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COMPARATIVE ANALYSIS OF ORAL MUCOSAL PH IN ORAL LEUKOPLAKIA, ORAL LICHEN PLANUS, RECURRENT APHTHOUS STOMATITIS, AND HEALTHY SUBJECTS

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ABSTRACT:

BACKGROUND: Saliva is a complex fluid, which influences oral health through specific and nonspecific physical and chemical properties.Saliva plays a major role in maintaining the neutrality of the pH in oral cavity. Alterations in salivary pH and flow can be affected by various pathological and physiological conditions.Hence determining the pH at the local site is essential to know the progression of the condition.Oral leukoplakia is defined as essentially an oral mucosal white lesion that cannot be considered as any other definable lesion with an increased risk of malignant transformation. Oral lichen planus (OLP) is a chronic mucocutaneous disorder of stratified squamous epithelium of uncertain etiology that affects oral and genital mucous membranes, skin, nails, and scalp. Recurrent aphthous ulcer is a self limiting painful mucosal condition which is often preceded by a prodromal burning sensation lasting for 24-48 hours.The management of such cases can be challenging,Hence determining the mucosal pH can be helpful as an Early Diagnostic Biomarker.
Aim: To Compare mucosal pH in patients with Oral leukoplakia,Oral lichen planus and Recurrent aphthous ulcers with healthy individuals.
Objectives: The purpose of this study has two aspects a) to determine the differences in mucosal pH in patients with Oral Leukoplakia,Oral Lichen planus and Recurrent aphthous ulcers and healthy individuals and b) if mucosal pH can be used as an early diagnostic biomarker.
Materials and Methods: The study included pH strips to access mucosal pH in 20 Oral leukoplakia patients , 20 Oral Lichen Planus , 10 Recurrent aphthous Stomatitis and 20 Healthy individuals(controls). We are permitted to take subjects from the Department Of Oral Medicine And Radiology based on our inclusion and exclusion criteria and the subjects are explained about the study. The pH strip is wetted with the saliva and is compared with the standard pH index.
Results: The analyzed data showed statistically significant differences in the mean pH of patients with OLP, OL and RAS patients when compared to that of the normal healthy controls. It also showed significant difference when all the subjects were compared with Gender and Age(p value = 0.0270 and 0.0029 respectively).In pairwise comparisons of RAS with OL and OLP there is a significant difference with p values 0.0034 and 0.0081 respectively. Comparison of 4 groups with mean pH showed a significant p value of 0.0142.
Conclusion: Mucosal pH plays a significant role in maintaining equilibrium of oral health. Therefore, its alteration may indirectly affect the disease and its treatment outcomes.

Keywords: Oral mucosal pH, Oral Lichen Planus, Oral Leukoplakia, Recurrent Aphthous Stomatitis.

1. INTRODUCTION

The oral mucosa, covered with stratified squamous epithelium, acts as a physical barrier to pathogens and provides a flexible protective covering for structures beneath it. Another distinctive feature of the oral mucosa is the presence of saliva, which plays a critical role in the maintenance of oral health (1). Saliva lubricates and protects the oral mucosa, has antibacterial activity, and its buffering action maintains tooth integrity. Hence, the salivary flow rate of saliva, the hydrogen ion concentration (pH), buffering capacity, and microflora influence the balance of oral health (2). The role of pH equilibrium and the development of dental caries has been well established (3). However, not many studies have been conducted regarding the pH of saliva and its theoretical association with the development of oral lesions or symptoms related to it. Yosipovitch G et al. believed that the change in the pH of saliva can cause irritation and stimulate neural receptors (4). Therefore, evaluation of oral pH at the local site is important to know and explain the symptomatology and progression of oral lesions. Moreover, physical and chemical determination of saliva can be effectively performed as a chairside investigation at a dental office, thus making it a useful tool in oral health assessment (5).

Lichen planus (LP) is a chronic inflammatory mucocutaneous T cell mediated disease that affects the skin, oral mucosa (oral lichen planus or OLP), genital mucosa, scalp, and nails. Lichen planus affects 0.02% to 1.2% of the world's population (7). Though it can be seen at any age, most cases occur between the ages of 30 and 60 years, with female predominance (8). OLP causes a negative impact on oral functions because of severe oral mucosal soreness, including burning and itching sensations, especially on food intake (9).

Oral leukoplakia is defined as a predominantly white lesion of the oral mucosa that cannot be characterized as any other definable lesion. This disorder can be further divided into a homogeneous and a nonhomogeneous type. The development of oral leukoplakia as premalignant lesions involves different genetic events. Most oral leukoplakias are seen in patients over the age of 50 and infrequently encountered below the age of 30. In population studies, leukoplakias are more common in men but a slight majority for women was found in reviews of referred materials. The typical homogeneous leukoplakia is clinically characterized as a white, well-demarcated plaque with an identical reaction pattern throughout the entire lesion. The nonhomogeneous type of oral leukoplakia may have white patches or plaque intermixed with red tissue elements. Due to the combined appearance of white and red areas, the nonhomogeneous oral leukoplakia has also been called erythroleukoplakia and speckled leukoplakia. Oral leukoplakia is a lesion with an increased risk of malignant transformation, which has great implications for the management of this oral mucosal disorder. Until biomarkers are developed, management of oral leukoplakias has to rely on traditional clinical and histopathologic criteria.

Recurrent Aphthous Stomatitis is a disorder characterized by recurring ulcers confined to the oral mucosa in patients with no other signs of disease. RAS is classified accord-ing to clinical characteristics: minor ulcers, major ulcers, and herpetiform ulcers. The major factors presently linked to RAS include genetic factors, hematologic deficiencies, immunologic abnor-malities, and local factors, such as trauma and smoking. More recent research has centered on dysfunction of the mucosal cytokine network. Most patients with RAS have between two and six lesions at each episode and experience several episodes a year. The disease is an annoyance for the majority of patients with mild RAS, but it can be disabling for patients with severe frequent lesions, especially those classified as major aphthous ulcers.

Management of certain cases is challenging due to multifactorial reasons. Therefore, probing for a factor that may cause alterations in the characteristics of lichen planus, leukoplakia and Recurrent Aphthous Stomatitis is important. Very few studies have been conducted concerning the changes in the salivary parameters and OLP, Oral Leukoplakia, RAS. The pH of saliva is

one such salivary parameter that needs to be explored in patients with OLP, Oral Leukoplakia and RAS as not many studies have been conducted to compare the pH of saliva and OLP, Oral Leukoplakia and RAS. Literature is scarce on the influence of pH in the occurrence, progression, and response to the treatment of OLP, Oral Leukoplakia and RAS which may leave behind an important aspect in the management of resistant cases. Moreover, the pH strip is readily available, economical, non-invasive, easy, and a patient-friendly method to evaluate the pH chairside. Hence, this comparative study aims to assess and compare the mucosal pH of saliva in patients with OLP, Oral Leukoplakia, RAS and a normal control group.

Aims and Objectives

This study aims to compare the oral mucosal pH levels in patients with Oral Lichen Planus, Oral leukoplakia and Recurrent Aphthous Stomatitis. The objectives of the study were:

a) to determine the differences in mucosal pH in patients with Oral Leukoplakia,Oral Lichen planus and Recurrent aphthous ulcers and healthy individuals

b) if mucosal pH can be used as an early diagnostic biomarker.

c) To compare the difference between the mucosal pH of healthy oral mucosa and oral mucosa affected by Oral Lichen Planus, Oral Leukoplakia and Recurrent Aphthous Stomatitis

2. SUBJECTS AND METHODS

This comparative study was carried out on 71 subjects; 20 subjects each in two groups which include Oral Lichen Planus and Healthy Individuals. 21 and 10 subjects in two groups which include Oral Leukoplakia and Recurrent Aphthous Stomatitis respectively. Institutional ethical clearance was taken (KIDS/IEC/2020/205). All the participants were explained about the procedure involved in the study. Procedures were performed after obtaining written informed consent from the participants.

Inclusion Criteria:

- Study group: 20 Patients clinically diagnosed with Oral Lichen Planus (based on WHO criteria), with no history of previous treatment, with an age range of 20 to 70 were included in the study, 20 Patients clinically diagnosed with Oral Leukoplakia (based on WHO criteria), with no history of previous treatment, with an age range of 20 t o 70 were included in the study, 10 Patients clinically diagnosed with Recurrent Aphthous Stomatitis (based on WHO criteria), with no history of previous treatment, with an age range of 20 to 70 were included in the study,
- Control group: 20 healthy volunteers with no history of habits and any significant medical history were included in the study.

Exclusion Criteria:

- Patients suffering from salivary gland disorders (such as autoimmune salivary gland diseases, irradiation, infections of salivary glands, developmental diseases, dehydration), that can affect flow of saliva (for the control group)
- Patients who are on medications such as nonsteroidal analgesics (diflunisal, ibuprofen, naproxen, and piroxicam), anorexigens and anti-parkinson's that can affect salivary parameters (for the control group)
- Patients who declined to provide consent for the study.

Criteria to Diagnose OLP (WHO Criteria): OLP was diagnosed based on clinical criteria by the presence of fine radiating lines on the mucosa, surrounded by an erythematous border or

presence of erosions/ ulcerations with an erythematous zone that is surrounded by white lacy lines.

Materials Used in This Study: A set of diagnostic instruments which includes kidney tray, mouth mirror, straight probe, tweezer, and commercially available pH strip (Figure 1)
Procedure: All the patients were explained about the procedure. Patient was abstained from eating or drinking 2 hours prior to the examination. For the OLP study group, clinical symptoms, duration, VAS scale for burning sensation, medical history, and the type of OLP were recorded. For the Oral Leukoplakia and RAS study group, clinical symptoms, duration, medical history, and the type of the lesion were recorded. After which, the pH strip was directly placed on the lesion to determine mucosal pH. If a patient had lesions on multiple areas, the most severe lesion was considered. The strip was kept on the lesion until the strip covers and is wetted completely by the saliva in that region, which was approximately 30 seconds. The color of the pH strip thus changed was compared and analyzed with the standard pH color given by the manufacturer to determine the pH of that area. For the control group, the procedure was repeated in a similar manner. Two researchers separately analyzed the color change and conferred the pH value. Any difference of opinion was discussed and the finalized pH value was decided after mutual agreement.

Determining pH: pH was determined using commercially available pH strips (amiciKart® universal pH test paper). This test paper can determine the pH of fluids ranging from 1 to 14, depending on the color change of the strip. This strip is compatible for determining the pH of urine, water or saliva. Principle of this strip is that a color change occurs when an acid or base accepts or donates a proton in the media to be tested. Therefore, depending on the salivary characteristics, the strip color changes indicating the pH.

Statistics:
Collected data was compiled in excel sheet 2010 version in a separate data sheet for control and study groups respectively, followed by data analysis using SPSS version 23 software. Pearson Chi square correlation test was performed to see the correlation between age and pH, gender and pH. One way ANOVA test was performed to compare the four groups with mean pH value. Pairwise comparisons were done by Tukey's multiple post hoc procedures. Kruskal Wallis ANOVA was performed to compare age groups with pH values and Clinical stages with pH values associated with OLP, Oral Leukoplakia and RAS. Mann-Whitney test was performed to compare the gender with pH values associated with OLP, Oral Leukoplakia and RAS. Mann-Whitney test was performed to compare the significant association between smoking and pH values associated with Oral leukoplakia. Association between age groups and gender with status of smoking in the Oral Leukoplakia group were recorded. Individual test was performed to compare sites with pH values in the OLP and Oral Leukoplakia group.

3. RESULTS

71 patients with an age range of 20 to 70 were included in this study as participants for the estimation of mucosal pH, as per our inclusion and exclusion criterias for the control and study groups respectively. For the case groups 40 patients consisting of clinically diagnosed cases of OLP, Oral Leukoplakia and 10 patients consisting of clinically diagnosed cases of RAS were included. For the control group 20 patients with no significant medical history and habit history were included.

Age

The control group had 20 participants, with 10 (50%) males and 10 (50%) females, with a mean age of 43.05 years. The Oral Lichen Planus study group had 20 participants, with 05 males (71.43%) and 15 females (75%), with a mean age of 49.70 $\pm$ 13.09. The Oral Leukoplakia study group had 20 participants, with 15 males (71.43%) and 06 females (28.57%), with a mean age of 51.14 $\pm$ 9.76. Similarly, the Recurrent Aphthous Stomatitis study group had 10 participants, with 4 males (40.00%) and 06 females (60.00%), with a mean age of 31.80 $\pm$ 16.13. In the Oral Lichen Planus group, there is a statistically significant difference between age and mucosal pH. In the Oral Leukoplakia group, Recurrent Aphthous Stomatitis and control group there were no statistically significant differences between age and salivary pH.

Gender

A total of 38 females participated in the four groups, accounting for 53.52%, of which 29 (76.31%) had an acidic pH, 05 (13.15%) had an optimal pH, and 4 (10.52%) had an alkaline pH .A total of 33 male participants were included, accounting for (46.47%) of the study population, of which 23(69.69%) were in the acidic range, with 5 (15.15%) and 5 (15.15%) for the optimal and alkaline pH, respectively. To check the correlation of gender with pH, a Chi-square test was performed. The number of female participants was greater, and there is significant difference in the pH values among the genders when all the groups are compared. In the Oral Leukoplakia study group based on the type of Oral Leukoplakia, the most common type was the Homogenous leukoplakia in males (60.0%) and the incidence of homogenous and non homogenous types is same in females of both groups (50.0%). In the Oral Lichen Planus study group based on the type of OLP, the most common type was the Erosive type (60.0%) and the least common type was the papular in females (13.33%). The most and least common types of OLP in males are erosive, ulcerative (50.0%) and reticular (20.0%) respectively. In the Recurrent Aphthous Stomatitis study group based on the type of RAS, the most and least common type in females are Minor (66.66%) and Major (33.33%) respectively. In males the incidence of both major and minor types are equal.

Site:

To determine site-specific variations of salivary pH in the control group, different intraoral sites including buccal mucosa, floor of the mouth, gingiva and dorsum of the tongue were selected. The buccal mucosa accounted for 34 (82.93%) of the 71 sites, with the tongue, floor of the mouth and gingiva accounting for 1 (2.44%) each. In the control group, all the sites showed optimal pH in 10 (50%) of participants, followed by 1(0.05%) and 9 (45.00%) of participants with a pH towards acidity and alkalinity . In our OLP study group it most frequently seen in the buccal mucosa (16, 72.72%), followed by the tongue (5, 22.72%) and gingiva (1, 4.5%). The most common forms of OLP were found to be erosive 55.0%, followed by reticular 25.0% and with the least common being the papular and ulcerative types at 10.0% in each. In the study group, acidic pH was found to be predominant in OLP, affecting gingiva, buccal mucosa, and retro-commissural areas. Whereas the buccal mucosa showed acidic pH scores ranging from 2,3 & 4 in 6(30.0%), 7(35.5%) & 4(20.0%) individuals respectively. Similarly the tongue showed the values of 2 , 3 in 3 (15.0%) , 2(10.0%) individuals respectively. In the Oral Leukoplakia study group it is most frequently seen in the buccal mucosa (17, 80.95%), followed by the tongue (4, 19.04%). In our Oral Leukoplakia study group, the most common forms of Oral Leukoplakia were found to be homogenous type 57.14%, followed by non homogenous 42.85%. In the OralLeukoplakia study group, acidic pH was found to be predominant, affecting buccal mucosa and the tongue. Whereas the buccal mucosa showed acidic pH scores ranging from 2,3 & 4 in 4(19.04%), 6(28.57%) & 7(33.33%) individuals respectively. Similarly the tongue showed the values of 2 , 3 in 2 (9.5%) , 2(9.5%)

individuals respectively. In the Recurrent Aphthous Stomatitis study group the most frequently involved type in our study is Minor RAS (n=6), followed by the major type (n=4). In this study group, acidic pH was found to be predominant in RAS which showed acidic pH scores ranging from 2 & 3 in 6(60.0%) & 4(40.0%) individuals respectively.

Duration, Symptoms, Habit, Medical History

In the present study, 26 (52.2%) patients reported having a burning sensation for a period less than three months, and 24 (48.0%) had moderate symptoms. Among them, only 4 (8.0%) had a history of adverse habits. There was no statistically significant association between the type of OLP,OL and RAS and the presence of medical history.

Medical History

In the study group, 18 (36.0%) of the patients had one or more medical histories, and 32 (64.0%) were without any significant medical history. Those participants with medical history had the erosive and ulcerative types of OLP as the most prevalent form, and the reticular and papular types of OLP as the least prevalent form. However, there was no statistically significant association between the oral conditions(OL & RAS) and the presence of medical history.

Treatment

In our study, all the patients with OLP were treated with topical triamcinolone 0.1%, clobetasol 0.05%, prednisolone 5mg, 10mg, 20mg, or a combination of these. And in OL, patients were treated with Candid cream and in Severe cases they were given Retinol-A and were recalled every two weeks. RAS patients were treated with Multivitamins and thorough clinical and hematological record were kept where patients were treated for underlying conditions such as anemia and were recalled for every two weeks.

pH

The mean pH in the control group was found to be 7,40$\pm$0.60 and in the Oral Lichen Planus, Oral Leukoplakia and Recurrent Aphthous Stomatitis study group was found to be 2.85$\pm$0.75, 3.10$\pm$0.77, 2.40$\pm$0.52 respectively. Independent sample analyses were performed to see the mean difference in the mucosal pH of the healthy oral mucosa and the oral mucosa affected by OLP, Oral Leukoplakia and Recurrent Aphthous Stomatitis. There was a significant mean difference in the mucosal pH between the study and control group as the p value was 0.05.

Tables

Table: Comparison of four groups with age

Age groups	**Oral Leukoplakia**	**%**	**Oral lichen planus**	**%**	**Recurrent aphthous stomatitis**	**%**	**Control**	**%**	**Total**	**%**
<=30yrs	1	4.76	2	10.00	6	60.00	7	35.00	16	22.54
31-40yrs	4	19.05	3	15.00	1	10.00	2	10.00	10	14.08
41-50yrs	6	28.57	5	25.00	1	10.00	2	10.00	14	19.72
51-60yrs	7	33.33	8	40.00	2	20.00	6	30.00	23	32.39

>=61yrs	3	14.29	2	10.00	0	0.00	3	15.00	8	11.27
Total	21	100.0	20	100.0	10	100.0	20	100.0	71	100.0
Chi-square=17.6820, p=0.1260										

Figure: Comparison of four groups with age

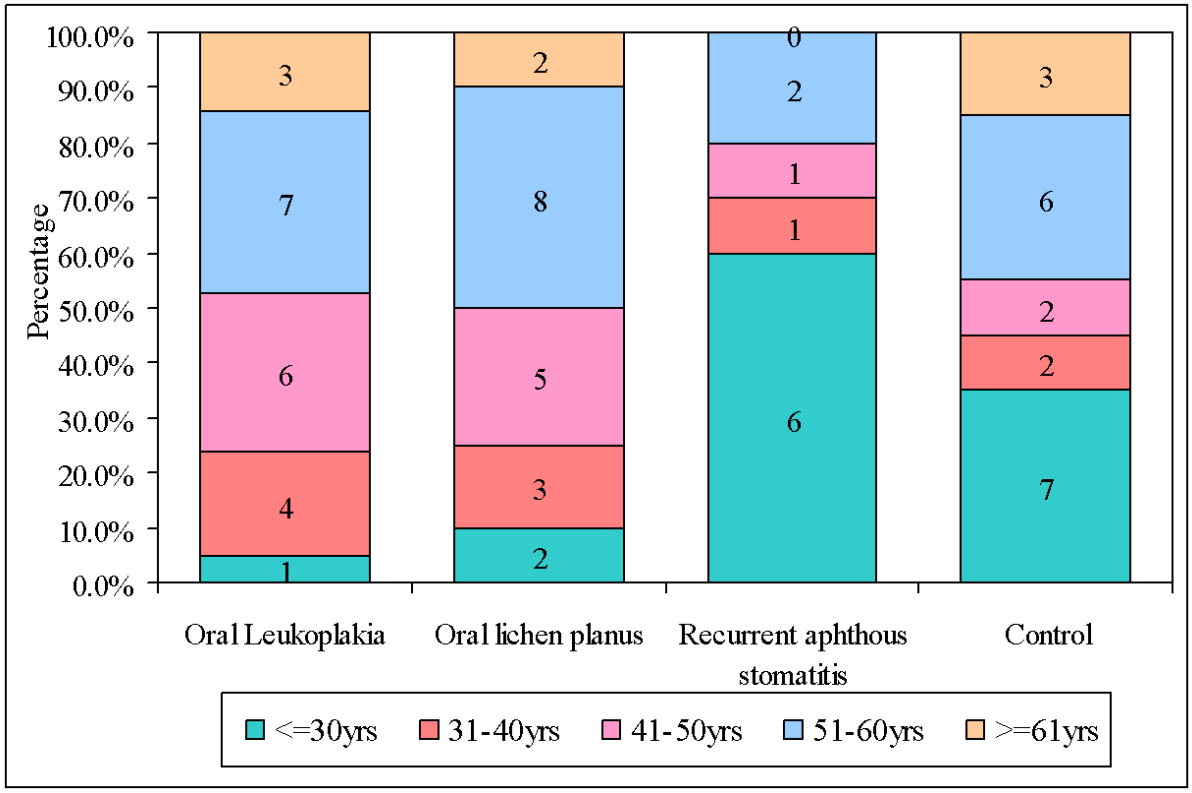

Table: Comparison of four groups with gender

Gender	**Oral Leukoplakia**	**%**	**Oral lichen planus**	**%**	**Recurrent aphthous stomatitis**	**%**	**Control**	**%**	**Total**	**%**
Male	15	71.43	5	25.00	4	40.00	10	50.00	34	47.89
Female	6	28.57	15	75.00	6	60.00	10	50.00	37	52.11
Total	21	100.0	20	100.0	10	100.0	20	100.0	71	100.0
Chi-square=9.1470, p=0.0270*										

*p<0.05

Figure: Comparison of four groups with gender

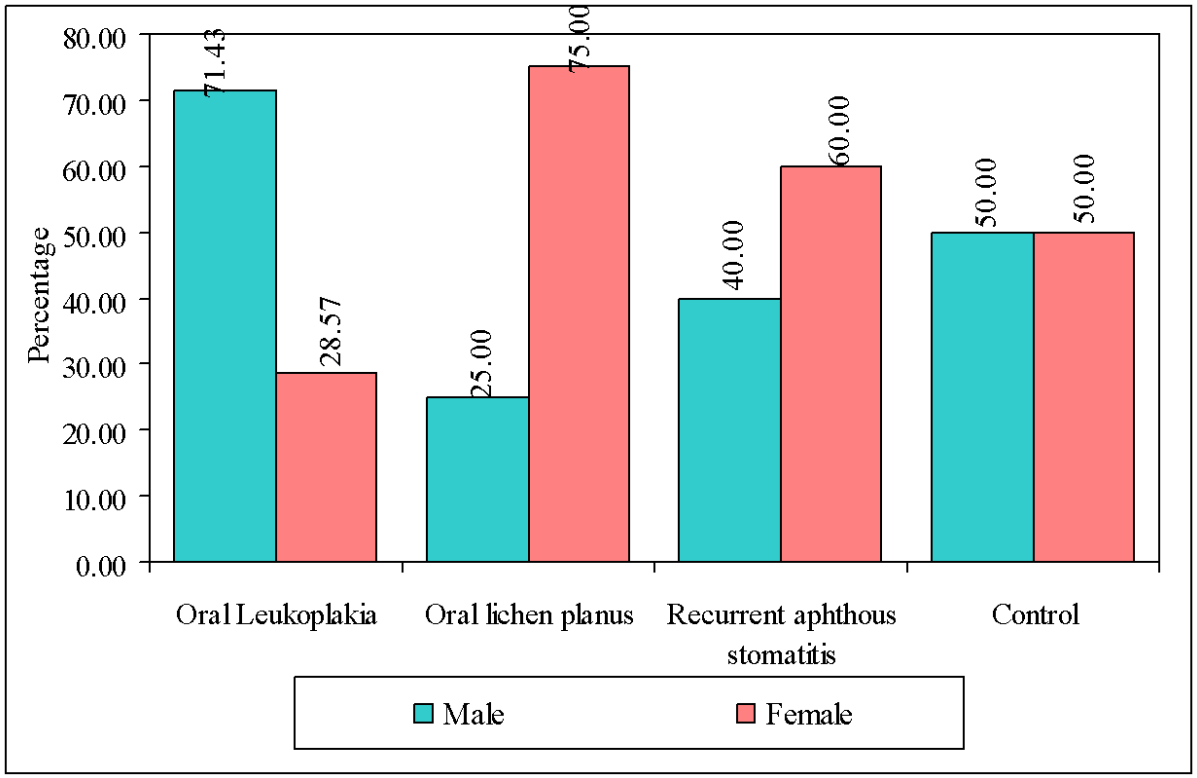

Table: Comparison of four groups with mean age by one way ANOVA

Groups	**Mean**	**Std.Dev.**
Oral Leukoplakia	51.14	9.76
Oral lichen planus	49.70	13.09
Recurrent aphthous stomatitis	31.80	16.13
Control	43.05	17.10
Total	45.73	15.15
F-value	5.1554	
p-value	0.0029*	
Pair wise comparisons by Tukeys multiple posthoc procedures		
Oral Leukoplakia vs Oral lichen planus	p=0.9875	
Oral Leukoplakia vs Recurrent aphthous stomatitis	p=0.0034*	
Oral Leukoplakia vs Control	p=0.2572	
Oral lichen planus vs Recurrent aphthous stomatitis	p=0.0081*	
Oral lichen planus vs Control	p=0.4396	
Recurrent aphthous stomatitis vs Control	p=0.1701	

*p<0.05

Figure: Comparison of four groups with mean age

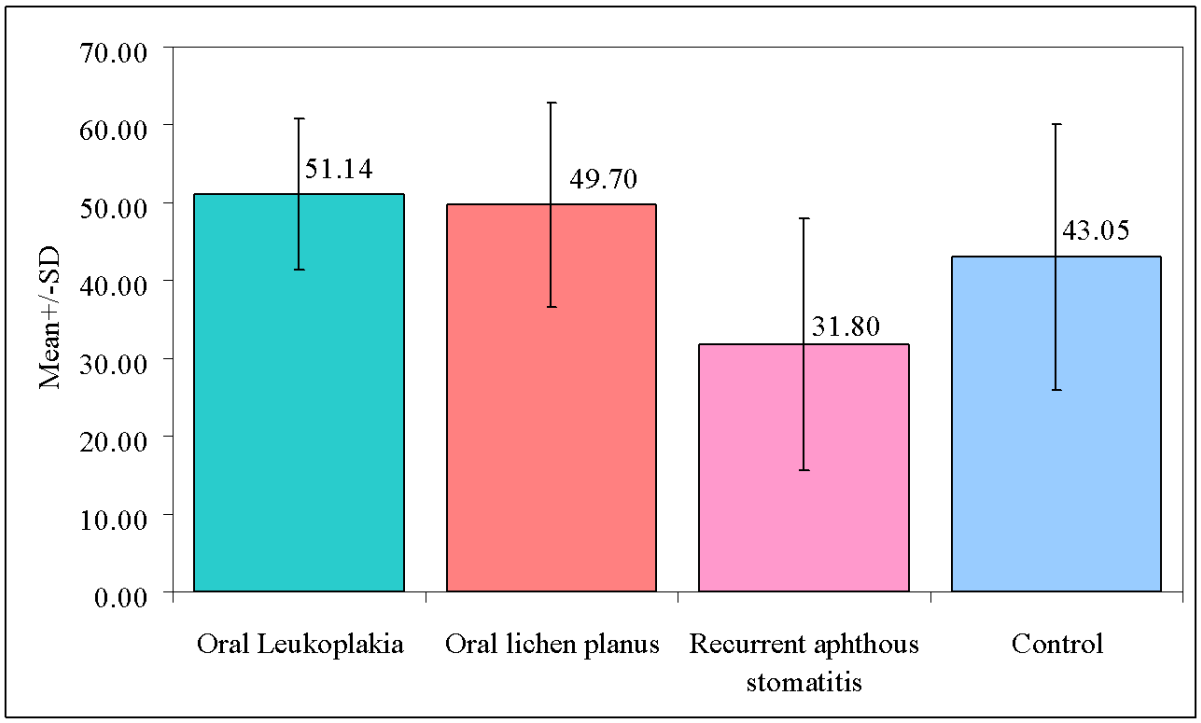

Table: Comparison of three groups with types

Types	Oral Leukoplakia	%	Oral lichen planus	%	Recurrent aphthous stomatitis	%	Total	%
Homogenous Leukoplakia	12	57.14	0	0.00	0	0.00	12	23.53
Non Homogenous Leukoplakia	3	14.29	0	0.00	0	0.00	3	5.88
Speckled Leukoplakia	6	28.57	0	0.00	0	0.00	6	11.76
Erosive Lichen Planus	0	0.00	11	55.00	0	0.00	11	21.57
Papular Lichen Planus	0	0.00	2	10.00	0	0.00	2	3.92
Reticular Lichen Planus	0	0.00	5	25.00	0	0.00	5	9.80
Ulcerative Lichen Planus	0	0.00	2	10.00	0	0.00	2	3.92
Major Recurrent Aphthous Stomatitis	0	0.00	0	0.00	4	40.00	4	7.84
Minor Recurrent Aphthous Stomatitis	0	0.00	0	0.00	6	60.00	6	11.76

Total	21	100.0	20	100.0	10	100.0	51	100.00

Table: Comparison of two groups with sites

Sites	**Oral Leukoplakia**	**%**	**Oral lichen planus**	**%**	**Total**	**%**
Buccal mucosa	18	85.71	16	80.00	34	82.93
Dorsum of the tongue	0	0.00	1	5.00	1	2.44
Floor of the mouth	1	4.76	0	0.00	1	2.44
Gingiva	0	0.00	1	5.00	1	2.44
Total	21	100.0	20	100.0	41	100.00

Figure: Comparison of two groups with sites

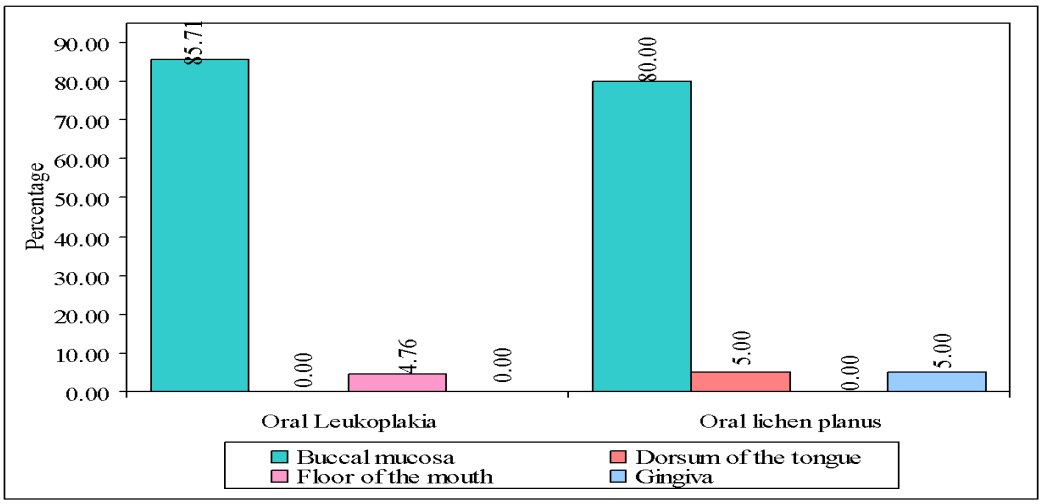

Table: Comparison of four groups with mean pH value by one way ANOVA

Groups	**Mean**	**Std.Dev.**
Oral Leukoplakia	3.10	0.77
Oral lichen planus	2.85	0.75
Recurrent aphthous stomatitis	2.40	0.52
Control	7.40	0.60
Total	4.14	2.17
F-value	211.6123	
p-value	0.0001*	
Pair wise comparisons by Tukeys multiple posthoc procedures		
Oral Leukoplakia vs Oral lichen planus	p=0.6641	
Oral Leukoplakia vs Recurrent aphthous stomatitis	p=0.0499*	
Oral Leukoplakia vs Control	p=0.0002*	
Oral lichen planus vs Recurrent aphthous stomatitis	p=0.3355	
Oral lichen planus vs Control	p=0.0002*	
Recurrent aphthous stomatitis vs Control	p=0.0002*	

*p<0.05

Figure: Comparison of four groups with mean pH value

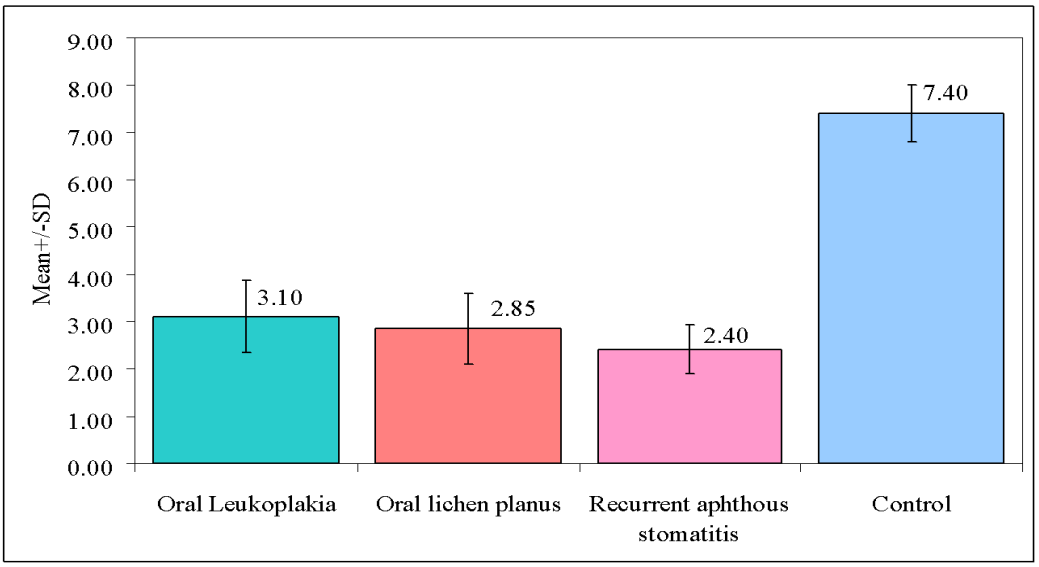

Figure: Comparison of age groups with pH values in Oral Leukoplakia group

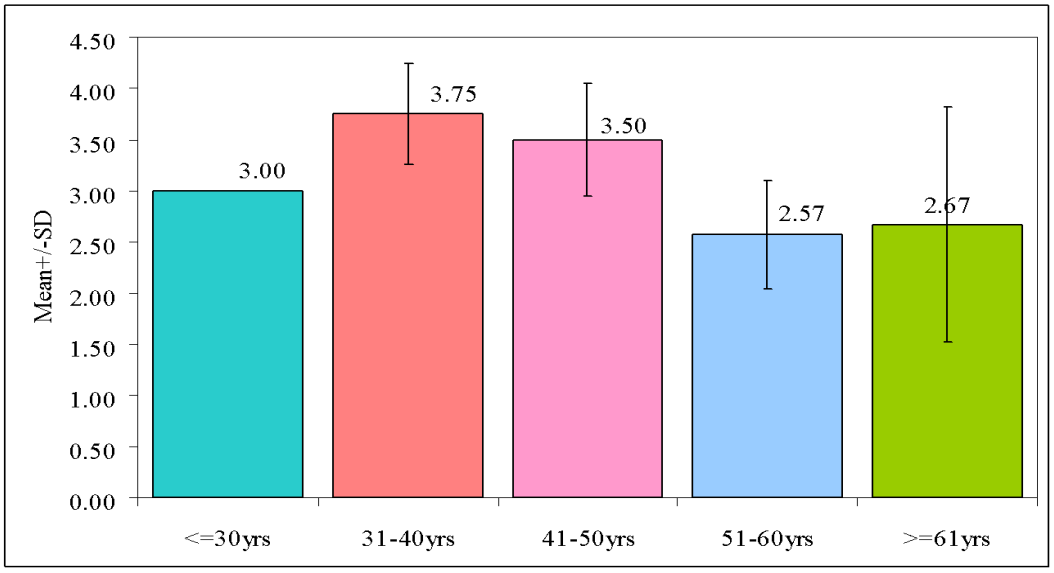

Table: Comparison of age groups with pH values in Oral Leukoplakia group by Kruskal Wallis ANOVA

Age groups	Means	Std.Dev.	Median	Mean ranks
<=30yrs	3.00	0.00	3.00	10.00
31-40yrs	3.75	0.50	4.00	16.00
41-50yrs	3.50	0.55	3.50	14.00
51-60yrs	2.57	0.53	3.00	7.00
>=61yrs	2.67	1.15	2.00	8.00
Total	3.10	0.77	3.00	
H-value	8.7500			
p-value	0.0680			

Table: Comparison of age groups with pH values in Oral lichen planus group by Kruskal Wallis ANOVA

Age groups	Means	Std.Dev.	Median	Mean ranks
<=30yrs	3.50	0.71	3.50	15.25
31-40yrs	3.33	0.58	3.00	14.17
41-50yrs	2.80	0.45	3.00	10.40
51-60yrs	2.25	0.46	2.00	6.00
>=61yrs	4.00	0.00	4.00	18.50
Total	2.85	0.75	3.00	
H-value	12.4732			
p-value	0.0142*			

*p<0.05

Figure: Comparison of age groups with pH values in Oral lichen planus group

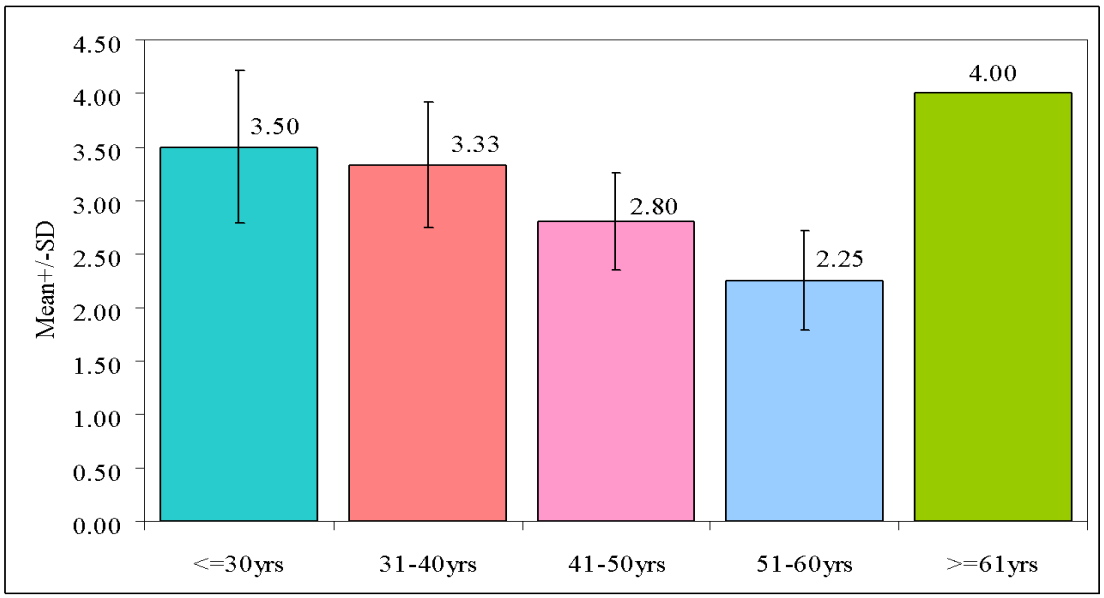

Table: Comparison of age groups with pH values in Recurrent Aphthous Stomatitis group by Kruskal Wallis ANOVA

Age groups	Means	Std.Dev.	Median	Mean ranks
<=30yrs	2.33	0.52	2.00	5.17
31-40yrs	3.00	0.00	3.00	8.50
41-50yrs	2.00	0.00	2.00	3.50
51-60yrs	2.50	0.71	2.50	6.00
>=61yrs	-	-	-	-
Total	2.40	0.52	2.00	
H-value	2.1250			
p-value	0.5469			

Figure: Comparison of age groups with pH values in Recurrent Aphthous Stomatitis group

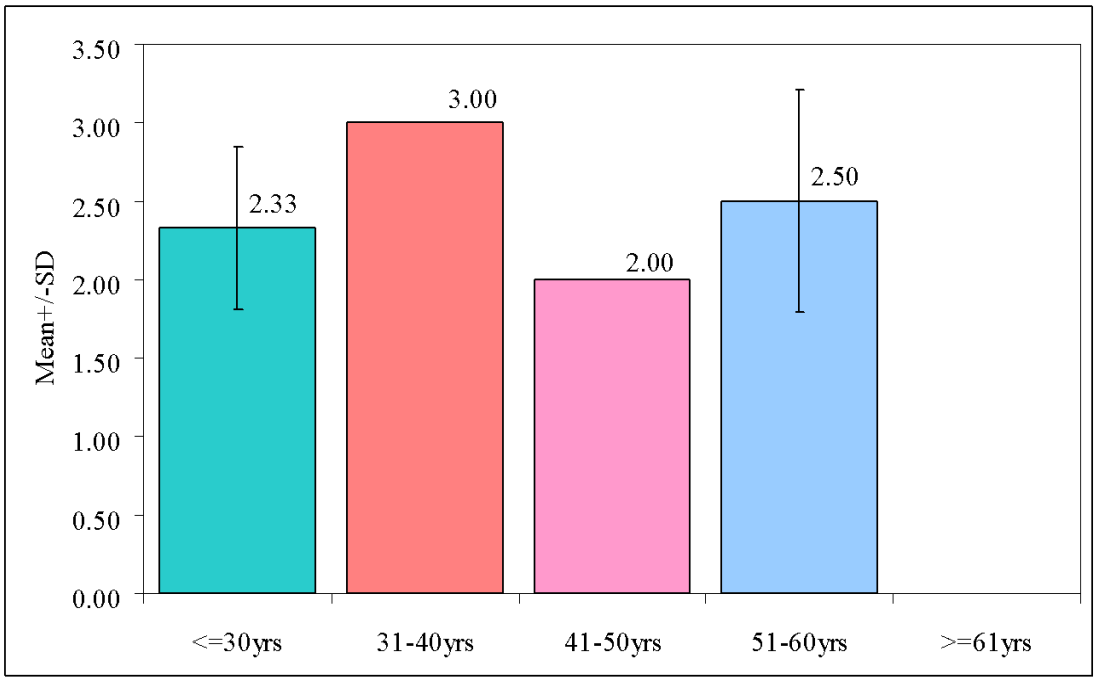

Table: Comparison of gender with pH values in Oral Leukoplakia group by Mann-Whitney U test

Gender	Means	Std.Dev.	Median	Mean ranks
Male	2.93	0.80	3.00	9.80
Female	3.50	0.55	3.50	14.00
Total	3.10	0.77	3.00	
Z-value	-1.3624			
p-value	0.1731			

Figure: Comparison of gender with pH values in Oral Leukoplakia group

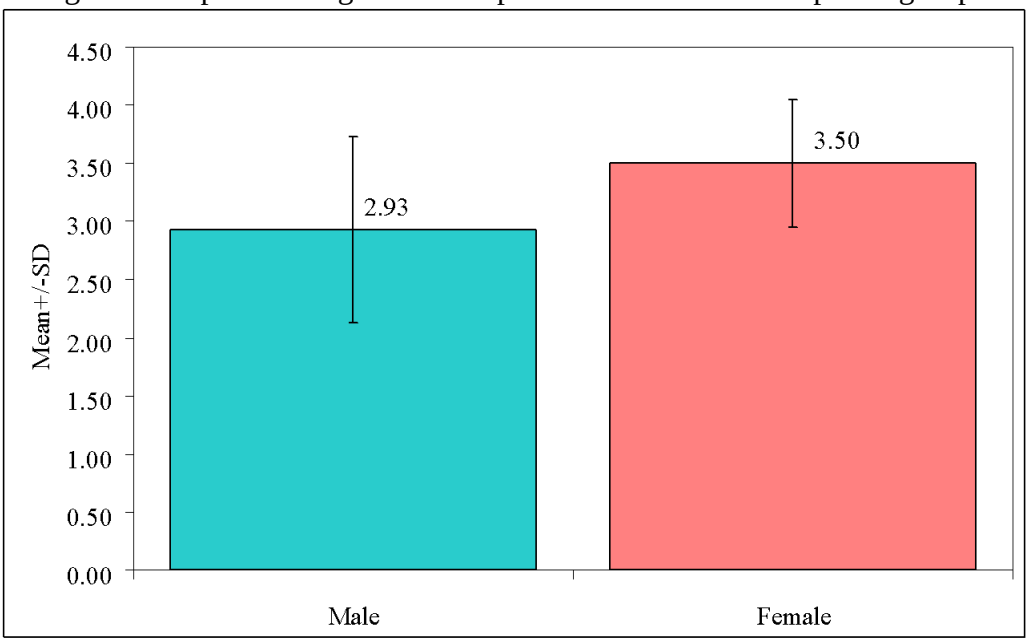

Table: Comparison of Gender with pH values in Oral lichen planus group by Mann-Whitney U test

Gender	Means	Std.Dev.	Median	Mean ranks
Male	2.60	0.89	2.00	8.50
Female	2.93	0.70	3.00	11.17
Total	2.85	0.75	3.00	
Z-value	-0.8292			
p-value	0.4070			

Figure: Comparison of Gender with pH values in Oral lichen planus group

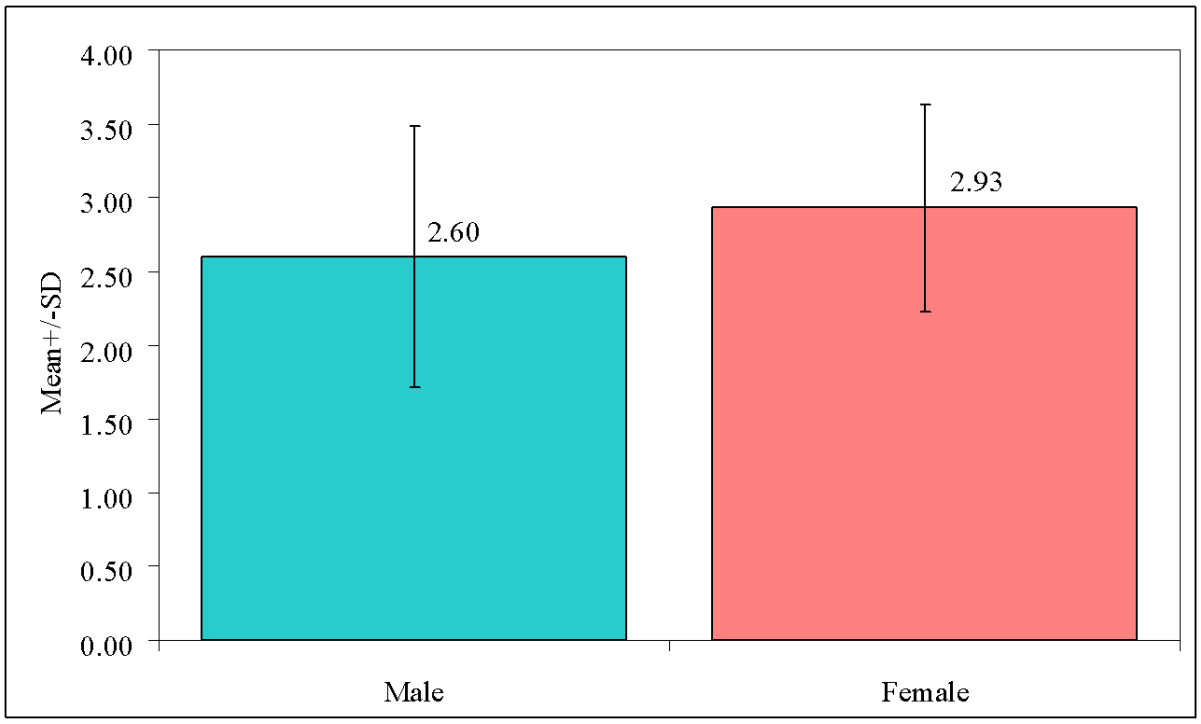

Table: Comparison of Gender with pH values in Recurrent Aphthous Stomatitis group by Mann-Whitney U test

Gender	Means	Std.Dev.	Median	Mean ranks
Male	2.50	0.58	2.50	6.00
Female	2.33	0.52	2.00	5.17
Total	2.40	0.52	2.00	
Z-value	0.3198			
p-value	0.7491			

Figure: Comparison of Gender with pH values in Recurrent Aphthous Stomatitis group

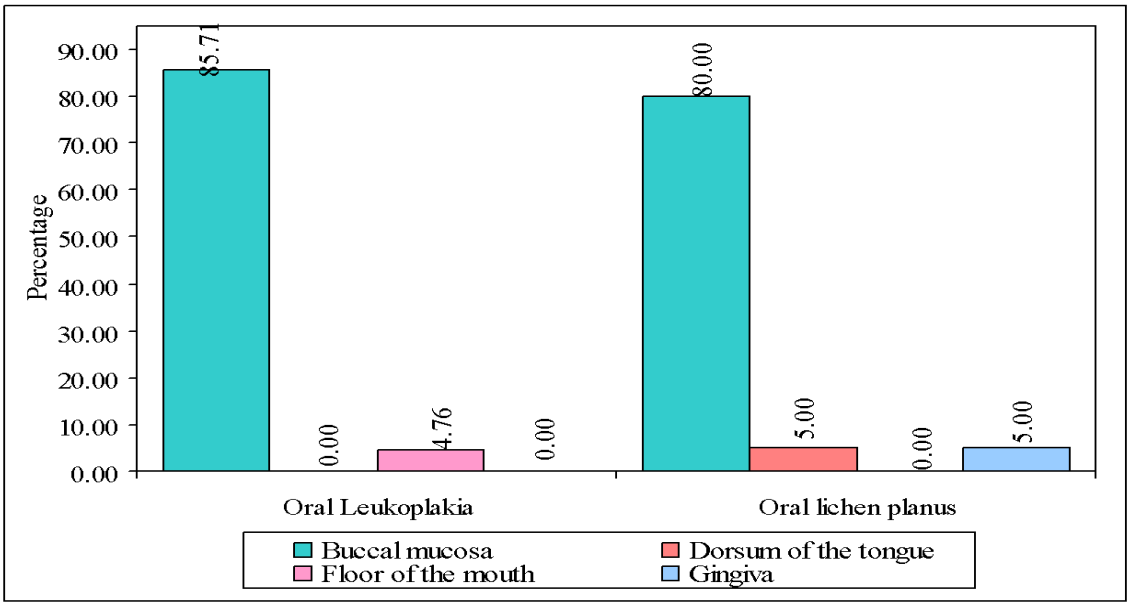

Figure: Association between age groups with status of smoking in Oral Leukoplakia group

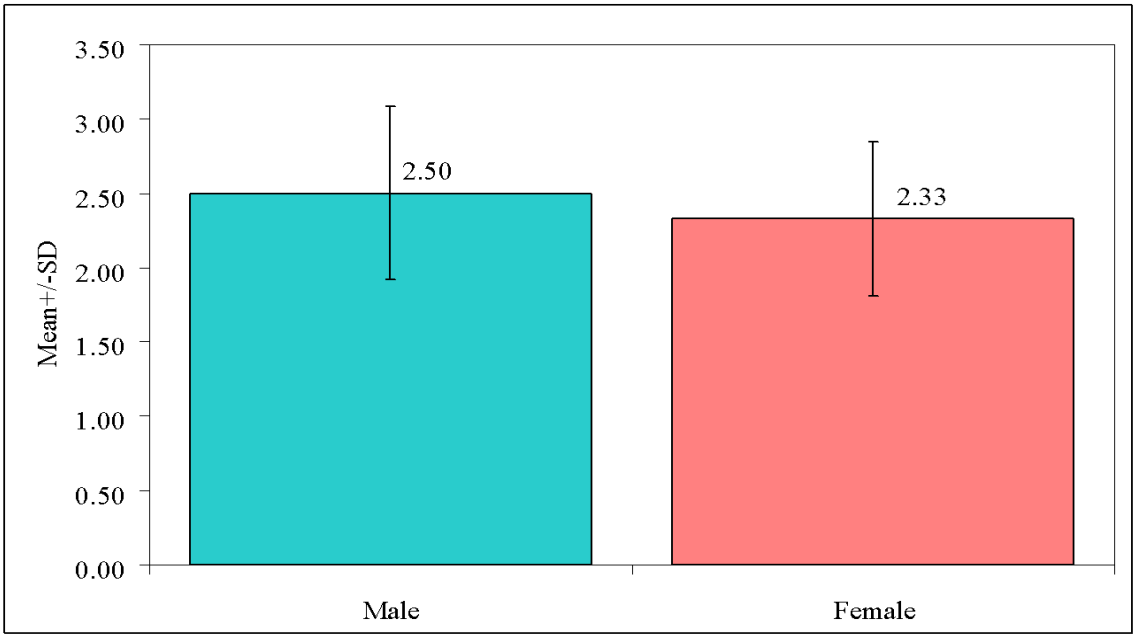

Table: Association between age groups with status of smoking in Oral Leukoplakia group

Age groups	Smokers	%	Non-smokers	%	Total	%
<=30yrs	1	10.00	0	0.00	1	4.76
31-40yrs	0	0.00	4	36.36	4	19.05
41-50yrs	0	0.00	6	54.55	6	28.57
51-60yrs	6	60.00	1	9.09	7	33.33
>=61yrs	3	30.00	0	0.00	3	14.29
Total	10	100.00	11	100.00	21	100.00

Table: Comparison of Clinical stages with pH values in Oral Leukoplakia group by Kruskal Wallis ANOVA

Clinical stages	Means	Std.Dev.	Median	Mean ranks
Homogenous Leukoplakia	3.17	0.72	3.00	11.50
Non Homogenous Leukoplakia	4.00	0.00	4.00	18.00
Speckled Leukoplakia	2.50	0.55	2.50	6.50
H-value	8.0804			
p-value	0.0176			

Figure: Comparison of Clinical stages with pH values in Oral Leukoplakia group

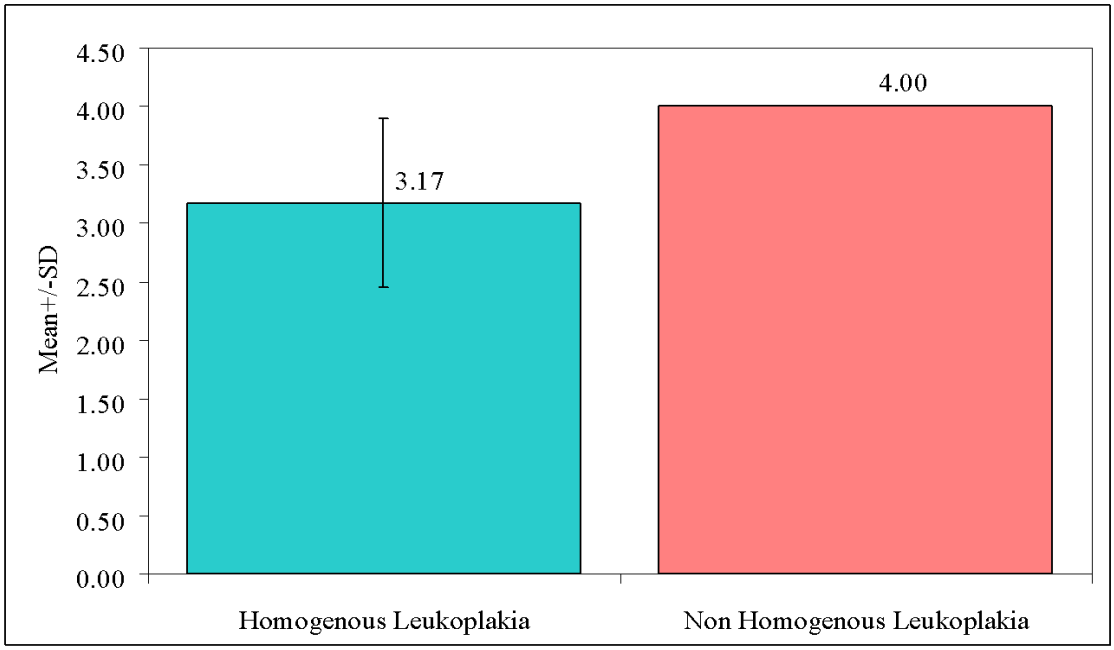

Table: Comparison of Clinical stages with pH values in Oral lichen planus group by Kruskal Wallis ANOVA

Clinical stages	Means	Std.Dev.	Median	Mean ranks
Erosive Lichen Planus	2.82	0.75	3.00	10.27
Reticular Lichen Planus	3.40	0.55	3.00	14.60
Papular Lichen Planus	2.50	0.71	2.50	8.00
Ulcerative Lichen Planus	2.00	0.00	2.00	4.00
H-value	6.0328			
p-value	0.1100			

Figure: Comparison of Clinical stages with pH values in Oral lichen planus group

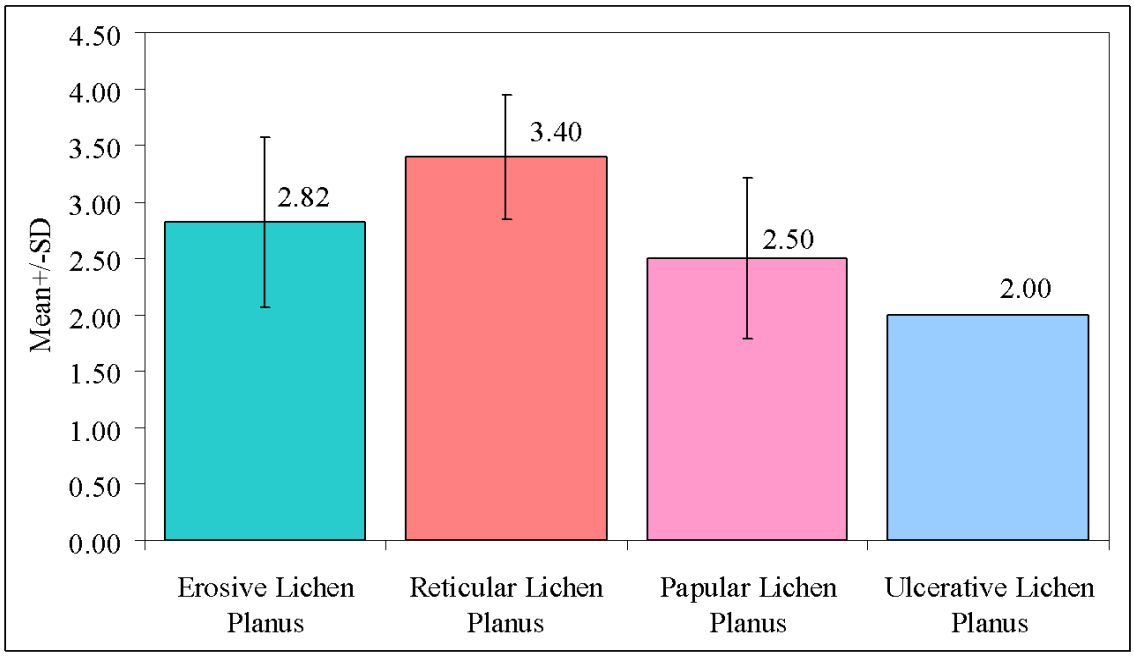

Table: Comparison of Clinical stages with pH values in Recurrent Aphthous Stomatitis group by Mann-Whitney U test

Clinical stages	**Means**	**Std.Dev.**	**Median**	**Mean ranks**
Major Recurrent Aphthous Stomatitis	2.00	0.00	2.00	3.50
Major Recurrent Aphthous Stomatitis	2.67	0.52	3.00	6.83
Z-value	-1.5990			
p-value	0.1098			

Figure: Comparison of Clinical stages with pH values in Recurrent Aphthous Stomatitis group

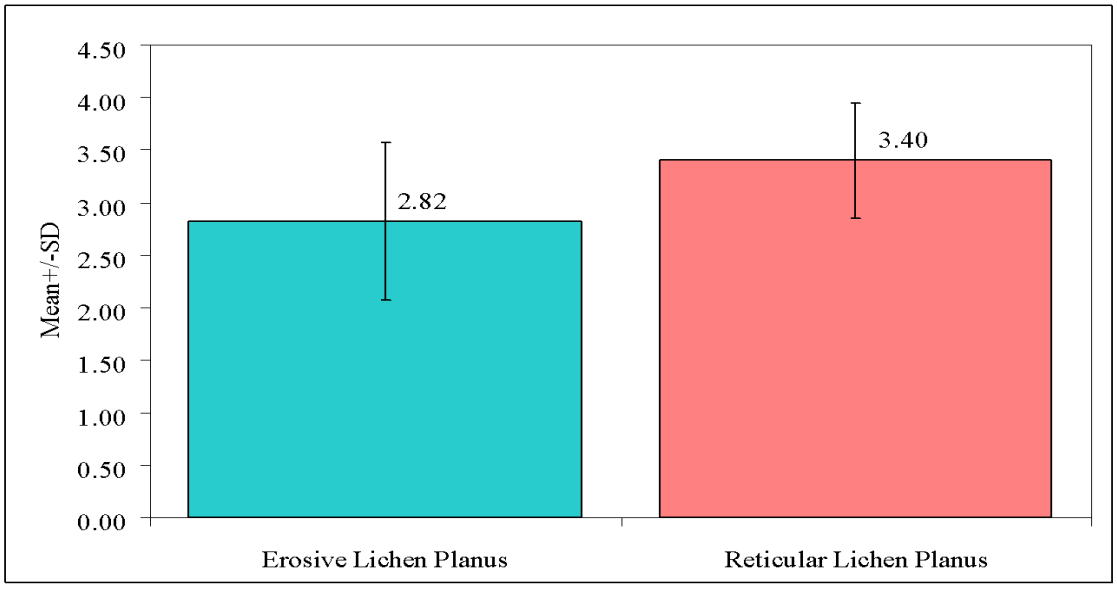

Table: Association between gender with status of smoking in Oral Leukoplakia group

Gender	Smokers	%	Non-smokers	%	Total	%
Male	10	100.00	5	45.45	15	71.43
Female	0	0.00	6	54.55	6	28.57
Total	10	100.00	11	100.00	21	100.00
Chi-square=7.6364, p=0.0057*						

*p<0.05

Figure: Association between gender with status of smoking in Oral Leukoplakia group

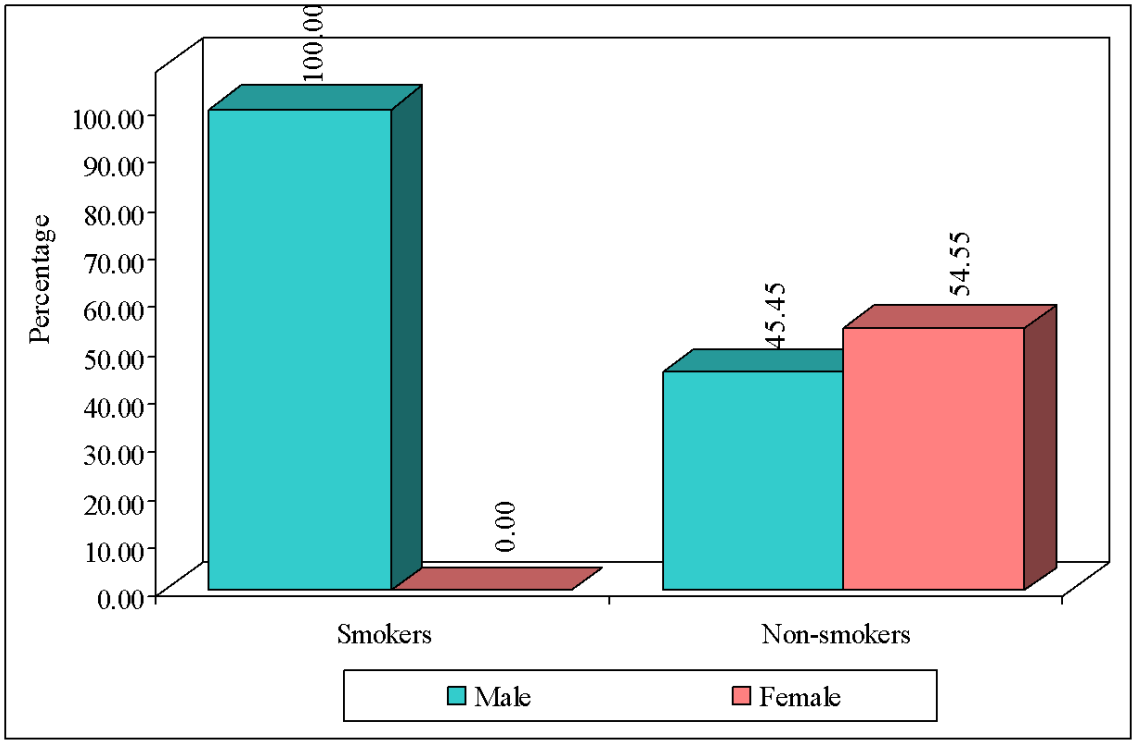

Table: Comparison of status of smoking with pH values in Oral Leukoplakia group by Mann-Whitney U test

Status of smoking	Means	Std.Dev.	Median	Mean ranks
Smokers	2.60	0.70	2.50	7.30
Non-smokers	3.55	0.52	4.00	14.36
Total	3.10	0.77	3.00	
Z-value	-2.5703			
p-value	0.0102			

Figure: Comparison of status of smoking with pH values in Oral Leukoplakia group

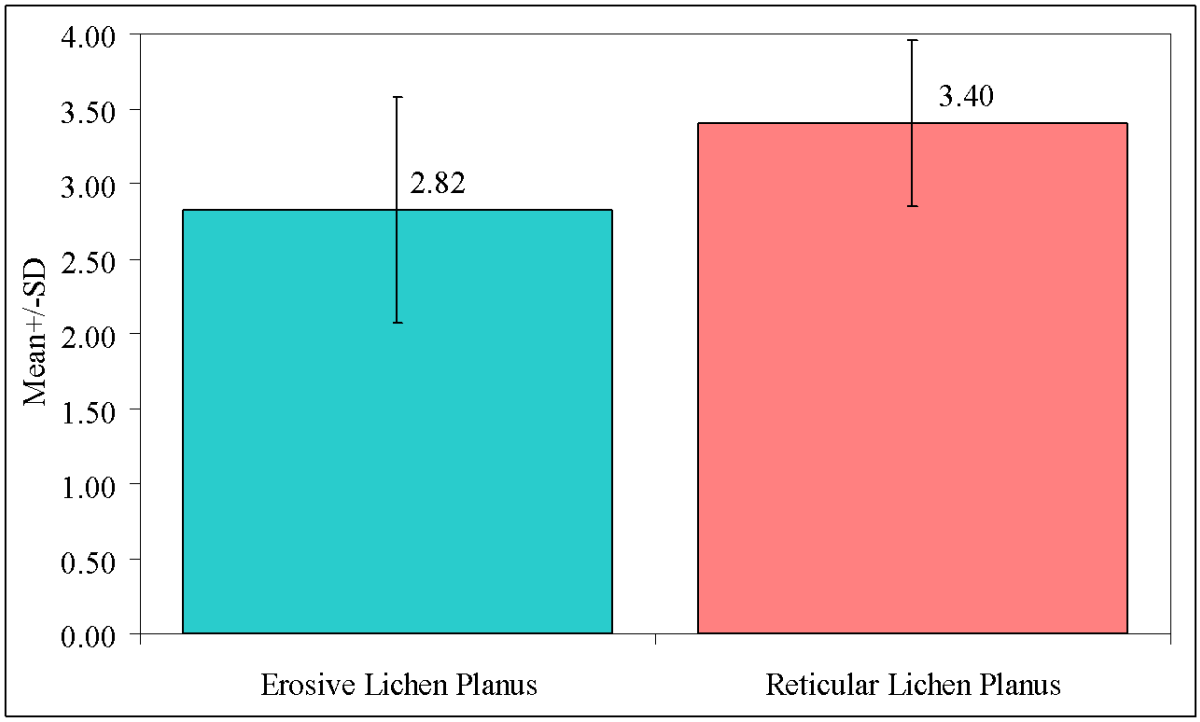

Table: Comparison of sites with pH values in Oral Leukoplakia group

Site	n	Mean	SD	Median
Buccal mucosa	18	3.2	0.8	3.0
Tongue	2	3.0	0.0	3.0
Floor of the mouth	1	2.0	0.0	2.0

Table: Comparison of sites with pH values in Oral lichen planus group

Site	n	Mean	SD	Median
Buccal mucosa	16	2.94	0.77	3.00
Tongue	2	2.50	0.71	2.50
Gingiva	1	3.00	0.00	3.00
Dorsum of the tongue	1	2.00	0.00	2.00

4. DISCUSSION

The etiology of OLP remains unclear, but it begins due to apoptosis of oral epithelial cells initiated by CD8+ T cells. According to Lundström IM et al, impaired salivary gland function may reduce mucous membrane protection, which could further influence the progression of OLP in the presence of an external stimuli. An alteration in the pH of saliva, which is maintained in homeostasis by the salivary glands, is one such change. Hence, we conducted this study to assess the alteration of pH in patients with OLP. Oral leukoplakia (OL) is the most frequent potentially malignant disorder of oral mucosa. Although OL has been mentioned in clinical reviews since 1969 (2), it was first defined by the World Health Organization in 1978 (3) as a white patch or plaque which cannot otherwise be characterized clinically or pathologically as any other disease. Downer and Petti reported that the annual malignant conversion incidence rate of leukoplakia was found to be between 6.2 and 29.1 cases per 100,000 people. In other study by the authors, Martorell-Calatayud et al determined the prevalence of leukoplakia to be in the range of 0.4% to 0.7%, whereas Feller et al. estimated

the prevalence towards higher range of 0.5% to 3.46%.9 Furthermore, the same study concluded that the malignant transformation rate of leukoplakia ranged from 0.7% to 2.9%. In one more study by Brouns et al showed the prevalence and annual malignant transformation is 2% and 1% respectively.9 The prevalence increases with increasing age.9 In general the reported prevalence ranges between 0.2 % and 5%, with exceptional differences in various regions of the globe: India (0.2-4.9%), Sweden (3.6%), Germany (1.6%), and Holland (1.4%). Recurrent aphthous stomatitis (RAS) is the most common oral mucosal disease in the general population (5% to 60% in different study groups). RAS is characterized by multiple recurrent round or ovoid inflammatory ulcerations with circumscribed margins, erythematous haloes, and yellow or gray floors (Jurge et al. 2006). RAS causes considerable pain, can interfere with oral functions (eating, speech, toothbrushing), and can thereby have a negative impact on quality of life (Al-Omiri et al. 2014).Studies have shown that the influence of various factors including stress, systemic diseases such as diabetes and hypertension, hypersensitivity to dental materials such as amalgams, drugs, hepatitis C virus, and genetic predisposition is known to modify the disease progression, severity, and the treatment response. However local factors such as saliva also may greatly influence disease outcome**.**

Our study assessed various parameters such as pH in 20 OLP, 21 OL and 10 RAS patients and 20 healthy controls along with symptoms, clinical characteristics, the presence or absence of systemic diseases or habits, and the treatment provided for patients with OLP, OL and RAS. OLP was most common in the age group of 45.22$\pm$11.803 years in our study. Whereas OL and RAS were most common in the age group of 51.14$\pm$9.76 years and 31.80$\pm$16.13 years respectively. González-Moles M discovered that the prevalence of OLP rises progressively and significantly after the age of 40 years in a meta-analysis of the global incidence of OLP ($p > 0.001$) (12). A study conducted by BK Gandara et al. stated that there were no significant statistical differences in age-related salivary flow rates among the patients with OLP and healthy controls (13). According to a study conducted by Amith Kumar Singh et al, the OL was highly prevalent in the fifth decade of life. However, our study showed an insignificant association between age and pH alterations in both study and control groups.

A study conducted by Jornet PL et al showed that the majority of the study group included in their study were females, which reflects OLP to be a more female predilection disease which is in agreement to various literatures. A review of Ana Contreras et al states that Oral leukoplakia is more commonly found in men 40 years of age or older [1], with higher prevalence in men and women over 70 [10]. The result of the study conducted by R Prithi and Sreedevi Dharman was that, out of 300 individuals, females were 71.3% and males were 30.6% affected by aphthous ulcer. The recurrence rate in females was 47.6% and male was 21.3%. However in our study, there was no significant association between the gender predilection and pH values of OLP, OL and RAS(15). But there is a significant p value of 0.0270 when the pH values are compared among the four groups with gender predominance.

The most common forms of OLP, OL and RAS in our study were Erosive OLP, Homogenous OL and Minor RAS. This was similar to a 4-year follow-up study by Rimkevicius A et al. in which the most prevalent forms were the reticular and ulcerative forms. However, there was no significant association between the form of OLP and local or systemic risk factors (15). In our study, 36% of patients with OLP had one or more systemic disorders, which was statistically insignificant. Similar results were obtained by Daye M et al., who found 60% of OLP patients with systemic diseases and found it statistically insignificant. Furthermore, they did not find any correlation between the severity of OLP and the presence or absence of systemic diseases. However, Krishnamoorthy et al. and Baykal et al found more involvement

of OLP with systemic disorders (16, 17, 18). Salivary buffering capacity depends on the amount of acid and bases present in the secreted saliva, and bicarbonate is the principal buffering agent. Bicarbonate's secretion increases as the salivary flow rate increases (19). Bonda PLF et al. found statistically significant decreased salivary flow rate and altered pH in patients with oral lesions when compared to patients without oral lesions. In their study, a decreased flow rate of 0.336 mL/min, and an increased pH of 6.69 were seen in their study. Though in this study, alteration of pH was noted in patients with oral lesions, the pH obtained was less than that of our study. This could be due, the presence of underlying systemic diseases such as hypertension and deleterious habits such as smoking, which are associated with oral lesions and could influence the pH greatly in their study. In our study, patients with a known habit history were limited, which could be the foremost reason for selecting only OLP patients, whereas in their study, other oral lesions were also considered (20).

Yosipovitch G et al. found a higher palatal pH in the control group when compared to the pH of the buccal mucosa, lip, or tongue. In our study, the mean pH of the control group was 7.40, without any site-specific difference in pH. Moreover, Yosipovitch G et al. found higher palatal pH in comparison with other sites and other lesions in patients with OLP (4). Osterberg et al believed that the higher the salivary flow rate, the higher the salivary mucosal pH (21). But the palatal salivary flow is less compared to the other areas, hence Yosipovitch G et al implied that salivary flow rate may not be the single factor determining pH. Although saliva encompasses the entire oral cavity, additional local elements such as oxidative stress, microbial flora, food intake, oral hygiene status, and mechanical and chemical stimulants, influence its characteristics and pH. Psychological disorders, neurological deficits, metabolic, hormonal, and nutritional imbalances all contribute to the altered oral pH, which may have a significant impact on oral lesions (22). Furthermore, the thickness of the salivary coating in the oral cavity might vary between 72 and 100 microns depending on its location in the oral cavity. This thickness is a balance between salivary secretion and fluid loss that may occur in the process of deglutition, mucosal absorption, and evaporation. OLP is an inflammatory disorder that can cause fluid imbalance. For example, atrophy and ulcers in OLP, can impact the fluid lubrication, absorption, and evaporation (23, 24). Shih-Wei Yang et al conducted a Retrospective Cohort Study of Oral Leukoplakia in Female Patients and stated that the predilection site of oral leukoplakia in male patients was buccal mucosa ($p = 0.0001$) and that for women patients was tongue ($p = 0.033$). The etiology of oral leukoplakia is multifactorial, and many causes are idiopathic. The most commonly associated risk factor is the use of tobacco in either smoke or smokeless form.In a study conducted by N. Prashanthi , the results showed that reduced Salivary flow rate and pH has a correlation with Oral Leukoplakia which is one of the potentially malignant disorders and oral cancer. Positive correlation was found between the flow rate and pH in recurrent oral ulcer patients in a study conducted by Mustafa Al-Ahmad et al. They also stated that patients with recurrent oral ulcers had higher flow rate and pH compared to the control group. These effects were exaggerated in female patients with ulcers

Numerous studies have indicated that pH changes can be seen in a variety of oral conditions and disorders. For chronic gingivitis and periodontitis, Baliga S et al. found alkaline pH (7.24 ± 0.010) and acidic pH (6.85 ± 0.11), respectively, while the control group's pH was 7.06 ± 0.04, which was statistically significant (25). Kumar CN et al. discovered significantly acidic pH in patients with chronic periodontitis who smoked compared to healthy volunteers and proposed that salivary pH can be used as a salivary biomarker (26)Sahu RK discovered altered pH in arecanut and tobacco chewers, which may predispose oral mucosa to toxic effects (27)Salivary flow rate and pH are altered in chronic gutkha chewers due to the release of harmful chemicals into the saliva. A prospective case-control study found a statistically significant reduction in

salivary pH in OSMF patients (28). However, Abdul Khader NF observed increased and decreased salivary flow rates among areca nut chewers and OSMF patients, respectively, without any significant alteration in salivary pH in either category (29). In an observational study by Migliario M, a significantly lower pH was found in the first trimester of pregnancy in comparison with non-pregnant women, which was attributed to acidity as a result of emetic phenomena (30). It is well established that pH below 5.5 is considered a critical pH, which is prone to the demineralization of enamel and the development of dental caries. Pyati SA observed a significant salivary pH reduction along with decreased salivary flow rate and increased total antioxidant activity in caries active children. (31). In case of OLP Free radicals cause oxidative damage, thus found to be important in the pathogenesis of OLP, and oxidant-antioxidant status in patients with OLP is an efficient and non-invasive marker to determine OLP progression. Darczuk D et al found significantly decreased total antioxidant capacity in OLP patients (32). Also, salivary antioxidant capacity acts as a defense mechanism against many oral diseases, including OLP (33). MUCHANDI S et al compared salivary antioxidant capacity and pH of saliva in caries free and active children. It was found that the antioxidant property of saliva is in an indirect relationship with the pH of saliva (34). In our study, pH in OLP patients was higher as compared to the control group, thus correlating with the decreased antioxidant capacity of saliva in OLP patients.

The causes of oral leukoplakia is multifactorial, some well known and identified such as tobacco, ill-fitted dentures ,Nutritional deficiency(Vitamin A, B complex, C, E and Beta-carotene deficiency), bacterial infections, Epstein Barr virus (EBV) and Candida species and some extracts of herbal plants. Local Factors such as Tobacco which is the main etiologic agent for leukoplakia. It is available in two forms: smoked and smokeless. The smoked form contains carbon monoxide, thiocyanate, hydrogen cyanide, nicotine and the metabolites of these constituents whereas smokeless tobacco contains nitrosamine, polycyclic aromatic hydrocarbons and nitrosoproline. The chemical constituents of tobacco and its combustion end products as tars and resins are irritating substances capable of causing leukoplakia. Over 300 carcinogens have been identified in tobacco smoke or in its water-soluble components which can be expected to leach into saliva. Other local factors such as Alcohol: It seems to have a strong synergistic effect with tobacco relative to oral cancer production and Sanguinaria which is a herbal extract used in the toothpaste and mouth rinse. It can cause true leukoplakia. This type of leukoplakia is called sanguinaria-associated keratosis and is usually located in the maxillary vestibule or on the alveolar mucosa of the maxilla. Continuous trauma or local irritation in the oral cavity is suspected as a causative agent for leukoplakia. In a study conducted by Dr. Mukundh Chathanya & Dr. Uma Maheshwari.T, the results showed that there is a significant decrease in the mean pH of Saliva in patients with tobacco consumption as compared with non-users, though there are other studies that show in contrast, this study is done to prove the significance of salivary pH change in users of smokeless and smoking in patients with oral leukoplakia. Association analysis of mean pH of patients with oral leukoplakia and Type of leukoplakia shows no statistical significance.

Univariate analysis conducted by P.L. Foglio-Bonda, K. Brilli, F. Pattarino, A. Foglio-Bonda showed that the presence of lichen and leukoplakia in the oral cavity reduces the UWSFR(Unstimulated Whole Salivary Flow Rate) values. Also in classification analyses, oral lesion plays an important role in discretizing UWSFR “Pathological” group from the UWSFR “Normal” one.

Higher pH in Oral lesions may be associated with altered microbial flora or changes in the epithelial barrier, influencing disease characteristics. In our study, topical and/or low-dose systemic corticosteroids were employed to treat OLP cases. Al-Janaby H et al. investigated the effect of topical corticosteroids on mouth dryness before and after OLP therapy and discovered

that, while they reduced mouth dryness, they had no effect on salivary flow rates, unstimulated salivary pH, or buffering capacity (24).

5. CONCLUSION

In our study, we found a statistically significant difference in the mean pH of patients with OLP, OL & RAS and normal healthy controls and pH determination can be used as chairside salivary biomarker. Hence, in the management of OLP, OL and RAS, patients can be advised to refrain from food that greatly alters the salivary pH, increase their hydration to balance the alkalinity of the oral mucosa, and follow appropriate stress reduction protocols that could indirectly affect the local pH, which could markedly enhance the patient's perception towards such conditions and also aid in effective treatment.

Limitations

This study used pH strips rather than pH meters to determine pH as it was economical, patient-compatible, and an easy-to-use option. However, a commercially available portable pH metre provides an accuracy of up to 2 decimal points. Additionally our study did not include equal size of samples as we were unable to find RAS patients to assess within the limited time period. Furthermore, we were unable to assess post-treatment pH in these patients. pH determination and comparison of pre and post treatment of OLP, OL & RAS can be done to assess and compare if pH is affected by the treatment outcomes or if there is an effect of pH in resistant cases of OLP, OL & RAS. Moreover, the effect of stimulated and unstimulated pH on OLP, OL & RAS can also be determined to investigate if there is any effect on treatment outcomes.

Future Prospects

Further studies with larger and equal sample sizes and a comparison of mucosal pH between different types of oral conditions could serve a great benefit.

6. REFERENCES

1. Erdem V, Yildiz M, Erdem T. The Evaluation of Saliva Flow Rate, pH, Buffer Capacity, Microbiological Content and Indice of Decayed, Missing and Filled Teeth in Behçet's Patients. Balkan Med J 2013; 30; 211-4
2. Humphrey SP, Williamson RT. A review of saliva: Normal composition, flow, and funetion. J Prosthet Dent 2001;85:162-9
3. Sreebny LM. Saliva in health and disease: an apprasial and update. Int Dent Res 2000;50:140-61
4. Yosipovitch G, Kaplan I, Calderon S, David M, Chan YH, Weinberger A. Distribution of Mucosal pH on the Bucca, Tongue, Lips and Palate. Acta Derm Venereol 2001; 81: 178–80
5. Yang, S.-W., Lee, Y.-S., Wu, P.-W., Chang, L.-C., Hwang, C.-C. A Retrospective Cohort Study of Oral Leukoplakia in Female Patients—Analysis of Risk Factors Related to Treatment Outcomes. Int. J. Environ. Res. Public Health 2021, 18, 8319
6. Erugula, Sridhar Reddy, Mohammed Umar Farooq, Divya Jahagirdar, Chillamcherla Dhanalakshmi Srija, Swetha Meruva and Gude Venkata Naga Sai Pratap. "Oral Leukoplakia Etiology, Risk Factors, Molecular Pathogenesis, Prevention and Treatment: A Review." (2020).
7. Qin R, Sukhov A, Faze N. Oral Mucosa Biology and Salivary Biomarker. Clinics in Dermatology (2017), doi: 10.1016/j.clindermatol.2017.06.00.

8. Canto AM, Müller H, Freitas RR, da Silva Santos PS . Oral lichen planus (OLP): clinical and complementary diagnosis. An Bras Dermatol. 2010;85(5):669-75
9. Lanfranchi-Tizeira HE, Aguas SC, Sano SM. Malignant transformation of atypical oral lichen planus: a review of 32 cases. Med Oral 2003; 8: 2-9
10. Lehman JS, Tollefson MM, Gibson LE. Lichen planus. Int J Dermatol. 2009;48(7):682-694
11. Ismail SB, Kumar SKS, Zain RB. Oral lichen planus and lichenoid reactions: etiopathogenesis, diagnosis, management and malignant transformation. J Oral Sci. 2007;49:89-106
12. Gupta S, Jawanda MK. Oral Lichen Planus: An Update on Etiology, Pathogenesis, Clinical Presentation, Diagnosis and Management. Indian J Dermatol. 2015 May-Jun;60(3):222-9
13. Lundström IM, Anneroth KG, Bergstedt HF. Salivary gland function and changes in patients with oral lichen planus. Scand J Dent Res. 1982 Dec;90(6):443-58
14. 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 Dis. 2021 May;27(4):813-828
15. Gandara, Beatrice K. et al. "Age-related Salivary Flow Rate Changes in Controls and Patients with Oral Lichen Planus." *Journal of Dental Research* 64 (1985): 1149 – 1151
16. Jornet PL, Perez FP, Fuster AP. Association of autoimmune diseases with oral lichen planus: a cross sectional, clinical study. Eur Acad Dermat Vener 2013; 28:895-9.
17. Rimkevičius A, Aleksejūnienė J, Pūrienė A, Šeinin D, Rastenienė R. Oral lichen planus: a 4-year clinical follow-up study. Turk J Med Sci. 2017 Apr 18;47(2):514-522
18. Daye M, Temiz SA, Isık B. The relationship between lichen planus and metabolic syndrome. J Cosmet Dermatol. 2021 Aug;20(8):2635-2639. doi: 10.1111/jocd.13905. Epub 2020 Dec 28. PMID: 33355985.
19. Baykal L, Arıca DA, Yaylı S, et al. Prevalence of metabolic syndrome in patients with mucosal lichen planus: A case–control study. Am J Clin Dermatol. 2015;16(5):439-445
20. Krishnamoorthy B, Suma GN, Mamatha NS, Sowbhagya MB, Garlapati K. Lipid profile and metabolic syndrome status in patients with oral lichen planus, oral lichenoid reaction and healthy individuals attending a dental college in northern India-a descriptive study. J Clin Diag Res. 2014;8(11):ZC92
21. Zhang, C., Li, B., Zeng, X. *et al.* The global prevalence of oral leukoplakia: a systematic review and meta-analysis from 1996 to 2022. *BMC Oral Health* 23, 645 (2023). https://doi.org/10.1186/s12903-023-03342-y
22. Dr. Mukundh Chaithanya.V, Dr. Uma Maheswari.T.N. Assessment Of Salivary pH in Patients With Oral Leukoplakia (2020). JCR. 2020: 3364-3371. Volume 7 Issue-12
23. Wang P, Zhou Y, Zhu YH, Lin HC. Unstimulated and stimulated salivary characteristics of 12-13 year-old schoolchildren with and without dental erosion. Arch Oral Biol 2011; 56: 1328-1332
24. Hijazi K, Lowe T, Meharg C, Berry SH, Foley J, Hold GL. Mucosal microbiome in patients with recurrent aphthous stomatitis. J Dent Res. 2015 Mar;94(3 Suppl):87S-94S. doi: 10.1177/0022034514565458. Epub 2014 Dec 24. PMID: 25540188; PMCID: PMC4541092.
25. Porter SR, Leao JC. Review article: oral ulcers and its relevance to systemic disorders. Aliment Pharmacol Ther. 2005 Feb 15;21(4):295-306. doi: 10.1111/j.1365-2036.2005.02333.x. PMID: 15709981.
26. Bonda PLF, Pattarino BF, Bonda AF. Salivary flow rate and pH in patients with oral pathologies. Eur Rew Med Pharmacol Sci 2017; 21: 369-374

27. Osterberg T, Landahl S, Hedegard B. Salivary flow, saliva, pH man and buffering capacity in 70-year-old men and women. J Oral Rehabil 1984; 11: 157–170
28. Thelin WR, Brennan MT, Lockhart PB, et al. The oral mucosa as a therapeutic target for xerostomia. Oral Dis 2008; 14(8): 683-9
29. Zhang GH, Castro R. Role of oral mucosal fluid and electrolyte absorption and secretion in dry mouth. Chin J Dent Res 2015; 18(3): 135-54
30. Al-Janaby H, El-Sakka H, Masood M, Ashani W Mendis W, M Slack-Smith L, Parsons R, M Frydrych A. Xerostomia and Salivary Gland Hypofunction in Patients with Oral Lichen Planus Before and After Treatment with Topical Corticosteroids. Open Dent J. 2017 Mar 31;11:155-163.
31. Baliga S, Muglikar S, Kale R. Salivary pH: A diagnostic biomarker. J Indian Soc Periodontol. 2013 Jul;17(4):461-5
32. Kumar CN, Rao SM, Jethlia A, Linganna CS, Bhargava M, Palve DH. Assessment of salivary thiocyanate levels and pH in the saliva of smokers and nonsmokers with chronic periodontitis – A comparative study. Indian J Dent Res 2021;32:74-8
33. Sahu RK, Patro S, Nayak B, Bardhan D, Panda S, Rajguru JP. Habit-associated salivary pH changes in oral submucous fibrosis: A cross-sectional study. Natl J Maxillofac Surg. 2021 Jan-Apr;12(1):78-82.
34. Tamgadge P, Wasekar R, Kulkarni S, Chandran A, Jain S, Chalapathi K, et al. Comparative evaluation of alteration in salivary pH among gutkha chewers with and without oral submucous fibrosis and healthy subjects: A prospective case-control study. J Curr Oncol 2020;3:8-16
35. Abdul Khader NF, Dyasanoor S. Assessment of Salivary Flow Rate and pH Among Areca Nut Chewers and Oral Submucous Fibrosis Subjects: A Comparative Study. J Cancer Prev. 2015 Sep;20(3):208-15
36. Migliario M, Bindi M, Surico D, De Pedrini A, Minsenti S, Pezzotti F, Mele B, Foglio Bonda PL. Changes in salivary flow rate and pH in pregnancy. Eur Rev Med Pharmacol Sci. 2021 Feb;25(4):1804-1810
37. Pyati SA, Naveen Kumar R, Kumar V, Praveen Kumar NH, Parveen Reddy KM. Salivary Flow Rate, pH, Buffering Capacity, Total Protein, Oxidative Stress and Antioxidant Capacity in Children with and without Dental Caries. J Clin Pediatr Dent. 2018;42(6):445-449
38. Darczuk D, Krzysciak W, Vyhouskaya P, Kesek B, Galecka-Wanatowicz D, Lipska W, Kaczmarzyk T, Gluch-Lutwin M, Mordyl B, Chomyszyn-Gajewska M. Salivary oxidative status in patients with oral lichen planus. J Physiol Pharmacol. 2016 Dec;67(6):885-894
39. Aly DG, Shahin RS. Oxidative stress in lichen planus. Acta Dermatovenerol Alp Pannonica Adriat 2010;19:3-11.
40. Muchandi S, Walimbe H, Bijle MN, Nankar M, Chaturvedi S, Karekar P. Comparative evaluation and correlation of salivary total antioxidant capacity and salivary pH in caries-free and severe early childhood caries children. J Contemp Dent Pract. 2015 Mar 1;16(3):234-7.