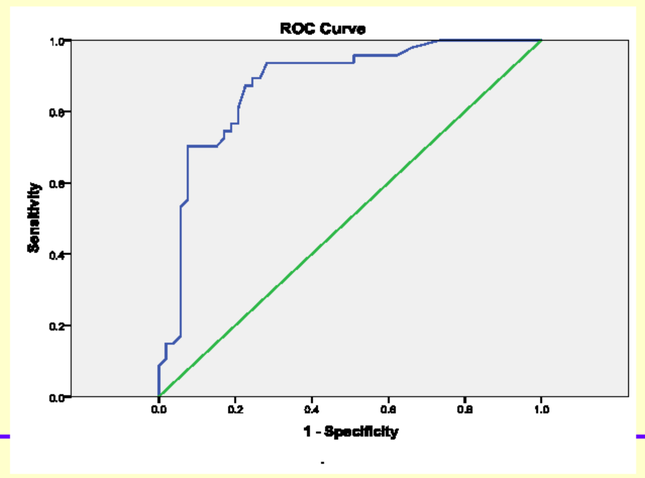

Fig. 1 ROC curve for concentrations of UA and LN

Results:

This was a cross-sectional study of a descriptive of consecutively patients with lupus nephritis in Mashhad Imam Reza hospital during 20 -20 .Six patients were male and 94 patients were female. Forty seven patients were suffered from LN. The average age of patients and disease duration were (31.76±9.22) years and (4.65±4.66) years respectively.

Table 1, represents mean ± standard deviation of serum uric acid, C3, C4, ANA, anti dsDNA, SLEDAI score in two study groups with and without LN. Serum uric acid levels (SUA) in In patients group with LN were significantly higher than that in non lupus nephritis (P value=0.03).

Spearman's correlation test showed a significant direct correlation between SUA with ANA, anti dsDNA and SLEDAI .However, there is an inverse significant correlation between SUA with C3 and C4 levels. Moreover, there is no statistically significant difference of serum uric acid level in different types of lupus nephritis (respect to WHO classification).

In non LN patients, serum uric acid had direct and significant correlation with ANA, anti dsDNA, duration of lupus disease, and there is reverse significant correlation with C3 levels.

There is reverse correlation between C3 levels and serum uric acid in LN patients.

In different cut of points, ROC curve was constructed. The area under the ROC curve was 0.875

The most valuable cut of points for SUA in identifying lupus nephritis was 4.95 µmg/dl(sensitivity 77%, specificity 82% and accuracy 87.5%).

Conclusions:

In this study, the average of serum uric acid in LN patients was significantly higher rather than 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 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-ds DNA was more. (1)In another research, Yang and et al, showed a positive correlation between serum urea, 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 (IQR) in Micromole/L, in LN and non LN patients were 416 µmol (338-561) and 279 µmol (217-329), respectively. They have also 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=330µ mol.

Other studies have also revealed the role of serum uric acid in renal diseases like preeclampsia 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 higher level of "under ROC curve area" in our study compare with Yang study.

Recent advanced researches have showed uric acid is able to activated infamasoame NLRP3, which owes a noteworthy character in many inflammatory responses like gouty nephritis; therefore it may have a considerable role in evolving of lupus nephritis. Hyperuricemia triggers endothelial dysfunction, renin angiotensin system (RAS) activation, oxidative stress and proliferative and preinflammatory process. (17)

Syrjanen J., et al and Ohno. I. et al studies, showed hyperuricemia is an independent risk factor in IgA nephropathy progress. (18, 19)

Iseki K. et al. study, revealed serum uric acid has a significant positive correlation in developing high serum creatinine in Japanese population.

Indeed, this study showed that uric acid increase is an imperative factor for prediction of renal failure progression compare with renal proteinuria. (20)

Interestingly, uric acid not only exacerbates kidney damage through Renin angiotensin system (RAS) activation, which increases systemic and glomerular pressure, but also through direct fibrogenic effects upon both renal and vascular cells. (21)

Conclusion:

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

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