

Correlation of Serum Urate Levels And Lichen Planus in Male and Female Patients

ABSTRACT

Aim: To correlate serum urate level in male and female patients with lichen planus (LP) presenting at Dermatology department, Liaquat University Hospital Jamshoro

Methodology: This Cross-sectional study was conducted from 2019 to 2020. Total 126 patients, divided into two equal groups male (n=63) and female (n=63), between the age of 20-50 years and duration of disease from one month after eruption of lesion to 18 months were incorporated in this study. The patients having gout, obesity, chronic kidney disease, Pregnant, smoker and those taking serum urate lowering drugs or steroids were excluded from this study. After taking history and clinical examination, patients were subject to height, weight, BMI, and duration of disease in months was stated. **Results:** Total 126 patients with age range between 20-50 years and the mean age was 32.5 ± 4.47 years in male and 35.3 ± 6.74 years in females were analyzed. The mean BMI was $23.6 \pm 2.68 \text{ kg/m}^2$ in male and 22.5 ± 3.47 in kg/m^2 females were recorded. The mean duration of disease was 35.4 ± 16.92 and 37.12 ± 18.92 weeks were recorded in male and female respectively. The mean serum urate level in Idiopathic Lichen Planus patients was $3.82 \pm 0.79 \text{ mg/dL}$ in male and $2.3 \pm 0.43 \text{ mg/dL}$ in female were observed. **Conclusion:** Our study results indicate that there is a positive correlation between LP and serum urate levels in male and female patients..

Keywords: Serum Uric Acid, Lichen Planus, BMI

1. INTRODUCTION

Lichen planus (LP) is seen in approximately 1% of all new patients visiting health care clinics. There is no considerable racial and geological and predisposition noted for LP. In most of the patients age ranges from 30-60 years; however, it can appear at any age [1]. The exact etiology is unknown but is likely an interaction between autoimmunity and environmental triggers. Environmental factors comprises medication, viruses (particularly hepatitis C), and allergic reactions to a foreign substance including metallic dental materials [2].

The typical lesions of lichen planus are described by 5 ps: Polygonal, Purple, pruritic, papules and/or plaque. [3]. It mostly involves wrist and ankles but can be anywhere and even generalized. Mucosal LP usually effects buccal mucosa or vulva. Cutaneous lesions of LP are not associated with risk of skin cancer, but erosive LP involving oral mucosa particularly in men and vulvar lesions in women, do carry a small risk of malignant transformation.. [4]

In humans, uric acid make about half of the antioxidant capacity of blood plasma [5]. Uric acid possesses strong antioxidant and scavenging activity for reactive oxygen

species (ROS) and peroxy nitrite. High concentration of uric acid are found in the cytoplasm of human and mammalian cells, especially in the hepatocytes [6], vascular endothelial cells, and in nasal secretions, where it acts as an antioxidant [5]. In fact, uric acid may exert a role in healing of tissues by initiating the inflammatory response that is required for tissue repair, hunting oxygen free radicals, and activating progenitor endothelial cells [7].

Low serum urate levels, which ultimately lead to a decrease in antioxidants, were found in patients having multiple sclerosis. Peroxynitrites and ROS are supposed to be liable for myelin sheath degeneration in multiple sclerosis (MS) which can be blocked by achieving high levels of serum urate. In support of this view, gout patients almost never developed multiple sclerosis (MS) [8]. There are a number of reports documenting association of low serum uric acid levels with MS [8,9] and other degenerative neurological disorders [10], i.e. Parkinson [11], and Alzheimer [12] disease. Similarly, Pemphigus vulgaris, (an autoimmune blistering disorder involving skin and mucous membranes), and lichen planus, (an autoimmune inflammatory disease involving skin, mucosa, even hair and nails)[13], were also found to be associated with low urate levels in serum and saliva [14].

2. MATERIAL AND METHODS

This Cross-sectional study was conducted from 2019 to 2020. A written consent was taken from all patients. Ethical approval was taken prior to conducting study from ethical review committee of CPSP. Total 126 patients, divided into two equal male (n=63) and female (n=63) groups, between the age of 20 to 50 years and duration of disease from one week after eruption of lesion to 18 months were included in this study. The patients on steroid or immune-suppression drugs or NSAIDs for last one month, gouty, obesity (BMI > 27), chronic kidney disease, Pregnant, smoker for >1 year and smoking more than 1 pack per day, and those taking serum urate lowering drugs were excluded from this study. After taking detailed history and full clinical examination, patients were subject to relevant investigations i.e. the patient's height, weight, BMI, and duration of disease in months was stated. The data was analyzed by using Statistical Package for Social Sciences (SPSS) Version.22.

3. RESULTS

Total 126 patients with age range between 20 to 50 years and the mean age was 32.5 ± 4.47 years in male and 35.3 ± 6.74 years in females were analyzed. The mean BMI was $23.6 \pm 2.68 \text{ kg/m}^2$ in male and 22.5 ± 3.47 in kg/m^2 females were recorded. The mean duration of disease was 35.4 ± 16.92 and 37.12 ± 18.92 weeks were recorded in male and female respectively. The mean serum urate level in Idiopathic Lichen Planus patients was $3.82 \pm 0.79 \text{ mg/dL}$ in male and $2.3 \pm 0.43 \text{ mg/dL}$ in female were observed. When the outcome variable was stratified with respect to age and duration of disease, significant difference was observed, shown in table 1. Similarly, when the outcome variable was stratified with respect to BMI and gender, no significant difference was observed, Shown in table 2

Table 1. Mean serum uric acid level stratification in age-related patients with LP in male and female.

SERUM URIC ACID	AGE	P-VALUE
-----------------	-----	---------

LEVEL (Mean \pm SD)	20-35 (n=36)	35-50 (n=27)	
Male	3.59 \pm 0.1	3.01 \pm 0.07	< 0.001
Female	1.9 \pm 0.43	2.4 \pm 0.03	< 0.001

Table 2. Mean serum uric acid level stratification in gender-specific patients with LP.

SERUM URIC ACID LEVEL	Gender		P-VALUE
	Male	Female (n=27)	
(Mean \pm SD)	3.82 \pm 0.79	2.3 \pm 0.43	< 0.001

Table 3. Stratification of the level of Mean Serum Uric Acid in weeks of disease duration in patients with Idiopathic Lichen Planus.

SERUM URIC ACID LEVEL	DURATION OF DISEASE (weeks)		P-VALUE
	1-40(weeks)	40- 72 (weeks)	
Male	3.94 \pm 0.1	3.68 \pm 0.2	< 0.001
Female	2.23 \pm 0.1	2.06 \pm 0.3	< 0.001

Table 4. Stratification of the level of Mean Serum Uric Acid in Idiopathic Lichen Planus Patients with respect to BMI.

SERUM URIC ACID LEVEL	BMI		P-VALUE
	18-25	>25 to <27	
Male	3.46 \pm 0.2	3.87 \pm 0.4	< 0.001
Female	2.28 \pm 0.3	2.46 \pm 0.5	< 0.001

4. DISCUSSION

Lichen planus is a chronic inflammatory disease. The skin has a number of defense mechanisms to prevent their deleterious effect, this interacts with ROS.[13] Serum urate is a natural end product for purine metabolism and is made in mammalian systems. There are evidence that higher serum urate levels are a risk factor for cardiovascular disease where oxidative stress plays a major role in pathophysiology.¹⁵This pollutes free radicals by inhibiting endothelial function under oxidative stress conditions inside a cell that discharges glutathione. There is growing evidence that the serum urate has an in vitro impact as antioxidant and antioxidant plasma potential increases with serum urate administration [15].

Our analysis showed a significant reduction in serum serum urate levels in patients, i.e. 4.32 ± 0.79 mg/dL. This study was related to Chakraborti et al, medium serum serum urate levels, 3.6 mg/dL in patients and 3.94 mg/dL controls [16] The mean difference is 0.34 mg/dl. There was also a significant decrease in serum urate levels in the sample of Italian LP patients [17]. On the contrary, Israel's report found that hyperuricemia was more common than the general population, although LP was not found to be a source of overproduction of uric acid. Saawarn et al stated that oxidative stress can play a role in oral LP, meanwhile, the strong antioxidant lycopene was found to be effective in another study in the oral LP's management. This therapeutic effect shows indirectly oxidative stress's function in LP pathogenesis [18]

This study demonstrates a significant correlation with serum serum urate levels between age of the patient and duration of the disease. However no significant gender and BMI relationship with serum serum urate was identified. Compared to other studies, there is no significant correlation between age and gender with serum serum urate in one study. Although a significant association between serum urate disease period was found similar to this research [16].

Indirect evidence of increased oxidative stress in LP is confirmed by the fact that saliva serum urate is decreased in oral LP patients.²²In addition, vitamin E and C levels in LP are decreased and supplementation of these may play a role in the management of LP [19].

serum urate is a potent free radical scavenger and, using two methodologically distinct assays, it has been demonstrated that systemic administration of serum urate improves ex vivo serum-free radical scavenging to a significantly greater extent than vitamin C, another effective aqueous physiological antioxidant. Administering antioxidants also raises serum urate levels [20].

4. CONCLUSION

Our study results show that LP can be correlated with serum urate depletion in male and female patients. Serum urate can be considered as a useful antioxidant biomarker in LP for the production and monitoring of treatment strategies.

CONSENT

All authors declare that written informed consent was obtained from the patient.

REFERENCES

1. Shah AK. Postoperative pathologic assessment of surgical margins in oral cancer: A contemporary review. *Journal of oral and maxillofacial pathology: JOMFP*. 2018 Jan;22(1):78.
2. Elenbaas A, Enciso R, Al-Eryani K. Oral Lichen Planus: A review of clinical features, etiologies, and treatments. *Dentistry Review*. 2021 Dec 1:100007.
3. Gholizadeh N, Sheykhbahaei N. Micronutrients profile in oral lichen planus: a review literature. *Biological trace element research*. 2021 Mar;199(3):912-24.
4. Yang JY, Wang F, Zhou G. Characterization and function of circulating mucosal-associated invariant T cells and $\gamma\delta$ T cells in oral lichen planus. *Journal of Oral Pathology & Medicine*. 2022 Jan;51(1):74-85.

5. González-Moles MÁ, Warnakulasuriya S, González-Ruiz I, González-Ruiz L, Ayén Á, Lenouvel D, Ruiz-Ávila I, Ramos-García P. Worldwide prevalence of oral lichen planus: A systematic review and meta-analysis. *Oral diseases*. 2021 May;27(4):813-28.
6. Shi B, Su Y, Duan Y, Chen S, Zuo W. A nanocomposite prepared from copper (II) and nitrogen-doped graphene quantum dots with peroxidase mimicking properties for chemiluminescent determination of uric acid. *Microchimica Acta*. 2019 Jul;186(7):1-0.
7. Kurajoh M, Fukumoto S, Yoshida S, Akari S, Murase T, Nakamura T, Ishii H, Yoshida H, Nagata Y, Morioka T, Mori K. Uric acid shown to contribute to increased oxidative stress level independent of xanthine oxidoreductase activity in MedCity21 health examination registry. *Scientific Reports*. 2021 Apr 1;11(1):1-9.
8. Kakoei S, Karbasi N, Raeiszadeh M, Tajadini H, Nekouei AH. The efficacy of henna (*Lawsonia inermis* L.) mouthwash versus chlorhexidine gluconate 0.2% mouthwash as adjuvant therapy of oral lichen planus: A randomized double-blind clinical trial. *Journal of Ethnopharmacology*. 2022;290:115037.
9. Scribante A, Gallo S, Pascadopoli M, Soleo R, Di Fonso F, Politi L, Venugopal A, Marya A, Butera A. Management of Periodontal Disease with Adjunctive Therapy with Ozone and Photobiomodulation (PBM): A Randomized Clinical Trial. In *Photonics 2022* Feb 26 (Vol. 9, No. 3, p. 138). MDPI.
10. Georgescu SR, Mitran CI, Mitran MI, Nicolae I, Matei C, Ene CD, Popa GL, Tampa M. Oxidative Stress in Cutaneous Lichen Planus—A Narrative Review. *Journal of Clinical Medicine*. 2021 Jun 18;10(12):2692.
11. Rehman M, Tabassum A, Mahboob T. EVALUATION OF OXIDATIVE STRESS BIOMARKERS IN DIFFERENT CANCER TYPES IN PAKISTANI POPULATION. *International Journal of Biology and Biotechnology*. 2018;15(3):589-96.
12. Wang J, Yang J, Wang C, Zhao Z, Fan Y. Systematic Review and Meta-Analysis of Oxidative Stress and Antioxidant Markers in Oral Lichen Planus. *Oxidative Medicine and Cellular Longevity*. 2021 Sep 27;2021.
13. Kushwaha RP, Rauniar GP, Rimal J. Clinical assessment of the effects of lycopene in the management of oral lichen planus. *International Dental & Medical Journal of Advanced Research*. 2019;5(1):1-5.
14. Shahi Y, Samadi FM, Mukherjee S. Plasma lipid peroxidation and antioxidant status in patients with oral precancerous lesions and oral cancer. *Oral Science International*. 2020 May;17(2):86-93.
15. Brown RS, Bottomley WK, Puente E, Lavigne GL. A retrospective evaluation of 193 patients with oral lichen planus. *J Oral Pathol Med*. 1993; 22(5):69-72.
16. Eberhardt MK. *Chemistry and medical consequences*. 1st ed. Florida: CRC Press; 2000. p. 261 – 302.
17. Jungell P. Oral lichen planus: a review. *Int J Oral Maxillofac Surg*. 1991;20(3):129-35.
18. Murrah VA, Perez LM. Oral lichen planus: parameters affecting accurate diagnosis and effective management. *Pract Periodontics Aesthet Dent*. 1997; 9(6):613-20.
19. Lewis JE, Beutner EH, Rostami R, Chorzelski TP. Chronic ulcerative stomatitis with stratified epithelium-specific antinuclear antibodies. *Int J Dermatol*. 1996;35(4):272-5.

20. Pynn BR, Burgess KL, Wade PS, McComb RJ. A retrospective survey of 2021 patients referred to the Toronto Hospital Mouth Clinic. *Ont Dent.* 1995; 72(1):21-4.

UNDER PEER REVIEW