Type of manuscript : *Original Study*

Prevalence of Vesiculobullous Lesions: A Hospital Based Retrospective Study

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Abstract

Vesiculobullous lesions, characterized as mucocutaneous, have a significant impact on quality of life when compared to other conditions, as they can lead to pain and difficulty in eating and speech, depending on the extent of the ulceration. The overlapping pattern of clinical presentation of vesiculobullous lesions in the oral mucous membranes makes it difficult for the clinicians to arrive at a proper diagnosis. Hence careful evaluation of clinical, histological and immunofluorescence data aids the clinician to arrive at a proper diagnosis. The aim of this study is determine the prevalence, age and gender variations of vesiculobullous lesions pertaining to oral mucosa among patients who have visited Saveetha Dental College, Chennai, India. A retrospective study was conducted and data collection was done from dental archives pertaining from June 2019 to April 2020. Data consisted of details of patients who presented with vesiculobullous lesions of the oral mucosa. Data was imported to IBM SPSS Version 20 for statistical analysis. Results were tabulated. Prevalence of vesiculobullous lesions pertaining to the oral cavity was more in females (51.8%) compared to males. (42.8%). Prevalence was more in patients belonging to the fourth decade of life (30.1%). Herpes labialis was found to be more prevalent among the vesiculobullous lesions seen in the oral cavity. Lesions were present in both the arch (44.6%) followed by lesions pertaining to only upper arch. Associations in this study were not statistically significant ($p>0.05$). The association between age and gender shows prevalence of herpes labialis to be the highest among all the age groups. There are very minimal studies done on the prevalence of vesiculobullous lesions pertaining to the oral cavity. In this study it has been found that vesiculobullous lesions of infectious origin (Herpes labialis) were found to be more prevalent compared to vesiculobullous lesions of autoimmune origin. This study was conducted in a single centre. Extensive multi centre study is to be done.

Keywords: *Vesiculobullous lesions, Mucocutaneous lesions, Herpes labialis, Vesicle, Bulla, Blisters*

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Introduction

Vesiculobullous lesions are a type of mucocutaneous disease that is characterised by vesicles and Bullae or blisters and secondary ulcers or erosions. Both vesicles and bullae are fluid-filled lesions, and they are distinguished by size, vesicles being less than 5–10 mm and bulla being larger than 5–10 mm, In the case of vesiculobullous diseases which are also immune disorders the term immunobullous is sometimes used.[1–3] These diseases, characterized as mucocutaneous, have

a significant impact on quality of life when compared to other conditions, as they can lead to pain and difficulty in eating and speech, depending on the extent of the ulceration.[4–8] Vesiculobullous disorders form a challenging domain for treating clinicians due to its varied presentation. The pattern of blistering disorders varies in different age groups. The etio-pathogenesis of vesiculobullous lesions can be categorised as inherited disorders, infectious, inflammatory, autoimmune, reactive and metabolic disorders.[9–11] Bulbous autoimmune dermatoses have a common pathogenic mechanism involving binding of autoantibodies to specific adhesion molecules in epidermal desmosomes and in some cases in the area of dermo-epidermal basement membrane zone. The binding of circulating autoantibodies and the induction of an inflammatory reaction in the area of target structures lead to loss of adhesion with subsequent intra or sub epithelial blister formation.[12–15]

The vesiculobullous lesions occurring in the oral cavity are bullous lichen planus, herpes simplex infection, pemphigus, bullous pemphigoid, bullous systemic lupus erythematosus, varicella-zoster infections, erythema multiforme, measles, mucous membranes pemphigoid, hand foot and mouth disease, paraneoplastic pemphigus, toxic epidermal necrolysis is and Stevens Johnson syndrome, dermatitis herpetiformis, herpangina, linear IgA disease and epidermolysis bullosa [1,16–18] The overlapping pattern of clinical presentation of vesiculobullous lesions in the oral mucous membranes makes it difficult for the clinicians to arrive at a proper diagnosis[19]. Hence careful evaluation of clinical, histological and immunofluorescence data aids the clinician to arrive at a proper diagnosis.[20–23] Clinicopathological correlation is always an essential prerequisite before coming to any final diagnosis.[24–27]

This study is done for epidemiological significance to check the current trends in prevalence of vesiculobullous lesions of oral mucosa among patients who visited Saveetha Dental College, Chennai, India and have undergone treatment for the same. The main aim of the study is to check the frequency distribution of different types of vesiculobullous lesions of the oral mucosa prevalent in the population. To determine the prevalence pattern of vesiculobullous lesions pertaining to oral mucosa among different age groups and gender. To determine the intra oral site (maxilla, mandible, both maxilla and mandible) that is most commonly affected. To determine if gender and age has any statistically significant association with the prevalence and type of vesiculobullous lesions involving oral mucosa. To determine if there is a statistically significant association between the type of vesiculobullous lesion and site involved – maxilla / mandible / both maxilla and mandible and also to check if there is any statistically significant association between age and gender and site involved.

Materials and Methods

Study setting:

A retrospective study was conducted in Saveetha Dental College, Chennai, Tamilnadu, India, by obtaining data from dental archives (single centre study). Ethical approval was obtained from the institutional ethics committee (Approval number: SDC/SIHEC/2020DIASDATA/0619-0320).

Sampling, data collection and tabulation:

Non probability convenience sampling method was employed. The data included records of patients who presented with vesiculobullous lesions in the oral mucosa; the type of vesiculobullous lesions and the location of the lesion. Data entries from June 2019 to April 2020 were obtained for the same and were tabulated. All the available data was included (without any sorting process) to reduce sampling bias. Data was analysed and censored data was excluded. The data was then verified by one external reviewer. A data of 83 patients (males – 48.2% ; females – 51.8%) 6 years – 66 years was obtained.

Data Analysis

The tabulated data was statistically analysed by IBM SPSS Version 20 to find the prevalence of vesiculobullous lesions among different age groups, gender, location – maxilla, mandible, both maxilla and mandible; type of vesiculobullous lesions – infectious type, inflammatory type; also find correlations between the type of vesiculobullous lesion with gender, age of the patient and location of the lesion – upper arch, lower arch and both arch. Data was imported and variables were analysed. Pearson's Chi square test was used. Results were tabulated and bar charts were plotted.

Results and Discussion

Age and gender:

Among the 83 patients, 43 (51.8%) were females and 40 (48.2%) were males. (Graph 1). 1 patient (1.2%) was less than 10 years, 1 patient (1.2%) belonged to the second decade, 14 patients (16.9%) belonged to the third decade, 25 patients (30.1%) belonged to the fourth decade, 17 patients, (20.5%) belonged to the fifth decade, 17 patients (20.5%) belonged to the sixth decade and 8 patients (9.6%) belonged to the seventh decade. (Graph 2)

Type of vesiculobullous lesion and location of the lesion:

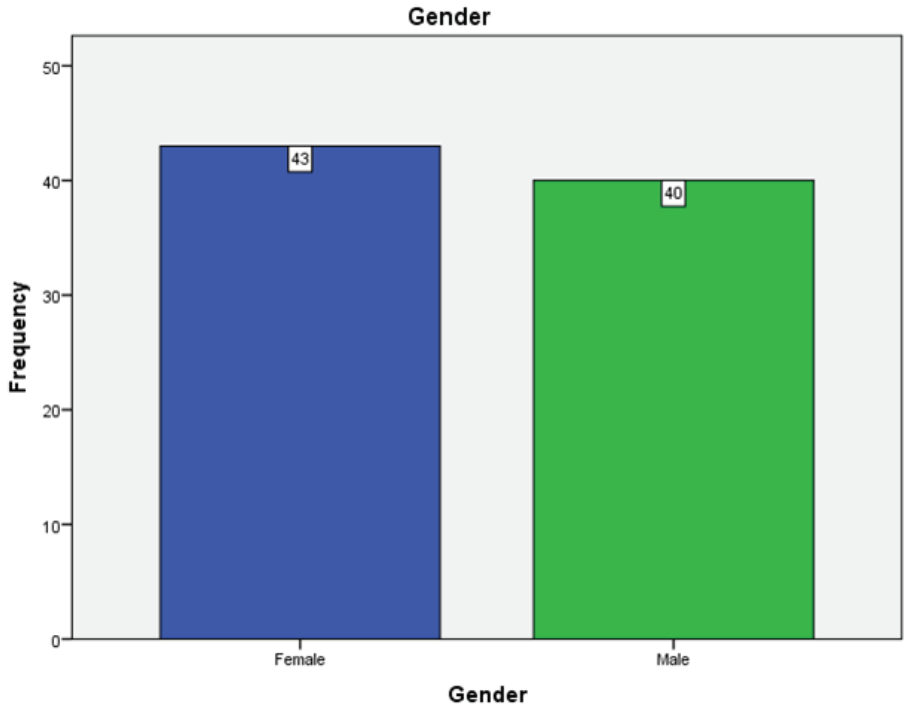
Among the 83 patients, 58 patients (69.9%) had herpes labialis, 5 patients (6%) had angina bullosa haemorrhagica, 1 patient (1.2%) had herpes zoster, 1 patient (1.2%) had bullous lichen planus, 7 patients had autoimmune vesiculobullous lesions (Pemphigus/ Pemphigoid / linear IgA disease/ dermatitis herpetiformis. 6 patients (7.2%) had primary herpetic gingivostomatitis, 3 patients (3.6%) had recurrent herpetic gingivostomatitis and two patients (2.4%) had secondary herpetic gingivostomatitis (Graph 3). 37 patients (44.6%) had lesions involving both in maxilla and mandible, 11 patients (13.3%) had lesions pertaining only to mandible and 35 patients (42.2%) had lesions involving only maxilla.(Graph 4)

Associations:

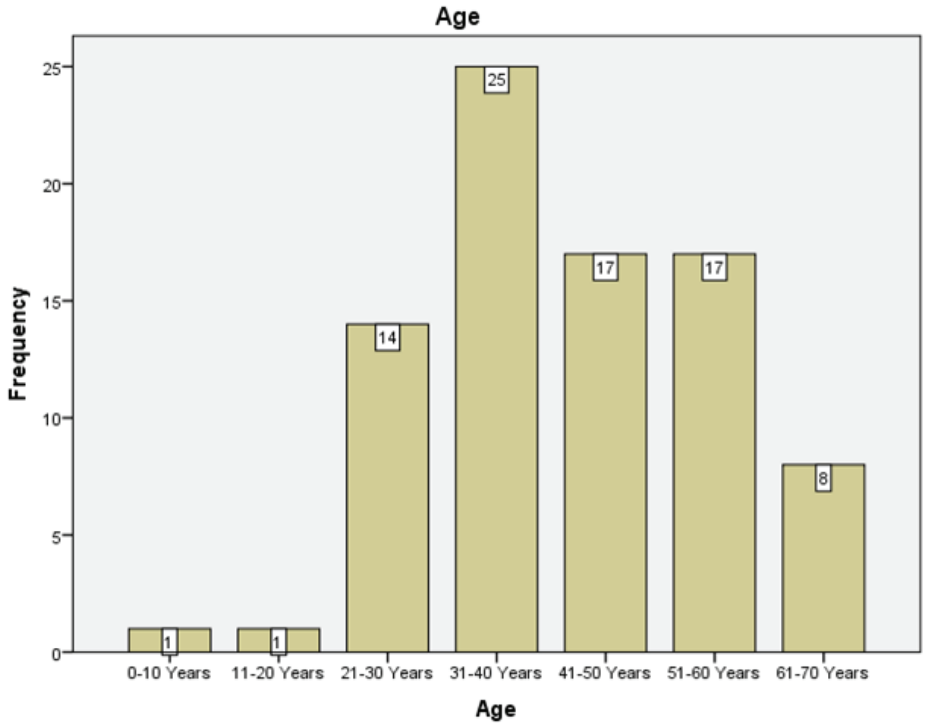
The association between gender and age is not statistically significant ($p>0.05$) but there is a female Predilection observed from the fourth decade (Graph 5). The association between age and the type of lesion shows an increased prevalence of herpes labialis in all age groups (Graph 6). The association between the location of the lesion and type of lesion shows that almost all types of vesiculobullous lesions occur in the upper arch followed by lesions occurring in both the arch. Herpes labialis most commonly affects both arch followed by upper arch. Herpes labialis in the lower arch is comparatively less (Graph 7). The association between gender and type of lesion shows that herpes labialis is the most prevalent type of vesiculobullous lesion seen in both males and females (no gender predilection) (Graph 8). All these associations are statistically insignificant ($p>0.05$).

In this study it is seen that females had more prevalence (51.8%) compared to males (48.2%) (Graph 1). This is in accordance with the studies done by Pavithra P et.al.,[28] Maharshank et.al.,[29] where females had more prevalence of vesiculobullous lesions compared to males. This may be due to genetic predisposition of female gender to vesiculobullous lesions. Hence, researching gender differences and the mechanisms of immune diseases is important to arrive at a conclusion. It is observed that prevalence was more in patients belonging to the fourth decade (30.1%) followed by the fifth and sixth decades (20.5% in each group) (Graph 2). In this study herpes labialis was found to be the most prevalent vesiculobullous lesion (69.9%). This shows that vesiculobullous lesions of infectious etiology is more prevalent than vesiculobullous lesions of autoimmune type. This is in accordance with various studies where the incidence of vesiculobullous lesions of infectious etiology was found to be ranging from 35.6% to 85.2%[30,31] The study results are in accordance with the study done by Embil JA et.al.,[32] where prevalence of herpes labialis is more in males than females. In the present study, 55.2% of patients with herpes labialis were males. This is also in accordance with several other studies.[33,34] The possible reason for male predominance may be due to habits and its role as a risk factor in prevalence of herpes labialis.[35,36] There is no significant association between gender, age; age, type of lesion; location and type of lesion; and gender, type of lesion.

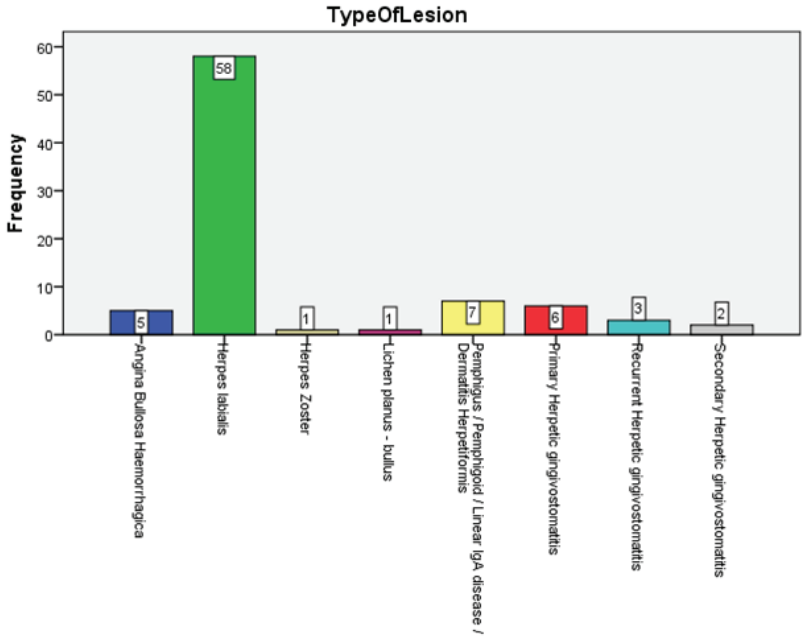
The study is a single centered study and samples were collected from a fixed time frame. Extensive research to be conducted – multi centre approach with a larger time frame to improve the scope of research. Also to evaluate the impact of geographical variations, race and habits in the prevalence, pattern and type of vesiculobullous lesions involving oral mucosa. The methodological problems faced during descriptive epidemiological studies are: case finding, using data sources such as hospital records, dental records and histopathological records often produce ascertainment bias, selection bias or both and multiple comparisons problems (i.e., the chance of occurrence of statistically significant findings). The resultant incidence and prevalence rates from studies with inadequate designs or inadequate data are limited and may be misleading.



Graph 1: Bar graph depicting the frequency of gender variations in patients with vesiculobullous lesions. X-axis shows gender and Y-axis shows the number of patients with vesiculobullous lesions. Blue colour denotes females and green colour denotes males. Prevalence was found to be more in females (51.8%) compared to males (48.2%).

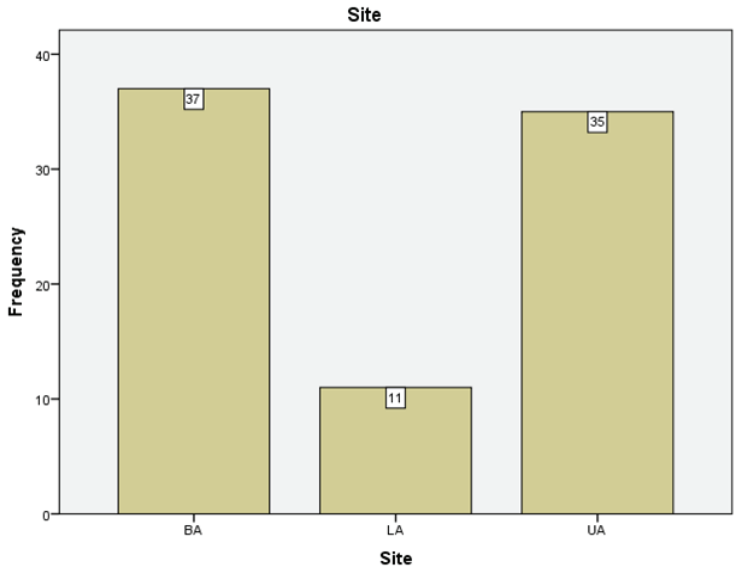


Graph 2: Bar graph depicting the frequency of vesiculobullous lesions among different age groups. X-axis shows the age groups and y -axis shows the number of patients with vesiculobullous lesions. Prevalence is more in the 4th decade (30.1%).



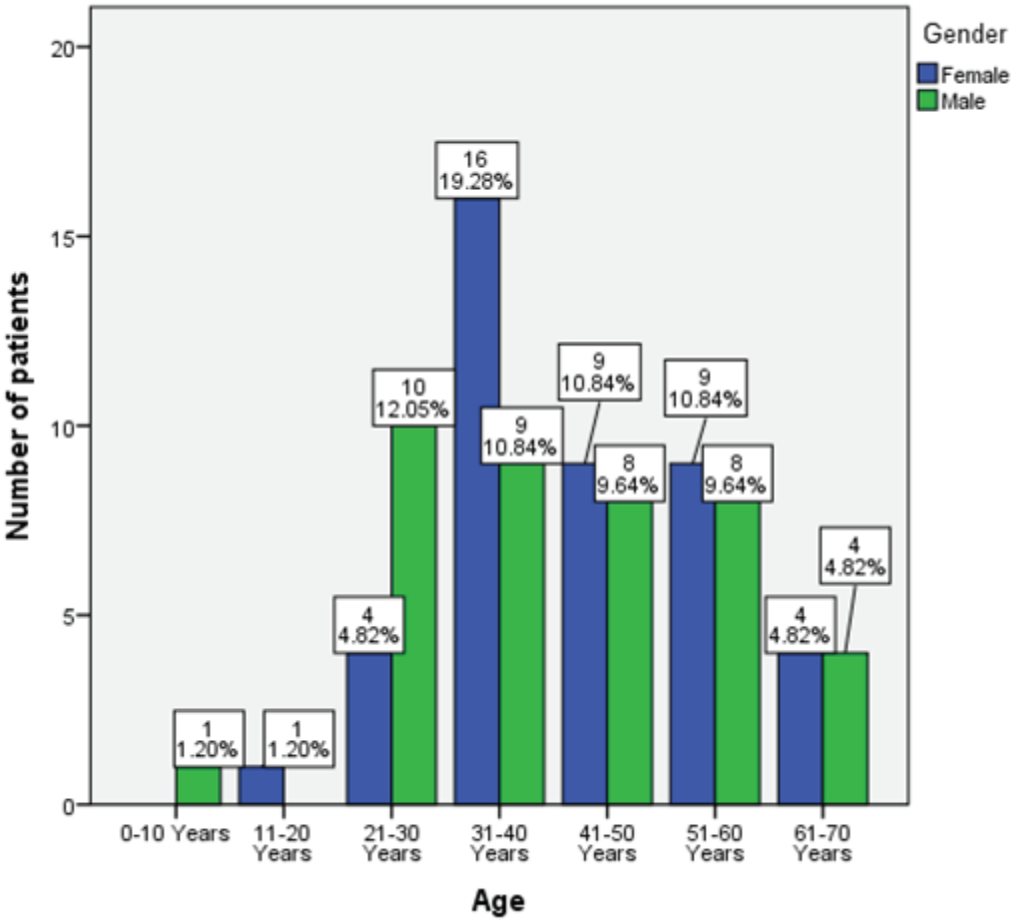
Graph 3:

Bar graph depicting the frequency of various vesiculobullous lesions in the oral cavity. X-axis shows the different vesiculobullous lesions and Y-axis shows the number of patients with vesiculobullous lesions. Blue colour denotes angina bullosa haemorrhagica, green colour denotes herpes labialis, beige colour denotes herpes zoster, purple colour denotes bullous lichen planus, yellow colour denotes pemphigus / pemphigoid / linear IgA disease / dermatitis herpetiformis red colour denotes primary herpetic gingivostomatitis, teal colour indicates recurrent herpetic gingivostomatitis and grey colour denotes secondary herpetic gingivostomatitis. Herpes labialis was found to be more prevalent (69.9%).

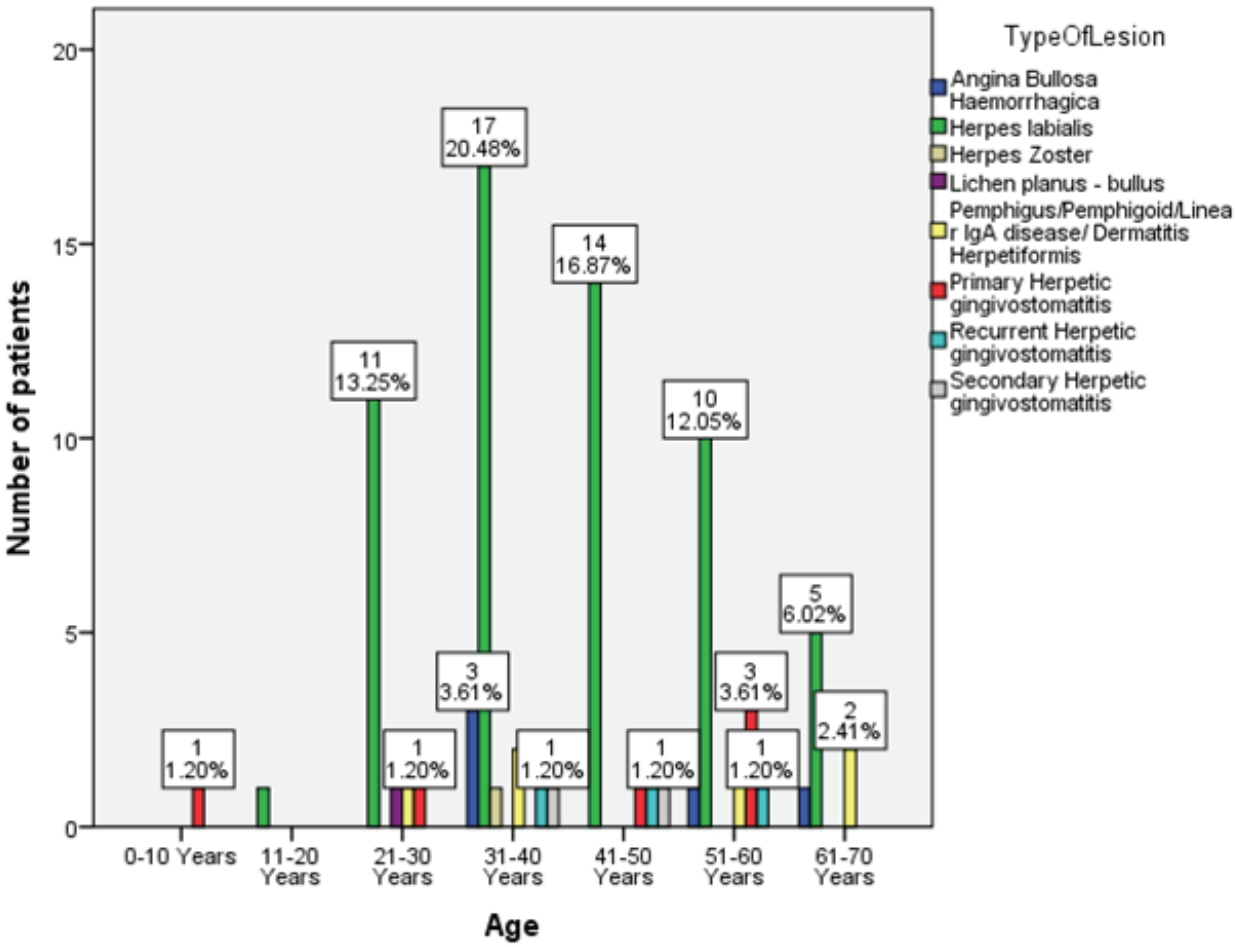


Graph 4:

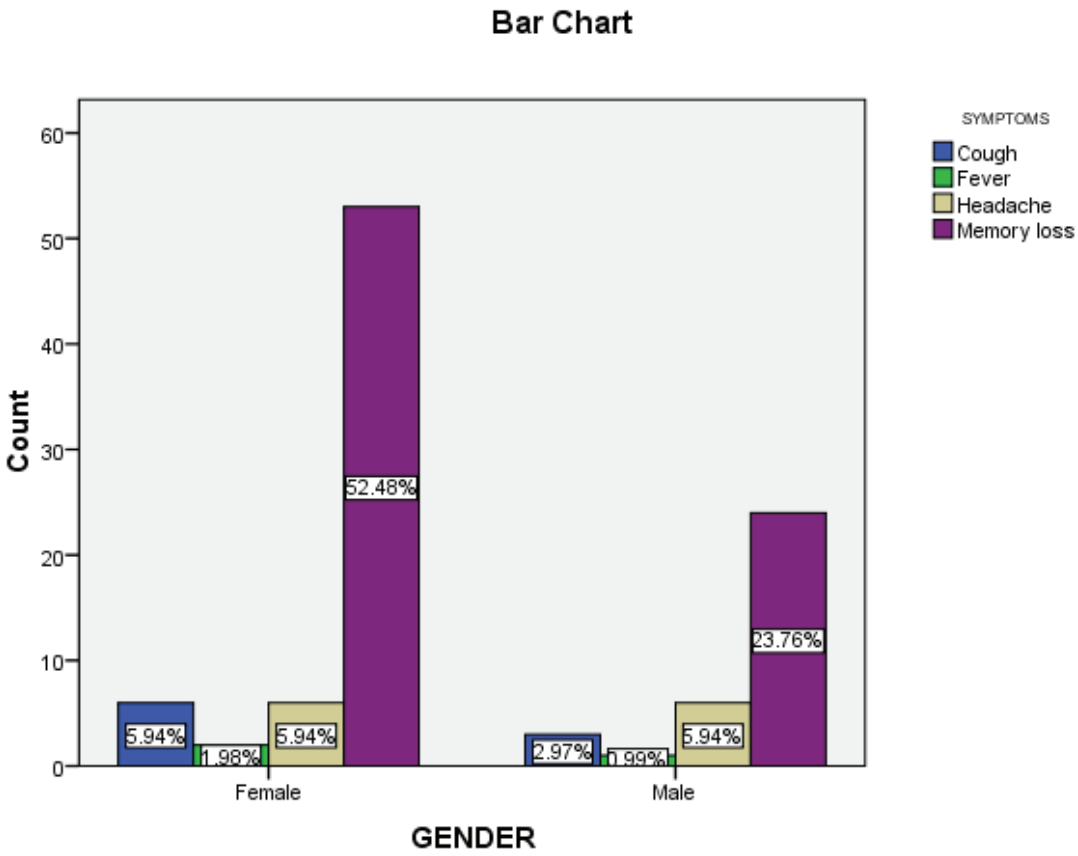
Bar graph depicting the site of prevalence of vesiculobullous lesions. X-axis shows the site of occurrence and Y-axis shows the number of patients with vesiculobullous lesions. It is commonly present in both the arches (44.6%).



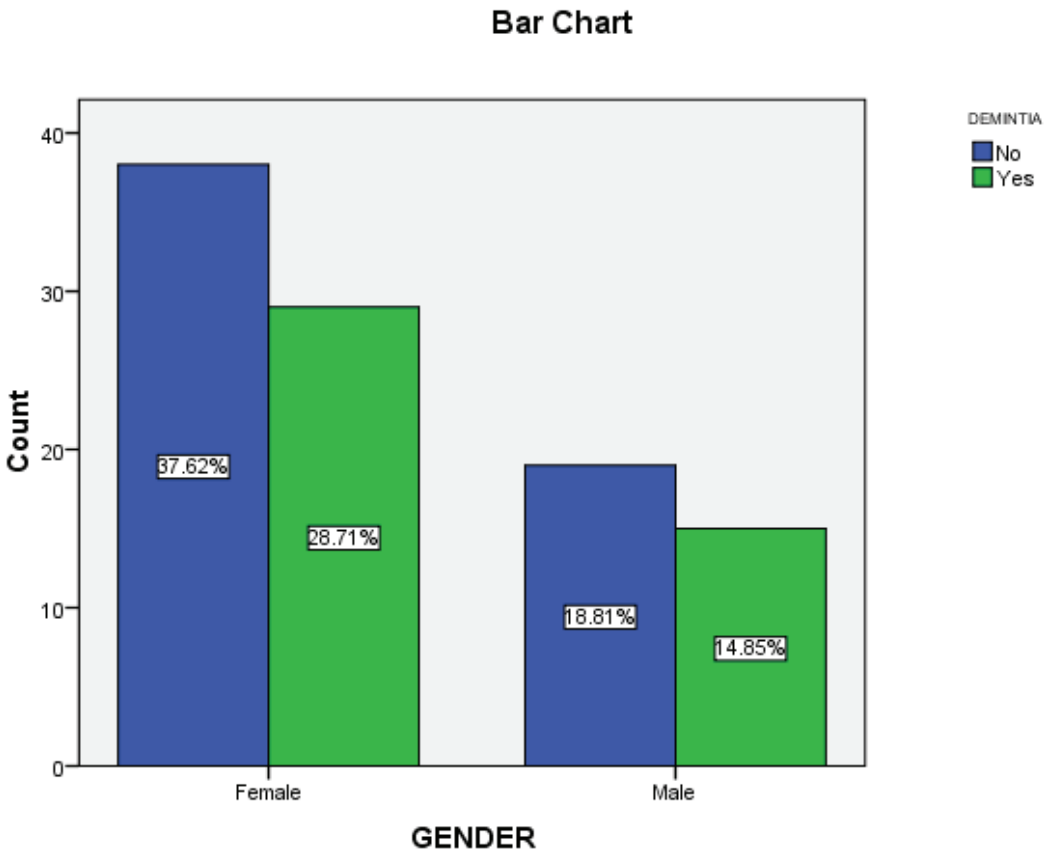
Graph 5: Bar graph depicting the association between age and gender. X-axis shows different age groups with gender variations and Y-axis shows the number of patients with vesiculobullous lesions. Blue colour denotes females and green colour denotes males. Prevalence among females was more in the 4th decade. Among males, prevalence was more in the third decade (12.50%). Prevalence was equal among both the genders in the 7th decade (4.82%) Chi-square test, P value 0.365; (>0.05 - statistically not significant).



Graph 6: **Bar graph depicting the association between age and type of lesion. X-axis shows the different age groups and types of vesiculobullous lesions and Y-axis shows the number of patients with vesiculobullous lesions. Blue colour denotes angina bullosa haemorrhagica, green colour denotes herpes labialis, beige colour denotes herpes zoster, purple colour denotes bullous lichen planus, yellow colour denotes pemphigus / pemphigoid / linear IgA disease / dermatitis herpetiformis red colour denotes primary herpetic gingivostomatitis, teal colour indicates recurrent herpetic gingivostomatitis and grey colour denotes secondary herpetic gingivostomatitis. Herpes labialis is more prevalent in all age groups with highest prevalence in the 4th decade of life (20.48%). In the first decade, primary herpetic gingivostomatitis is seen (1.20%). Chi-square test, P value 0.652; (>0.05 - statistically not significant).**



Graph 7: Bar graph depicting the association between site and type of lesion. X-axis shows the site of occurrence and type of vesiculobullous lesion. Y-axis shows the number of patients with vesiculobullous lesions. Blue colour denotes angina bullosa haemorrhagica, green colour denotes herpes labialis, beige colour denotes herpes zoster, purple colour denotes bullous lichen planus, yellow colour denotes pemphigus / pemphigoid / linear IgA disease / dermatitis herpetiformis. red colour denotes primary herpetic gingivostomatitis, teal colour indicates recurrent herpetic gingivostomatitis and grey colour denotes secondary herpetic gingivostomatitis. Almost all lesions are more prevalent in the upper arch. Herpes labialis is the more prevalent vesiculobullous lesion and it occurs in both the arch (32.53%). Chi-square test, P value 0.213; (>0.05 - statistically not significant).



Graph 8: Bar graph depicting the association between gender and type of lesion. X-axis shows gender and the type of vesiculobullous lesion. Y-axis shows the number of patients with vesiculobullous lesions. Blue colour denotes females and green colour denotes males. It is observed that herpes labialis (38.55%) and primary herpetic gingivostomatitis (4.82%) was more prevalent in males compared to females. All the other lesions were more prevalent in females. Chi-square test, P value 0.143; (>0.05 - statistically not significant).

Conclusion

From this study it has been found that vesiculobullous lesions are prevalent more in females than in males and in patients belonging to the 4th decade of life. Herpes labialis was found to be the most common vesiculobullous lesion occurring in the oral cavity with increased prevalence in males. The study was conducted in a single centre. Extensive multi centre study to be done.

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Conflict of Interest: No conflict of Interest.

Source of Funding: Self.

Ethical Clearance: It is taken from "Saveetha Institute Human Ethical Committee" (Ethical Approval Number- SDC/SIHEC/2020/DIASDATA/0619-0320)

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Graphs