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Original Research Article

Original Research Article: Study of Evaluation of Serum Uric Acid Level in Systemic Lupus Erythematous Patients & Its Correlation with Pulmonary Artery Pressure

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Conflict of interest: Nil

Abstract:

Background: Systemic lupus erythematosus (SLE) as a multisystem autoimmune disorder has diverse phenotypic expression affecting any organ system. Kidney, heart and pulmonary system are the most frequently affected organ in systemic lupus erythematosus.

Objectives: The objectives of the study is to measure serum uric acid level in patients with systemic lupus erythematosus and to study correlation of serum uric acid level with pulmonary artery pressure in SLE patients.

Methodology: This Hospital based case control study includes 40 patients of SLE. All patients of SLE admitted in our hospital and attending O.P.D. were included. Pulmonary artery pressure in patients was measured by echocardiogram. Blood samples was taken from each patient. Serum uric acid was measured by Kit. Duration of illness was extracted from patients' records. The relationship of serum uric acid level with pulmonary arterial pressure and duration of the disease was evaluated.

Results: In our study, maximum 67.50% patients were from 21-40 yrs age group followed by 20.00% patients in 41-60 yrs age group , 7.5% patients were from >60 yrs age group and 5.00% . Serum uric acid level was significantly higher in PAH patients (10.74±1.97 mg/dl) as compared to patients without PAH (6.42±2.02 mg/dl). Serum creatinine level was significantly higher in PAH patients (2.32±2.05 mg/dl) as compared to patients without PAH (1.30±0.74 mg/dl). 45.00% patient's EF was more than 55% , followed by 22.50% patients with EF 46-55%, 20.00% patient's EF was 35-45% and 12.50% patient's EF was <35.00. The EF was lower in patients with PAH (44.91±9.32%) as compared to patients without PAH (46.65±10.32%). This difference was statistically insignificant. The association between EF and serum uric acid was found to be statistically insignificant.

Conclusion: We conclude that serum uric acid is strongly associated with development of PAH in SLE patients. SLE patients with increased serum uric acid level are likely to have PAH and patients with normal serum uric acid level are likely to have normal pulmonary artery pressure. Being a low cost test and easily done everywhere, serum uric acid estimation will help to reduce clinical demand for echocardiography in SLE patients with normal uric acid levels.

Keywords: SLE, Uric Acid, EF, PAH.

Introduction

Annual incidence of Systemic Lupus Erythematosus (SLE) is 2.8 per 1,00,000 in United States and Europe. Estimates of total number with this disease ranges from 20 – 60 per 1,00,000. More than 80% are females. [1,2] Highest incidence is between 20 – 50 years of age. The frequency of Systemic Lupus Erythematosus concordance in monozygotic twin is 25% and with 1- 2% among dizygotic twins. More than 100 auto-antibodies have been found in the sera of patients with SLE. Autoantibodies found in SLE patients are anti-nuclear antibody (ANA), anti-dsDNA antibody and anti-extractable nuclear antigen (ENA) antibody, anti-ENA antibodies include anti-smith (Sm), anti-ribonucleoprotein 2 (RNP), anti-Ro and anti-La antibodies. The etiology of autoimmune diseases such as SLE remains unknown. [3,4] Genetic, hormonal and

environmental factors and immune deficiencies appear to be effective. Studies reported that autoimmune diseases affect 7% of the population in the United States (reference). SLE is associated with various complications, pulmonary arterial hypertension is one of them.

The prevalence of pulmonary hypertension in SLE is about 1.8%-14% [11] however multiple factors are implicated in increased pulmonary hypertension in SLE disease, but the cause is vague. Moreover, Pulmonary arterial hypertension (PAH) [7,8] is the third leading cause of mortality among patients with systemic lupus erythematosus. Other studies also reported that PAH was considered as the most frequent cause of mortality among these patients. [5]

Some studies have shown that high level of uric acid is observed in patients with lupus and high pulmonary arterial pressure. Considering the role of uric acid as pro-inflammatory compound in SLE disease and the relationship between high pulmonary arterial pressure and the lack of sufficient studies in our country, the aim of this study was to measure serum uric acid level in patients with systemic lupus erythematosus and its association with pulmonary artery pressure. [6]

Material and Methods

This Hospital based case control study was conducted at Department of General Medicine, S.P. Medical College and P.B.M Hospital, Bikaner, Rajasthan from Aug 2021 to July 2024

Sample size: All patients of SLE admitted in our hospital and attending O.P.D. were included.

Sampling Method: Consecutive sampling

Inclusion Criteria: Those who are giving informed consent. Age>18 year. Patients with SLE

Exclusion Criteria:

Patients with previous history of hypertension, valvular heart disease, thromboembolism, heart failure, chronic obstructive pulmonary disease, kidney failure, consumption of excess Alcoholics beverages, gout, use of drugs which increases serum uric acid example diuretics (thiazides, loop diuretics), Salicylates, pyrazinamide, ethambutol, Cyclosporin, cytotoxic agents, was exclude from the study.

Data Collection: Pulmonary artery pressure in patients was measured by echocardiogram. Blood samples was taken from each patient. Serum uric acid was measured by Kit. Duration of illness was extracted from patients' records.

The relationship of serum uric acid level with pulmonary arterial pressure and duration of the disease was evaluated.

Data Analysis:

To collect required information from eligible patients a pre-structured proforma was used. For data analysis data was analyzed with the help of frequencies, figures, proportions, measures of central tendency, appropriate statistical test**.**

Results

Table no 1 shows that maximum 67.50% patients were from 21-40 yrs followed by 20.00% patients were from 41-60 yrs age, 7.5%patien were from >60 yrs and 5.00% patients were from <20 yrs. Table no 2 shows that maximum (97.50%) patients were female.

Table 1. Age wise distribution of study subject

Age in yrs	No of patients	Percentage
<20	2	5.00
21-40	27	67.50
41-60	8	20.00
>60	3	7.5
Total	40	100.00

Table 2: Sex wise distribution of study subject

Sex	No of patients	Percentage
Male	1	2.50
Female	39	97.50
Total	40	100.00

Table 3: Socio-economic status wise distribution of study subject

SES	No of patients	Percentage
Lower	27	67.50
Middle	9	27.50
Upper	4	10.00
Total	40	100.00

Table no 3 shows that 67.50% patients were from lower SES followed by 27.50% patients were from middle SES and 10.00% patients were from upper SES.

Table 4: Presence of PAH in SLE patients

PAH	No of patients	Percentage
Present	5	12.50
Absent	35	87.50
Total	40	100.00

Table no 4 shows that 12.50% patients were present with PAH.

Table 5: Association between uric acid and PAH in SLE patients

Uric acid (mg/dl)	PAH		p-value
	Present	Absent	
Mean	10.74	6.42	0.001
SD	1.97	2.02	

Table no 5 shows that the uric acid was significantly higher in with PAH patients (10.74±1.97 mg/dl) as compare to without PAH (6.42±2.02 mg/dl).

Table 6: Association between creatinine and PAH in SLE patients

Creatinine (mg/dl)	PAH		p-value
	Present	Absent	
Mean	2.32	1.30	0.03
SD	2.05	0.74	

Table no 6 shows that the creatinine was significantly higher in with PAH patients (2.32±2.05 mg/dl) as compare to without PAH (1.30±0.74 mg/dl). Table no 7 shows that 15.00% patient's serum uric acid was increased.

Table 7: Serum uric acid level wise distribution

Serum uric acid	No of patients	Percentage
Increased	6	15.00
Normal	34	85.00
Total	40	100.00

Table 8: EF finding wise distribution

Ef finding	No of patients	Percentage
>55 %	18	45.00
46-55%	9	22.50
35-45%	8	20.00
<35%	5	12.50
Total	40	100.00

Table no 8 shows that 45.00% patients EF was more than 55% followed by 22.50% patients EF was 46-55%, 20.00% patients EF was 35-45% and 2.50% patients EF was <35.00%.
Table no 9 shows that the association between EF and serum uric acid was found statistically Insignificant.

Table 9: Association between uric acid and PAH

EF in %	Serum uric acid		p-value
	Increased	Normal	
Mean	43.12	48.36	0.102
SD	10.21	9.32	

Discussion

This hospital based cross-sectional study was carried out in Department of General Medicine, Sardar Patel Medical College and associated group of hospitals, Bikaner to evaluate serum uric acid level in patients with systemic lupus erythematosus and its co-relation with pulmonary artery pressure.

In this study, 40 patients with systemic lupus ery-

thematosus were evaluated. All patients underwent echocardiography and serum level of uric acid was measured.In our study, maximum 67.50% patients were from 21-40 yrs age group followed by 20.00% patients in 41-60 yrs age group , 7.5% patients were from >60 yrs age group and 5.00% patients were less than 20 yrs of age group. In our study majority patients (97.50%) were female. Similar to our study Aghdashi M et al [7] in their study found that among 75 patients with systemic lupus erythematosus 70 (93.3%) were female and 5 patients (6.7%) male. This may be because autoimmune diseases are more common in females, probably because of hormonal factors. Similarly Elera-Fitzcarrald C et al [8] in their study evaluated two hundred and thirty-seven patients with SLE. 220 patients (92.8%) were women and mean age (SD) at diagnosis was 35.9 (13.1) years. Jingya Wang et al [9,10] studied 80 patients with CTD-PAH. In their study also majority of patients (47) were female with mean age 38.5 ±0.3 years and 3 male with mean age 49.3 ±13.7 years.

In our study 67.50% patients were from lower SES followed by 27.50% patients from middle SES and 10.00% patients were from upper SES. 70.00% patients were from rural area. Similar result were found by Elera-Fitzcarrald C et al [8], they found that maximum patients were from middle and lower class. This may be because two third population of India is from rural area (population census 2011).

In our study 12.50% patients presented with PAH. The presence of PAH in SLE is estimated to be 0.5% to 43% in some older studies [11] and 0.5% to 17.5% in two newer French studies. The estimated prevalence range is wide, caused by multiple factors such as varied population groups, lack of a uniform PAH definition and different diagnostic approaches (echocardiogram versus right heart catheterization (RHC)) [12]. In a large community-based lupus cohort from the United Kingdom (n = 288), the prevalence of SLE-aPAH was 4.2%. The association between uric acid levels and damage occured in patients with SLE was evaluated in earlier studies and serum uric acid level was found to be associated with the development of new damage in these patients. Previous studies have found an association between hyperuricemia and hypertension, metabolic syndrome and renal disease, as well as with organ failure or damage, especially renal. [13]

In several autoimmune diseases, high serum uric acid levels play an important role in the development and risk of certain comorbidities; for example, in rheumatoid arthritis, uric acid is a cardiovascular risk factor reflected in the increased thickness of the carotid artery. On the other hand, in systemic sclerosis, Gigante et al found that serum uric acid levels were higher in those with more microvascular damage as compared with those with less microvascular damage. [14]. Kim *et al., also* found significant association between serum uric acid and high pulmonary arterial pressure [15]. Zhang *et al.,* also reported that serum uric acid was increased in more than one half of patients with pulmonary artery hypertension. Moreover, they reported that serum uric acid level is associated with severity of pulmonary artery hypertension and ventricular dysfunction [16]. Although in our study we did not evaluate the association of serum uric acid and severity of pulmonary hypertension. Sheikh *et al.,* in another study found that high level of uric acid was significantly associated with hypertension independent of age and BMI. They believed that hyperuricemia has a main role in hypertension *via* several mechanisms. Uric acid activates the renin-angiotensin system and down regulates production of nitric oxide (NO), leading to vasoconstriction [17]

Castillo-Grayson *et al.* found a significantly increased risk of hypertension in subjects with hyperuricemia [18] In present study we also assessed EF in SLE patients with and without PAH. EF was lower in with PAH patients (44.91±9.32%) as compared to those without PAH (46.65±10.32%). Although this association was not statistically significant. On reviewing available literature we could not find any study that evaluated association of EF with PAH in SLE patients .Further studies with larger sample size may be required to derive at any conclusion.

In our study uric acid was higher in PAH patients (10.74±1.97 mg/dl) as compared to patients without PAH (6.42±2.02 mg/dl) and this association was statistically significant. Out of 40 patients, six patients had increased serum uric acid level and five patients had PAH. Out of 5 patients who had PAH, 4 were found with increased serum uric acid level. Our finding are consistent with study done by Aghdashi M et al [7] they also studied serum uric acid level in patients with and without pulmonary arterial hypertension. Serum uric acid level was 2.13 ±6.20 and 1.74 ±4.19 *mg/dl* in patients with and without pulmonary arterial hypertension and they found it statistically significant.

Our study shows that SLE patients with increased serum uric acid level are likely to have PAH and patients with normal serum uric acid level are likely to have normal pulmonary artery pressure. Gold standard test to diagnose PAH is RHC but it is invasive and requires expertise and cannot be done in all health setup. 2D echocardiography though non-invasive way of assessing pulmonary artery pressure but it too requires expertise and not easily available, besides having cost issue. Serum uric acid estimation on the other hand is very cost effective and can be done easily in all health set up. So serum uric acid level can be used for initial screen-

ing of PAH in SLE patients particularly in those health set up where 2D-ECHO is not available or cannot be done in all patients due resource limitation. Patients having increased serum uric acid level can be subjected to 2D-ECHO or RHC as required. SLE patients having increased serum uric level but no evidence of PAH should be regularly followed up so as to pick up elevated pulmonary artery pressure early, as majority cases of mildly increased pulmonary artery pressure remain asymptomatic in initial course of disease. This may have significant impact on patient management and disease prognosis.

Conclusion

We conclude that serum uric acid is strongly associated with development of PAH in SLE patients. SLE patients with increased serum uric acid level are likely to have PAH and patients with normal serum uric acid level are likely to have normal pulmonary artery pressure. Being a low cost test and easily done everywhere, serum uric acid estimation will help to reduce clinical demand for echocardiography in SLE patients with normal uric acid levels. SLE patients with increased serum uric acid level but with normal pulmonary artery pressure should be regularly followed up to pick up PAH early in such patients. Further studies with larger sample size will be helpful to strengthen our observations.

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