

# Association Of Oral Lichen Planus And Thyroid Disease - A Case Control Study

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Running Title: Oral Lichen Planus and Thyroid disease correlation

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**Abstract :** *Introduction: Lichen planus, is a chronic autoimmune, mucocutaneous disease affecting the oral mucosa besides the skin, genital mucosa, scalp and nails. The exact etiology of oral lichen planus is unknown. The disease most commonly affects middle-aged females. Oral lichen planus usually presents as white striations (Wickham's striae), white papules, white plaque, atrophic, ulcerative, erosive or as blisters. There is a well established correlation between oral lichen planus and liver disease. Opinion amongst researchers vary on terminology of lichen planus and lichenoid drug reaction. Recent literature reported association between lichen planus and thyroid disease.*

*Aim: The main aim of this study is to evaluate the association between oral lichen planus and thyroid disease and its prevalence amongst patients visiting our dental institute.*

*Materials and methods: 67 case sheets of patients, diagnosed with oral lichen planus between June 2019 and March-2020 were retrieved from the electronic database. Collected data were entered into the Excel sheet and was analysed using SPSS analysis.*

*Results: Results showed a positive association between oral lichen planus and thyroid disease, mainly hypothyroidism (7.46%). Females were more affected than males (53.7%). The erosive variant of oral lichen planus was more prevalent among the study population (44.7%). There was a positive correlation between predominant clinical variety of Lichen planus and site involved. The positive correlation between hypothyroid state and lichen planus is also reported.*

*Conclusion: In conclusion, our study establishes an association between oral lichen planus and a coexisting thyroid disorder mainly hypothyroidism.*

*Keywords: Hypothyroidism, Lichen planus, Lichenoid reaction, Medication, Thyroid disease*

## 1. INTRODUCTION :

Oral lichen planus is a chronic, immune-mediated [1], inflammatory, mucocutaneous disease, affecting 0.5-2% of the general population [2],[3],[4]. It

is derived from the Greek word "leichen" means tree moss and Latin word "planus" means flat. Clinically, oral lichen planus is classified into seven forms: Atrophic, bullous, erosive, pigmented, plaque-like, or reticular. The patients with reticular lesions, the most common form, generally have no clinical symptoms, while atrophic, bullous, and erosive lesions cause pain<sup>[5],[6]</sup>, ranging from mild to severe. Notably, erosive oral lichen planus shows a significantly higher rate of malignant transformation than non erosive oral lichen planus<sup>[7]</sup>. Though there are theories that show that a complex series of immune-modulated events is responsible for OLP, the factor responsible for the etiology of oral lichen planus is unknown. Other factors like genetic background, stress, poor oral hygiene<sup>[8],[9],[10],[11]</sup>, Hepatitis C virus infection, smoking<sup>[12]</sup> are also found to be associated with oral lichen planus<sup>[13],[14],[15],[16],[17]</sup>. Among these factors, thyroid disease was considered to be a common factor observed among people<sup>[18]</sup>. Diagnosis of OLP is established either by clinical examination only or by clinical examination with histopathologic confirmation. Direct immunofluorescence examination is only used as an adjunct to the above method of diagnosis and to rule out specific autoimmune diseases such as pemphigus and pemphigoid. Early and accurate diagnosis of lichen planus plays an important role, since lichen planus lesions may undergo malignant transformation<sup>[19],[20],[21],[22],[23],[24],[25]</sup>.

Thyroid is a secretory organ secreting thyroid hormones, which are responsible for development, regeneration and metabolism<sup>[26]</sup>. Thyroid hormones (THs) play an important role in the physiology of humans. These hormones regulate human hematopoiesis in the bone marrow. The most common thyroid disorders include thyroid nodules, hypothyroidism, hyperthyroidism and autoimmune thyroid disease. Hypothyroidism and hyperthyroidism affect renal function by direct renal effects as well as metabolic and cardiovascular effects<sup>[27]</sup>. Thyroid disease is quite common, affecting majority of the adult female population and a smaller percentage of adult males. This gender-specific prevalence results from the underlying autoimmune mechanism for the most common forms of thyroid disease, which include both Graves' and Hashimoto's disease. With increase in age, specifically beyond the eighth decade of life, the male and female predilection becomes equal<sup>[28]</sup>. Limited literature is available on association between thyroid disease and lichen planus or the prevalence of lichen planus in patients with thyroid disease.

The main aim of this study is to determine the lichen planus - thyroid disease association and prevalence of oral lichen planus in patients with thyroid diseases.

## **2. MATERIALS AND METHODS:**

The study was set in University setting and Institutional Ethics Committee approval was obtained (ethical approval number SDC/SIHEC/2020/DIASDATA/0619-0320) and 67 case sheets of patients who underwent treatment for oral lichen planus between June 2019-March 2020 were retrieved from the oral medicine department<sup>[29]</sup>. The case sheets, clinical photographs, medical history, medication history, underlying thyroid disease if any was recorded. The data was analysed by 2 reviewers - the primary researcher and department faculty. Data collection was done by entering data into Microsoft Excel and then transferred into statistical package for Social Sciences (SPSS) software. The independent variables present in the study were age, sex, oral lichen planus variant and thyroid disease. The dependent variables were severity of lesion, presence of pain, duration and quality of living. The type of analysis used for this study was correlation and association.

## **3. RESULTS :**

Data of 67 patients with oral lichen planus were analysed in this study. Among the study population, the participants under age group 50-60 years were found to be highest (35.8%) (Graph-I). Females were (53.7%) found to be the highest among the gender distribution of

study population graph (Graph-II). Among oral lichen planus variant, erosive variant was found to be more prevalent among study population (46.2%) (Graph-III) and was more common among females (29.8%) (Graph-V) with buccal mucosa being most involved site (44.7%) (Graph-VI). Buccal mucosa was the most commonly observed site of all oral lichen planus variants among the study population (71.6%) (Graph-IV). It was also observed that (7.46%) of OLP patients with hypothyroidism (Graph-VII). Chi square analysis reported a positive correlation between oral lichen planus clinical type, site and coexisting thyroid disorder.

#### 4. DISCUSSION:

Oral lichen planus is known as autoimmune mucocutaneous disease and it is more common among females. The findings of this study, where females affected were 53.7%, also were similar to previous studies by Tak MM et al.<sup>[30]</sup>, Xue JL et al.<sup>[31]</sup> and Brown RS et al.<sup>[32]</sup>, where it was shown that oral lichen planus was more prevalent among women than in men. This was contradictory to the findings of studies by Zhou T et al.<sup>[33]</sup> and Munde A et al.<sup>[34]</sup>, where males were found to be affected by oral lichen planus. In this study, patients affected by oral lichen planus were under the age group 50-60 years. Similar results were observed in previous studies by Ingafou M et al.<sup>[35]</sup>, and Gandolfo et al.<sup>[36]</sup>, where the average age of patients affected by oral lichen planus were 50 and 52 years respectively, falling under the age group 50-60 years.

It was also observed that the erosive variant was found to be the most common oral lichen planus variant among the study population (46.2%). This was contradictory to the finding of previous study by Sachdev R et al.<sup>[37]</sup>, where the reticular variant was found to be more prevalent oral lichen planus variant (67.6%). In this study, the erosive variant was found to be more common among females (29.8%) and reticular variant was most common among male population (25.3%). This was consistent with the findings of previous studies by Munde A et al.<sup>[34]</sup>, where it was shown that reticular variant was more prevalent among males (n=76) and erosive and atrophic variants were more common among females (n=15). Buccal mucosa was found to be the most common site for oral lichen planus. This finding was consistent with previous studies by Bermejo-Fenoll et al.<sup>[38]</sup> and Birsay G et al.<sup>[39]</sup>, where 40-90% of patients had buccal mucosa as the site of oral lichen planus which was consistent with the findings of this study.

It was also observed in our study that 7.46% of patients with a history of hypothyroidism had oral lichen planus. The findings were similar to that of Siponen M et al.<sup>[40]</sup>, Laváee F et al.<sup>[41]</sup>, Garcia Pola MJ et al.<sup>[42]</sup>, where it was seen that oral lichen planus patients had a history of thyroid disease, among which hypothyroidism was most common. Siponen et al., analyzed retrospectively 222 OLP/OLL patients and 222 controls, with a marginal significant association (95% confidence interval [CI] 1.03 to 4.90) between OLP/OLL and hypothyroidism (10% versus 5% in controls). This can be attributed to the fact that oral lichen planus is considered to be a T-cell mediated auto-immune disease in which auto-cytotoxic CD8+ T-cells trigger apoptosis of basal cells of oral epithelium<sup>[43],[44]</sup>. The mechanism between oral lichen planus and thyroid disease was based on a hypothesis that structural similarities between microbial antigens and human autoimmune reactions can turn a defense immune reaction into an autoimmune reaction<sup>[45]</sup>. The hypothyroid patients were on medications for the systemic illness. It can also be postulated that the oral lesions could be a lichenoid reaction to the hypothyroid medications.

## 5. CONCLUSION:

Within the limits of this study, positive correlation between thyroid disease, mainly hypothyroidism and oral lichen planus was observed. Further multicentric study with a larger population, longer follow up with wider parameters needs to be done to firmly establish the correlations and association between oral lichen planus and thyroid disorders which would open avenues for research as to whether, treating the underlying thyroid disorder could cause regression of oral lichen planus.

## 6. ACKNOWLEDGEMENTS:

The authors thank and acknowledge Saveetha Dental College for providing access to use the retrospective data from the oral medicine department for the study.

## AUTHOR CONTRIBUTIONS:

The authors have contributed to study design, data collection, analysis of data, tabulation of results, manuscript typing and formatting, and critical reviewing.

## CONFLICT OF INTEREST:

This research project is self funded and is not sponsored or aided by any third party. There is no conflict of interest.

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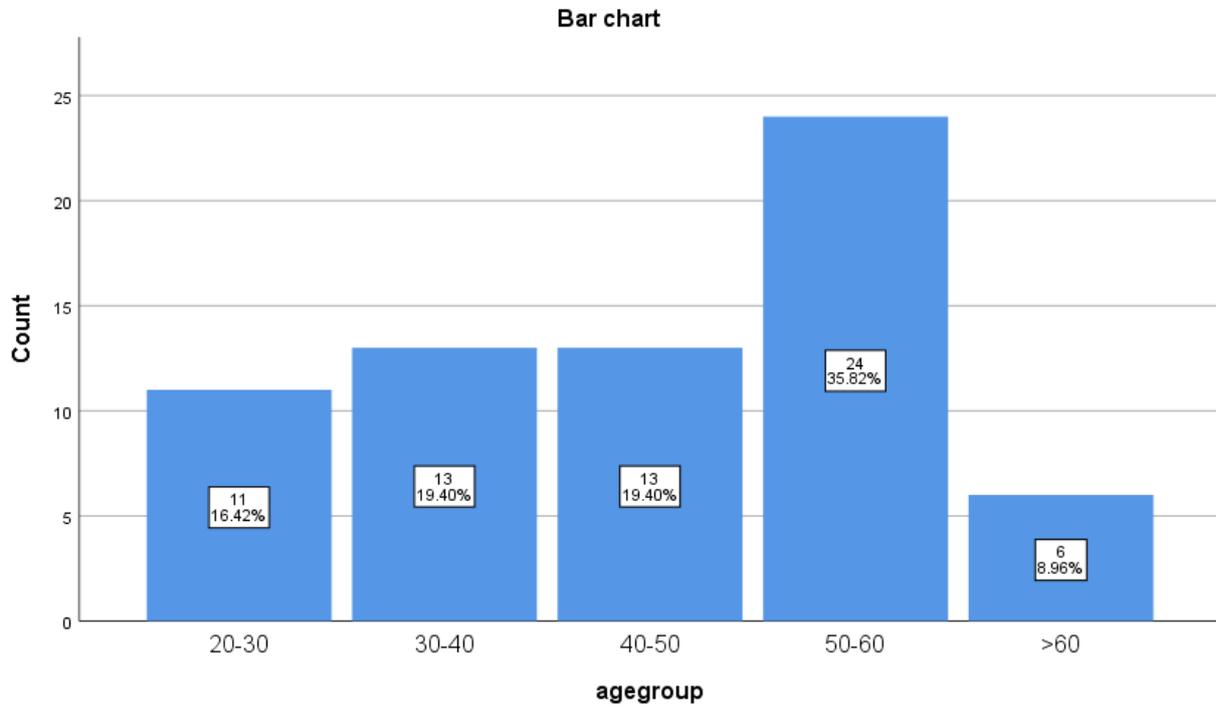
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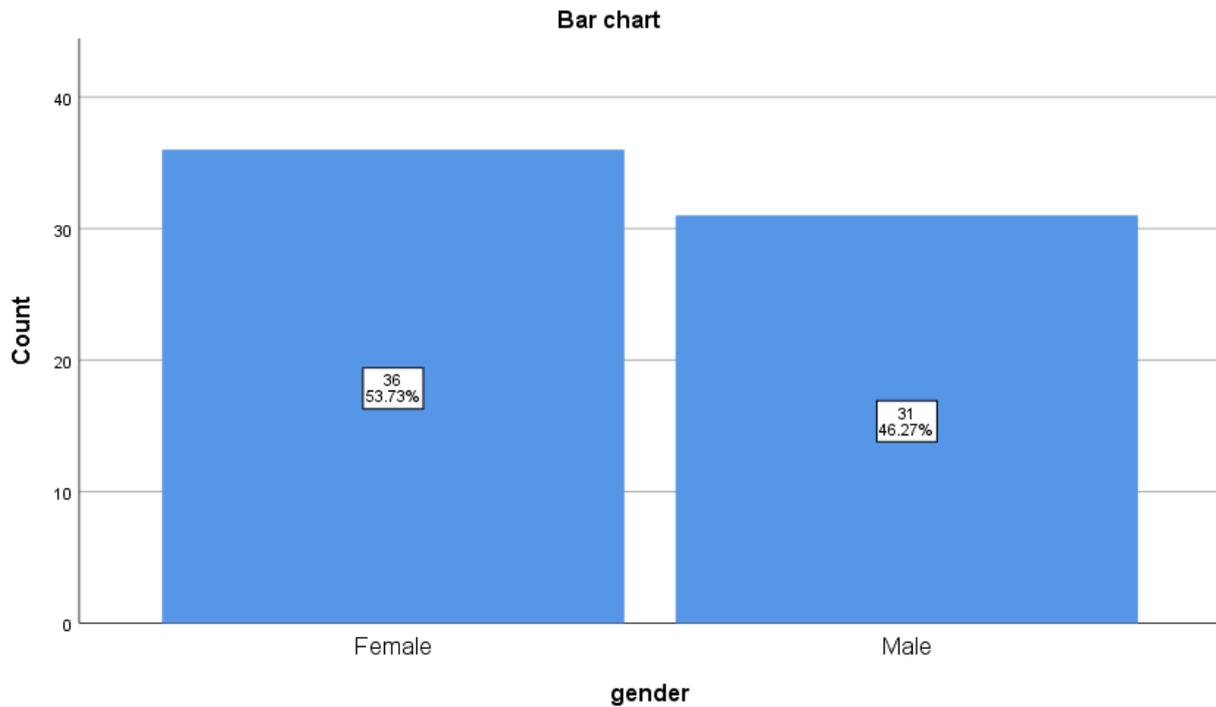
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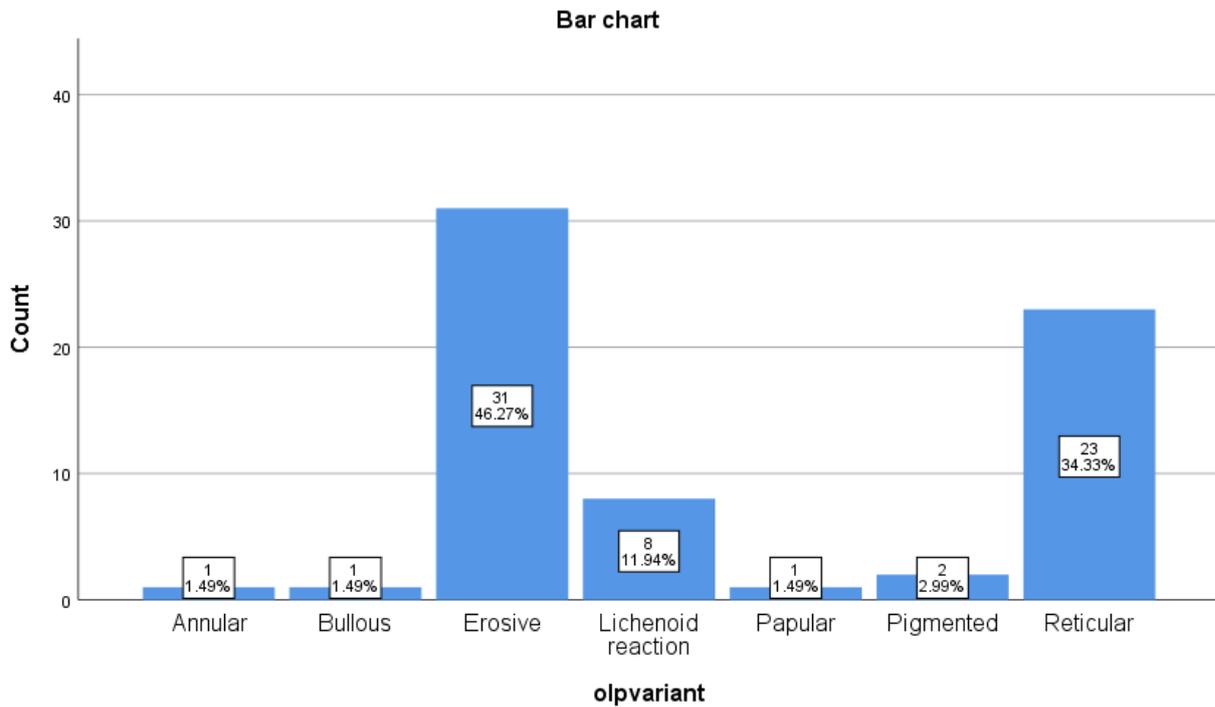
**GRAPHS AND TABLES :**



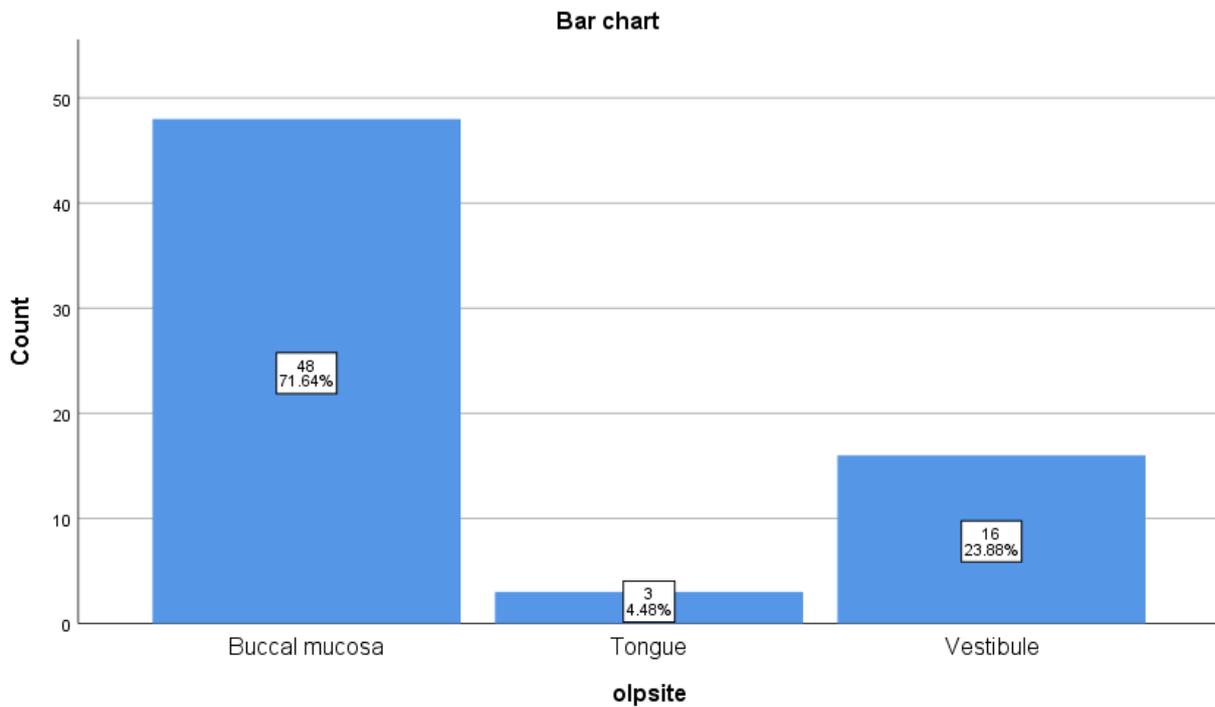
Graph I : This bar graph represents the distribution of the age among the study population. X axis represents the age and Y axis represents the number of cases. The maximum number of patients were in the age group of 50-60 years (n=24, 35.82%). Age groups 30-40 and 40-50 had 13 cases (19.40%) each. There were 11 patients (16.42%) and 6 patients (8.96%) in age group 20-30 and above 60 years respectively.



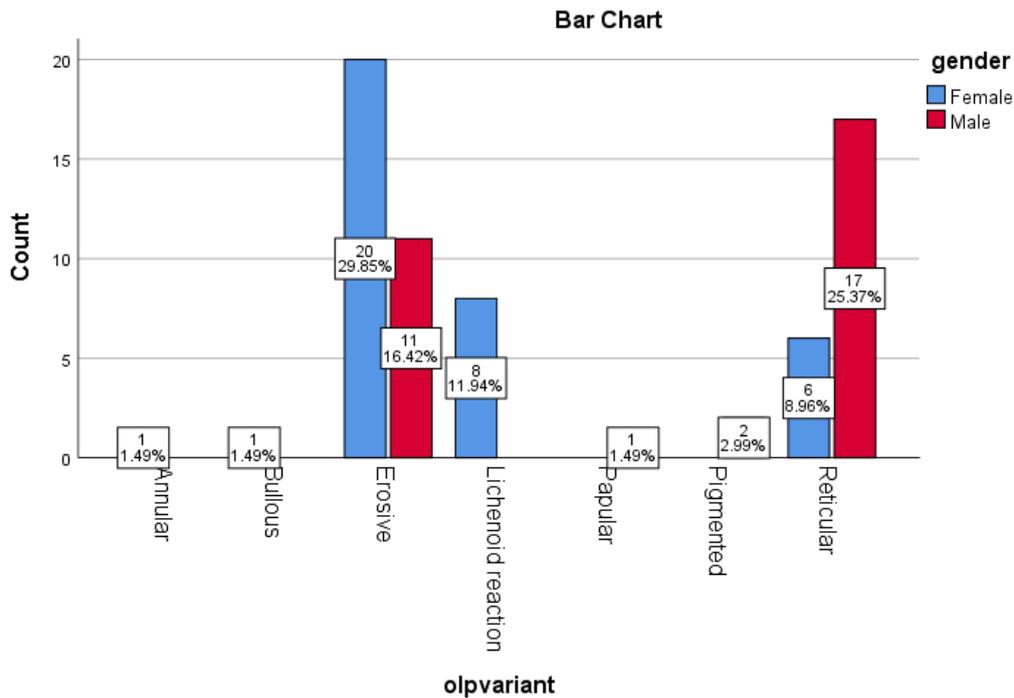
Graph II : This bar graph represents the distribution of the gender among the study population. X axis represents the gender and Y axis represents the number of cases. There was more female predilection (n =36,53.73%) when compared to males (n=31, 46.27%).



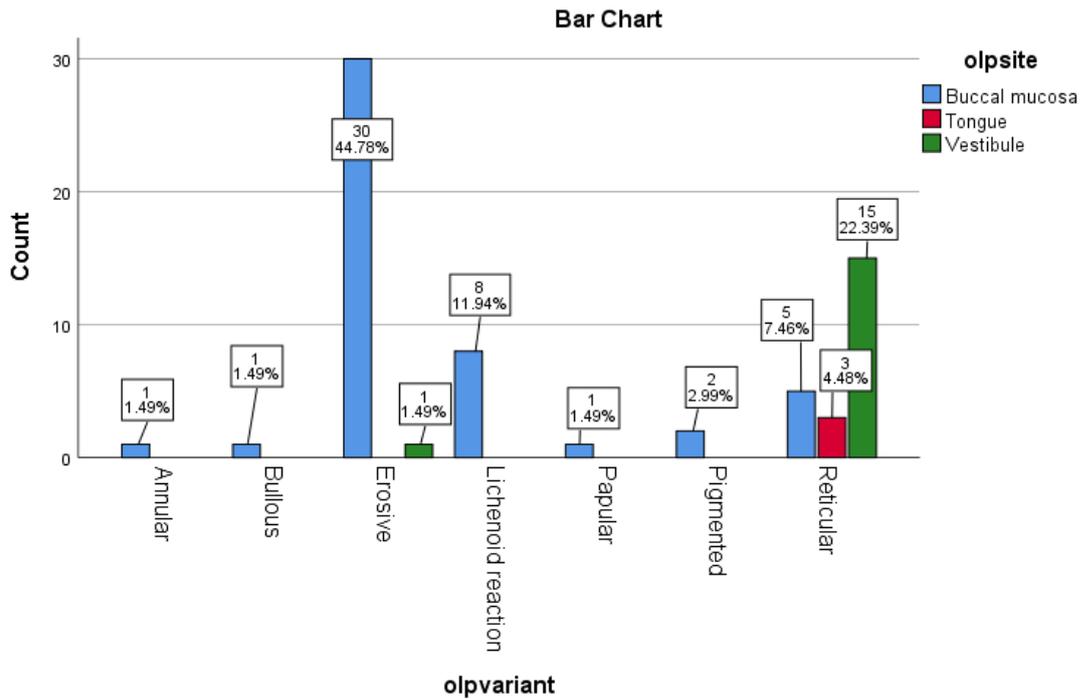
Graph III : This bar graph represents the distribution of the clinical variants of oral lichen planus (OLP) among the study population. X axis represents the clinical variant of oral lichen planus and Y axis represents the number of cases. Erosive lichen planus (46.27%) was most common variety in the study population followed by reticular (34.33%), Lichenoid (11.94%). Annular and bullous varieties had a prevalence of 1.49%.



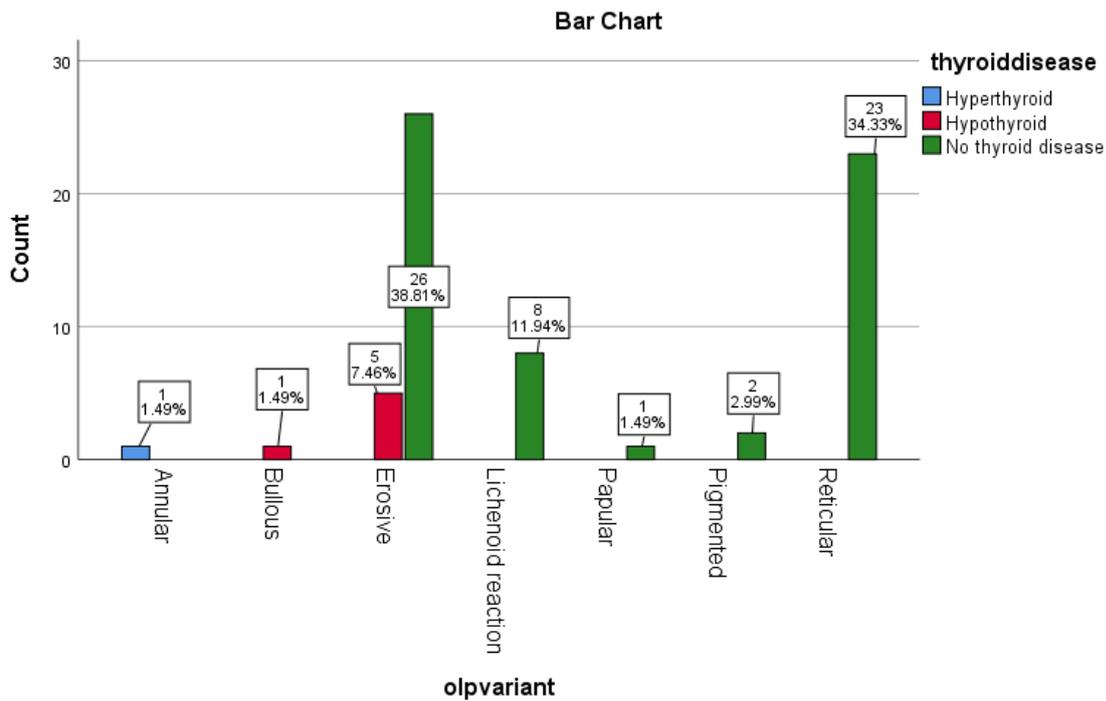
Graph IV : This bar graph represents the distribution of the site of oral lichen planus(OLP) among the study population.X axis represents the site of oral lichen planus and Y axis represents the percentage of cases. The buccal mucosa (71.64%) is the most common site of oral lichen planus among the study population, followed by vestibular region (23.88%) and tongue (4.48%).



Graph V : This cluster bar graph represents the association of the variant of oral lichen planus(OLP) with the gender. X axis represents the clinical variant and Y axis represents the percentage of cases. Blue colour represents females and red colour represents males. The Erosive variant was found to be most common among the female study population( 29.8% ). The reticular variant was found to be most common among male patients (25.3%). A Chi square analysis was done to compare the OLP variant and gender, (chi square 22.346;p-0.02((P<0.05)) which was statistically significant. There is a significant association of occurrence of erosive variety in females and reticular variant in males.



Graph VI : This cluster bar graph represents the association of the variant of oral lichen planus(OLP) with the site of Oral lichen planus. X axis represents the clinical variant and Y axis represents the case count. Blue colour represents buccal mucosa, red colour represents tongue and green colour represents vestibular mucosa. The buccal mucosa was found to be most common site of the erosive variant of oral lichen planus among the study population(44.7%). A Chi square analysis was done to compare the OLP variant and OLP site, (chi square 48.429;p-0.00((P<0.05)) which was statistically significant. There is a positive correlation between the clinical variety of and the site of occurrence of the predominant clinical variety of lichen planus.



Graph VII : This cluster bar graph represents the association of the variant of oral lichen planus(OLP) with the thyroid disease distribution among the study population. X axis represents the clinical variant and Y axis represents the percentage of cases. Blue colour represents hyperthyroid, red colour represents hypothyroid and green colour represents no thyroid disease. Hypothyroid state was found to be common among patients affected by the erosive variant in the study population( 7.46%) and bullous lichen planus (1,49%). A Chi square analysis was done to compare the OLP variant and thyroid disease distribution, (chi square 82.819,p-0.000((P<0.05)) which was statistically significant. Of the various thyroid states , hypothyroidism had a positive correlation with erosive lichen planus.

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- Graph : I - Age distribution among study population
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