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Comparison Between Salivary Biomarkers (*Macrophage Inflammatory Protein-1α And 1β)* Among Patients With Oral Lichen Planus And Oral Lichen Planus With Skin Lesions

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Abstract: *A common, chronic, inflammatory, T-cell-drivenoral. Mucosal condition is oral ichen planus (OLP). A. particular. cause.for.oral lichen planus hasn't been established yet. It has been believed that immune cell-mediated aberrances are the cause.. A lot of specialists suggest that macrophage inflammatory protein-1α (MIP-1α) and macrophage inflammatory protein-1β (MIP-1β) could have a role in the development of this disease. MIP-1α and MIP-1β have beeninvestigated for their possible implications as factors that contri bute to in the onset of oral lichen planus . Demographic, social,. medical and pharmaceutical histories were kept on file for each patient. Betw een 8 and 11 a.m., salivary samples from the patient were collected . Each p atient provided three to four milliliters of saliva for analysis . ELISA kits for measuring the levels of salivary macrophage inflammatory protein 1α and 1β in lichenplanus patients with oral and skin lesions and those with oral and ski n lesions are available . To take part in this study, each patient had to complete a consent form . There were fifty patients in total that took part . In this study, the participants were divided into two groups: group 1 included (25) patients with oral lichen planus (OLP) (17 females and 8 males), with mean±SD (47±18.35); and group 2 included (25) patients with OLP associated with skin lesions (14 females and 11 males), with mean±SD (45±16. 23); and the age range for both groups was between (30 and 70) . Regarding salivary (macrophage inflammatory protein-1α and 1β) , the present study showed no significant difference between patients with OLP group and patients with oral and skin lesions of lichen planus group, although, Mean salivary macrophage inflammatory protein-1α and 1β was higher in patients with oral and skin lesions of lichen planus group than patients with OLP group .*

Keywords: ***Oral Lichen Planus, macrophage inflammatory protein-1α and 1β, Salivary biomarkers, Oral Lesion .***

1.Introduction

The tissues of the body, including those in the oral cavity, might change as a result of someisorders . There is a chance that certain di sorders will affect the oral cavity . So, it has been said that the oral cavity serves as a mirror that reflects one's overall health . The mucosa

lining the oral cavity can disclose systemic problems when there are changes indicative of disease [1]. It is highly recommended that Pemphigus Vulgaris (PV) be included to the list of painful oral disorders and that dental care providers become more knowledgeable about this illness through ongoing education programs [2] . A mucous membrane that lines the oral cavity acts as a barrier between the body and the outside world . The oral cavity serves a variety of purposes, including protection, sensation, secretion, and temperature regulation [3] . An oral mucosal illness with an unknown cause called oral lichen planus (OLP) is a chronic inflammatory T-cell-mediated condition [3] . Infectious agents, psychological conditions, and genetic factors can all operate as causes or triggers [4] . It has been discovered that all potential causes of OLP lesion generation have the ability to alter the oxidative status [5], and this is supported by the fact that OLP patients have lower salivary anti-oxidant capability [6] . Clinically speaking, it can be classified as reticular, papular, plaque-like, erosive, atrophic, or bullous kinds . Reticular lesions and erosive lesions are the two main types of oral lesions [7]. Erosive lichen planus is the term used to describe the disease's atrophic, ulcerative, and bullous forms [7] . The most frequent clinical appearance is a reticular pattern, which takes the shape of a network of connections with underlying white lines [8] coupled with a few symptoms and indicating a more mild form of the illness [9] . The most damaging type of OLP, which also produces significant oral discomfort, is erosive-ulcerative OLP [9]. The number of patients with positive p53 expression increased from lichen planus to dysplasia [10] . 62% of PMD patients were disease-free after laser removal of dysplastic mucosal lesions, and the risk of malignant transformation remained low at 2 to 5% [11] . Although the specific pathophysiology is unknown, humoral and cell-mediated immunity have been linked . The primary cause of LP pathogenesis is activation of the cell-mediated immune response that is destined to cause keratinocyte apoptosis . LP-specific antigen recognition, cytotoxic lymphocyte activation, and keratinocyte death are the three stages that follow one another in the procedure [12]. Patients with oral lichen planus had reduced salivary melatonin levels [13]. Matrix metalloproteinase (MMP1) levels in saliva may also be important in the development of oral lichen planus [14]. Additionally, Epstein-Barr viruses were abundant in oral lichen planus [15] . Macrophage inflammatory protein MIP -1α and 1β is a chemotactic chemokine released by macrophages . It carries out a variety of biological processes, including the recruitment of inflammatory cells, the healing of wounds, the suppression of stem cells, and the maintenance of effector immune responses . Sites of inflammation and bone resorption have more cells that release MIP -1α and 1β [16] . Periodontitis, multiple myeloma, Sjogren syndrome, and rheumatoid arthritis are just a few examples of disorders that include bone resorption as a symptom . MIP -1α and 1β also plays a significant part in the pathogenesis of these conditions . Patients with these disorders have higher levels of MIP -1α and 1β in their biological fluids, such as their saliva . This discovery suggests that MIP -1α and 1β protein may have diagnostic value for the identification of a number of inflammatory illnesses and disorders [16] . OLP results from an unbalanced immunological response mediated by T helper 1 and T helper 2 . The pathophysiology of OLP may be influenced by a Th1/Th2 immune response imbalance also . MIP-1α and MIP-1β, which have a strong potential as biomarkers for diagnosing and predicting the prognosis of OLP, are positively linked with the severity of OLP . In OLP patients, increased MIP -1α and 1β levels in the saliva, particularly in symptomatic lesions, have also been documented [17].

Methodology :

In this clinical study, each patient with OLP provided their informed consent to participate in this study in accordance with ethical standards . The disease was either clinically (reticular type) or clinically diagnosed (erosive types) .. This study was carried out between January and September 2022 at the University of Baghdad's College of Dentistry and dermatology department of Al-Sader Medical City in Al-Najaf Al Ashraf government . Prior to doing a clinical examination on a patient, the patient's name, age, gender, and occupation were recorded, along with details about their medical history, medications, family history, social background, and OLP lesions (type, location, size) . Starting with the hard and soft palate, gingiva, alveolar ridges, upper and lower labial mucosa, vestibule, labial commissures, buccal mucosa, tongue (dorsal, ventral surfaces, and edges) . Every subject had a set daily time between 8 and 11 am when their saliva was collected' 'The collected saliva was entire and accounted for 3–4 ml . To allow for the removal of particles, a person was instructed to give their mouth a thorough water rinse . In order to clean the water, the first mouthful of saliva was expelled' 'Afterward, the patients were instructed to spit into graduated tubes all of their saliva . The extracted saliva was centrifuged at 3000 rpm for 20 minutes, and the clear supernatants were removed and kept frozen at (-70 c) pending analysis . The ELISA kits for measuring macrophage inflammatory protein-1α and 1β use the sandwich ELISA technique' 'Using an ELISA Reader and spectrophotometry at a wavelength of 450 nm, the optical density was estimated . it determined the concentration of human macrophage inflammatory protein-1α and 1β in each sample by comparing the optical density of each sample to the standard curve . Data entry was double-checked before being entered into an excel database . The statistical analysis was then performed using SPSS-26, a statistical software for social sciences . Along with averages and standard deviation, the study also provides descriptive analysis to display frequency distribution and percentages . In this investigation, Pearson correlation and the t-test were utilized to compare means . P values lower than 0.05 were deemed significant .

Results

This study uses fifty patients who took part in the study and were split into two groups: group 1 had 25 patients with oral lichen planus (OLP) (17 females and 8 males), mean SD (47±18.35), and Group 2 had 25 patients with OLP along with skin lesions (14 females and 11 males), meanSD (45±16. 23), and ages ranging from 30 to 70 (Table 1) .

Table 1: Distribution of patients of OLP study groups according to the age .

Age of OLP Years)(	OLP Group No.=25	OLP+Skin Group No.=25	P-value
30-39	2	6	*P = 0.8322 NS
40-49	7	5	
50-59	10	8	
60-69	6	6	
mean±SD	47±18.35	45±16. 23	

According to gender, Of the 25 OLP patients seventeen (73.4%) were females and eight (26.6%) were males; of the 25 OLP+Skin group patients, fourteen (54.2%) were females and eleven (45.8%) were males (Table 2) .

Table 2 : Distribution of the OLP study groups according to gender .

Study groups	Gender	N	percent	P-value
OLP NO.=25	male	8	26.6%	0.0352
	female	17	73.4%	
OLP+Skin NO.=25	male	11	45.8%	0.0356
	female	14	54.2%	

According to how the lesions presented clinically, patients with oral lichen planus were split into two subgroups . Patients (17,

21) had the reticular form of OLP, while (8, 4) had the erosive form (Table 3) .

Table (3) : Frequency distribution of patients groups according to the types of OLP .

Types of OLP	OLP Group No.=25	OLP+Skin Group No.=25	P-value
Reticular form	17 (73.4%)	**21 (84.6%)**	0.0374
Erosive form	8 (26.6%)	**4 (15.4%)**	0.163
Total %	25(100%)	25(100%)	

According to the salivary Markers (MIP-1α and 1β) , the present study revealed higher salivary (MIP-1α and 1β) levels in (OLP+Skin) group in comparison with (OLP) group (table 4) .

Table (4) : Descriptive statistic of (OLP) and (OLP+ skin) groups according to the affected Markers (MIP-1α and 1β) .

Study Groups	Statistic	MIP-1A	MIP-1B
OLP	Number	25	25
	Mean	6.181	4.671
	Std Dev	0.77	0.902
	Min	4.9839	3.0837
	Max	7.6215	6.2483
	% Of Total	56.96%	43.04%
OLP+Skin	Number	25	25
	Mean	9.295	8.857
	Std Dev	1.487	2.6652
	Min	7.2603	6.1956
	Max	11.3175	20.5773
	% Of Total	51.21%	48.79%

Regarding salivary Markers (MIP-1α and 1β) , the present study showed a significant difference in patients of (the OLP) group, while in patients of (OLP+ Skin) group, there is no significant difference (table 5) .

Table (5) : Statistical analysis of oral lichen planus and oral lichen planus+ skin groups according to affected markers (MIP-1α and 1β) .

Parameters	Item	Number	Mean	Std Err Mean	Confidence Interval (CI)		F ratio	P < value	Significant
					Lower 95%	Upper 95%			
OLP	MIP-1A	25	6.1811	0.168	5.8423	6.5200	40.145	<.0001 *	HS
	MIP-1B	25	4.6711	0.168	4.3323	5.0100			
OLP + skin	MIP-1A	25	9.29566	0.4316	8.4277	10.164	0.5159	0.4761	NS
	MIP-1B	25	8.8571	0.431	7.9892	9.725			

Discussion

MIP-1α and MIP-1β are two chemokines, or signaling proteins, produced by cells of the immune system . They are both members of the CC (cysteine-cysteine) chemokine family and share high sequence homology . When there is inflammation or another immune response, MIP-1α and MIP-1β have a role in controlling the activity and migration of different immune cells, such as monocytes, macrophages, T cells, and natural killer cells . MIP-1α and MIP-1β play important roles in the activation and modulation of inflammatory and host defense responses . It is essential for the attraction of macrophages and T-cell lymphocytes from circulatory systems to sites of infection or injury, and thereby orchestrates acute and chronic inflammatory host responses . As a result, MIP-1α and MIP-1β is a major proteins that plays a significant pathogenic function in the development of numerous inflammatory and autoimmune disorders such as rheumatoid arthritis, Sjogren syndrome, respiratory disease, and cardiovascular disease . Evaluating MIP-1α and MIP-1β levels in biological fluids allows for the early detection of a variety of inflammatory diseases and disorders . According to the World Health Organization's standards, OLP is a potentially malignant disease of the oral cavity; erosive lesions, in particular, could

considerably enhance the risk of cancer [18,19].

In this study, the level of salivary (MIP-1α and MIP-1β) in OLP patients was estimated . The salivary levels of both (MIP-1α and MIP-1β) were specifically elevated in the OLP research groups . Increased cytokine production by inflammatory cells or keratinocytes may explain the higher cytokine levels found in the saliva of OLP patients [20,21] . In this study, salivary cytokine (MIP-1α and MIP-1β) expression has been examined to gain an understanding of the pathophysiology of OLP . Many investigations have found that females are more impacted by OLP than males [22, 23], which is consistent with the findings of the present study . The vast majority of the patients were beyond the age of fifty, and this was in accordance with this study [24,25] . It is commonly recognized that Th1/Th2 immune imbalance plays an important role in inflammatory and/or immunologic diseases; therefore, based on these results, a disturbance in the Th1/Th2 immune response may play an crucial part in the pathogenesis of OLP [26]. In this study, the salivary MIP-1α and MIP-1β levels was higher in patients with OLP lesions that associated with skin lesions group than patients with OLP lesions group, Some of the results agreed with those of prior studies . MIP-1α and MIP-1β are members of the CC chemokine class that chemotactically affect T lymphocytes by attaching to surface receptors . The most distinguishing histologic feature of OLP is a thick, band-like infiltration of T-cell lymphocytes . The subepithelium and the lamina propria are dominated by CD4+ T cells, whereas the bulk of T-cell lymphocytes infiltrated in OLP lesions have been activated CD8+ lymphocytes . It is thought that elevated MIP-1α and MIP-1β levels are related to the collection of CD8+ T-cell lymphocytes at OLP areas; additionally, cytotoxic (activated CD8+) T-cells produced extensive basal cell disruption and keratinocyte apoptosis, which caused erosive lesions . MIP-1α and MIP-1β are biologically active proteins with comparable roles, but their expression profiles and regulation are different . Compared to MIP-1b, MIP-1a is produced by a wider variety of cells and is activated by a wider range of stimuli, such as bacterial or viral infections, whereas MIP-1b is largely produced by T cells and plays a greater role in controlling immune cell trafficking and function during chronic inflammatory disorders . Macrophage inflammatory protein-1a (MIP-1a) and MIP-1b are chemokines that are crucial for attracting and activating immune cells during inflammatory processes . Numerous studies have examined the concentrations of these biomarkers in the saliva of OLP patients to evaluate their potential as prognostic or diagnostic indicators for the illness .

Conclusion

In the OLP study groups (OLP and OLP with skin lesions), the salivary levels of both (MIP-1α and MIP-1β) were specifically increased . The OLP patients group showed a highly significant difference in salivary markers Macrophage Inflammatory Protein (MIP-1α and MIP-1β), while the OLP with skin lesions group showed no statistically significant difference .

Ethical approval

The Declaration of Helsinki's ethical guidelines were followed in the study . Patients' verbal and written consent was obtained before it was done . A local ethics committee evaluated and approved the study protocol, subject information, and permission form in accordance with document number 437, which also included the date of (27/12/2021) .

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