

# The Association between Uric and Ascorbial Acid Serum and Lichen Planus Pathogenesis

Sara Mohamed Mohamed<sup>1\*</sup>, Sahar Mohamed Abd El fattah , El-Sayed Mohamed Galal , and HodaAbdeen Ibrahim

<sup>1,2,3</sup>Department of Dermatology, Venereology and Andrology Faculty of Medicine, Zagazig University, Egypt.

<sup>4</sup>Department of Pathology, Faculty of Medicine, Zagazig University, Egypt.

## Authors

Sara Mohamed Mohamed, Dermatology Resident, Al-Qenayat Central Hospital, Ash-Sharkia, Egypt.  
Email: [sarahassanin282@gmail.com](mailto:sarahassanin282@gmail.com)

Sahar Mohamed Abd El fattah, Professor of Dermatology, Venereology and Andrology, Faculty of Medicine, Zagazig University, Egypt.

El-Sayed Mohamed Galal, Assistant Professor of Dermatology, Venereology and Andrology, Faculty of Medicine, Zagazig University, Egypt.

HodaAbdeen Ibrahim, Assistant Professor of Pathology, Faculty of Medicine, Zagazig University, Egypt.

**Corresponding Author:** Sara Mohamed Mohamed

Email: [sarahassanin282@gmail.com](mailto:sarahassanin282@gmail.com)

## Abstract:

**Background:** Lichen planus (LP) is a common disorder whose etiopathogenesis is not clear. Recently, it has been suggested that increased reactive oxygen species (ROS) play important roles in the underlying mechanism of LP. Free radicals have an important involvement in the underlying mechanism of lichen planus and also various skin diseases. The aim of the study was to evaluate serum uric acid (UA) levels as a measure of the antioxidant defense status in lichen planus patients.

**Methods:** A case control study was performed on 17 patients with lichen planus and 17 healthy subjects as a control group. We estimated Serum level of uric acid and ascorbic acid using ELISA.

**Results:** The mean of serum levels of uric acid and ascorbic acid was lower in patient group compared to healthy group with no significant difference between the two studied groups.

**Conclusion:** Lichen planus pathogens are not specifically affected by antioxidants as uric acid and ascorbic acid. However, in addition to other interactive variables, the difference in the level of serum for these anti-oxidants between lichen planus patients and healthy subjects alight not important– may suggest their involvement.

**Keywords:** Lichen planus, Uric acid, Ascorbic acid, Antioxidants.

## Introduction

Lichen planus is a subacute to chronic, inflammatory, papulosquamous disorder characterized by typical lesions. Small, shiny, flat-topped, polygonal, faintly erythematous to violaceous papules that may coalesce into plaques which involve the skin, mucous membrane, and nail. Lichen planus can clinically present in various forms including classical, hypertrophic, actinic, annular, follicular, eruptive, and linear types. It affects all races and occurs usually from 30 to 70 years of age[1].

An abnormal immune response is probably the basis of this disease and the pathogenesis includes lymphocytic infiltration and keratinocyte necrosis. It has been suggested that free radicals have an important involvement in the underlying mechanism of various skin diseases. In lichen planus, the inflammatory cellular infiltrate, which consists mainly of CD4+ lymphocytes, is a well-known source of reactive oxygen species (ROS) [2].

In high concentrations ROS damages endothelial cells, and subsequently intercellular adhesion molecule (ICAM) 1 is further upregulated and expressed. T lymphocytes are recruited at the site of inflammation by this expression of ICAM-1. This process may cause perivascular infiltration of T-cells and exocytosis of lymphocytes as observed in lichen planus[3].

In addition, oxidative stress may activate nuclear factor kappa-light-chain-enhancer of activated B cells (NF- $\kappa$ B), which is an important transcription factor. It controls transcription of various cytokine genes that include interleukin (IL)-2 and tumor necrosis factor (TNF)- $\alpha$ , and also major histocompatibility complex (MHC) class 1 gene and IL-2 receptor gene [4].

It is estimated that physiological concentrations of vitamin C diminish the harmful effects of free radicals and reactive intermediates. At high concentrations, vitamin C could exacerbate oxidative stress [3].

The primary defense mechanisms against oxidative stress include antioxidants like some enzymes, vitamins and uric acid which is one of the important antioxidants in plasma. It can scavenge ROS and can chelate metal ions. Thus, monitoring uric acid level in serum as an indicator of the antioxidant defense (oxidative balance) could be important for the clinicians' treatment strategy [5].

## Subjects and methods

We conducted this case control study in outpatient clinic of Dermatology, Venereology and Andrology Department at Zagazig University Hospitals., Egypt between February 2019 and July 2019.

This study included 2 groups: **Group 1:** included 17 patients diagnosed with lichen planus. **Group 2:** included 17 apparently healthy subjects of matched age and sex with the patients. Our inclusion criteria was patients with different types of lichen planus from both sexes and all ages. Our exclusion criteria was: Concurrent use of vitamin supplements, corticosteroids and immunosuppressant drugs or alcoholics in last 6 months, Smokers, children, elderly, dialysis patients, Patients with irritable bowel syndrome, malabsorption, anemia, uricosuria, allergies, disorders of the skeletal system, blood coagulation disorders, patients who underwent to surgical interventions, pregnant and breastfeeding women.

All subjects of this study were subjected to detailed history taking include age, sex, occupation, special habits and dermatological history including (onset, course, duration, site and history of previous treatment for the disease). General physical examination were done.

We estimated Serum level of uric acid and ascorbic acid using ELISA.

### **Ethical consideration**

Written informed consent was obtained from all patients and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (Institutional Research Board IRB). The work has been carried out in accordance with the code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

### **Statistical Analysis:**

All data were collected, tabulated and statistically analyzed using SPSS 20.0 for windows (SPSS Inc., Chicago, IL, USA) & MedCalc 13 for windows (MedCalc Software bvba, Ostend, Belgium).

Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ( $\chi^2$ ) and Fisher exact was used to calculate difference between qualitative variables as indicated. Quantitative data were expressed as mean  $\pm$  SD (Standard deviation) for parametric and median and range for non-parametric data. Independent T test and Mann Whitney test were used to calculate difference between quantitative variables in two groups for parametric and non-parametric variables respectively.

Pearson's correlation tests were used for correlating variables. The (+) sign was considered as indication for direct correlation i.e. increased frequency of independent leads to increased frequency of dependent and (-) sign as indication for inverse correlation i.e. increased frequency of independent leads to decreased frequency of dependent. Values near to 1 were considered as strong correlation and values near 0 as weak correlation.

All statistical comparisons were two tailed with significance level of P-value  $\leq$  0.05 indicates significant while P > 0.05 indicates nonsignificant.

### **Results**

Mean $\pm$ SD for age in cases and controls were 43.7 $\pm$ 13.8 and 42.82 $\pm$ 8.82 years respectively with no significant difference between the two groups, P value was 0.832. Regarding sex; females were more than half of both groups with no significant difference between them, P value was 0.49 (Table 1).

The duration of disease varied from 1 month to 36 months with mean  $\pm$  SD 7.11 $\pm$ 10.57, range 1-36 and median 3.0. Major sites were legs (47%) then mucosa (23.5%) with decreased frequency of other sites. Regarding type of lesion; papules were majority in 58.8%. Multiple lesions were found in 76.5% of cases (Table 2).

Serum levels of both uric acid and ascorbic acid were lower among patients than among control subjects but there were no significant differences, P values were 0.616 and 0.425 respectively (Table 3).

**Table (1) Age and sex distribution between cases and controls**

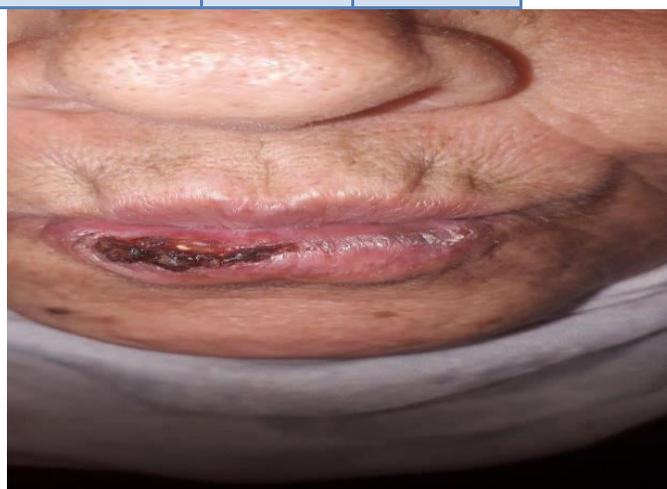
			Cases	Controls	t/ X <sup>2</sup>	P
<b>Age mean± SD</b>			<b>43.7±13.8</b>	<b>42.82±8.82</b>	<b>0.214</b>	<b>0.832</b>
<b>Range (years)</b>			<b>(18-60)</b>	<b>(30-60)</b>		<b>NS</b>
<b>Sex</b>	<b>Female</b>	<b>N</b>	<b>11</b>	<b>9</b>	<b>0.48</b>	<b>0.49</b>
		<b>%</b>	<b>64.7%</b>	<b>52.9%</b>		
	<b>Male</b>	<b>N</b>	<b>6</b>	<b>8</b>		
		<b>%</b>	<b>35.3%</b>	<b>47.1%</b>		
<b>Total</b>		<b>N</b>	<b>17</b>	<b>17</b>		
		<b>%</b>	<b>100.0%</b>	<b>100.0%</b>		

**Table (2) Clinical findings in patient group**

<b>Duration / months</b>	<b>Mean± SD</b>	<b>7.11±10.57</b>	
	<b>Median (Range)</b>	<b>3.0 (1-36)</b>	
		<b>N</b>	<b>%</b>
<b>Site</b>	<b>Legs</b>	<b>8</b>	<b>47.0</b>
	<b>Mucosa Lips only</b>	<b>2</b>	<b>11.8</b>
	<b>Buccal cavity and lips</b>	<b>2</b>	<b>11.8</b>
	<b>Hand and thigh</b>	<b>2</b>	<b>11.8</b>
	<b>Hand</b>	<b>1</b>	<b>5.9</b>
	<b>Axilla &amp; abdomen</b>	<b>1</b>	<b>5.9</b>
<b>Types of lesion</b>	<b>Wrist</b>	<b>1</b>	<b>5.9</b>
	<b>Papular</b>	<b>10</b>	<b>58.8</b>
	<b>Erosive</b>	<b>4</b>	<b>23.5</b>
<b>N of lesion</b>	<b>Hypertrophic</b>	<b>3</b>	<b>17.7</b>
	<b>Single</b>	<b>4</b>	<b>23.5</b>
	<b>Multiple</b>	<b>13</b>	<b>76.5</b>
		<b>Total</b>	<b>17</b>
			<b>100.0</b>

**Table (3) Comparison of serum levels of uric acid and ascorbic acid between both groups**

Serum level (mg/dl)	Cases	Control	t	P
Uric acid mean± SD Range	4.42±1.14 (1.9-8)	4.65±1.47 (2.9-6.4)	-0.507	0.616 NS
Ascorbic acid mean± SD range	0.79±0.27 (0.21-1.4)	0.83±0.28 (0.38-1.6)	0.680	0.425 NS

**Figure (1):** Papular lichen planus on right foot**Figure (2):** Erosive lichen planus on the lower lip

## Discussion

The aim of this study was to measure serum level of uric acid and ascorbic acid in lichen planus patients. Yasuda et al[5]found that uric acid and ascorbic acid have an important role as antioxidant in the body as it can scavenge ROS and chelate metal ions. Ascorbic acid in its physiological concentrations diminish the harmful effects of free radicals and reactive intermediates. Thus, monitoring uric acid and ascorbic acid levels in serum as indicator of the antioxidant defense (oxidative balance) could be important for the treatment strategy.

Barikbinet al [6]studied the mean plasma level of uric acid and ascorbic acid in a group of 30 patients diagnosed as having oral lichen planus compared with a control group of 30 age- and sex-matched healthy individuals and concluded that there was no significant difference in plasma uric acid level as the present study concluded. On the other hand they reported that mean plasma level of ascorbic acid was lower in patients than in controls.

Georgescu et al[7]detected serum level of uric acid in 70 lichen planus patients with hepatitis C and 50 normal subjects and reported that serum level of uric acid did not have statistically significant variations between patients and control. The results of the present study showed also no significant difference in serum level of uric acid, however patients with hepatitis C were excluded.

There are some studies concerning uric acid in specimens other than the serum in cases of lichen planus. For example; Battino et al[8] compared the serum and salivary levels of uric acid in patients with 20 oral lichen planus and 20 normal subjects, and found lower significant levels of uric acid in saliva and sera in the patient group, leading them to conclude that it might be a useful marker of oxidative stress.

As regarding ascorbic acid; Nicolae, et al[9] detected urinary ascorbic acid level in 77 patients with lichen planus (cutaneous lichen planus-49 cases; oral lichen planus -28 cases) and 50 control subjects and concluded that compared to the control group the level of ascorbic acid was significantly lower both in patients with cutaneous lichen planus and in those with oral lichen planus.

### Conclusion

Lichen planus pathogens are not specifically affected by antioxidants as uric acid and ascorbic acid. However, in addition to other interactive variables, the difference in the level of serum for these antioxidants between lichen planus patients and healthy subjects alight not important– may suggest their involvement.

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