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Thirteen-Year Retrospective Analysis of Biopsied Gingival and Alveolar Mucosal Lesions

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ABSTRACT

Gingiva and alveolar mucosa are exposed to similar chronic mechanical irritations in the oral cavity. They are common sites for plaque-induced and nonplaque-induced diseases. This study aims to compare the categories, frequencies, and age distribution of the biopsied gingival and alveolar mucosal lesions, as well as to report their distribution at these two sites. This retrospective study was performed on biopsied gingival and alveolar mucosal lesions taken for 13 years. The necessary information was noted, tabulated, and subjected to statistical analysis. Of 5068 biopsies, 302 (5.95%) gingival and 70 (1.38%) alveolar mucosal biopsies were obtained, with female (61.82%) and male dominance (38.17%), respectively. Among gingival biopsies, reactive lesions were the most common (86.75%), followed by inflammatory and immune conditions and lesions (5.29%), neoplasms (3.64%), specific infections (0.33%), and gingival pigmentation (0.33%). The alveolar mucosal biopsies were most commonly diagnosed as well-differentiated squamous cell carcinoma (58.57%), followed by moderately differentiated (28.57%), poorly differentiated squamous cell carcinoma (5.71%), adenoid cystic carcinoma (2.85%), malignant salivary gland tumor (2.85%), and pyogenic granuloma (1.42%). The study results show a high prevalence of gingival and alveolar mucosal biopsied lesions. Most reports suggested a prevalence of reactive lesions in gingival biopsies; on the contrary, alveolar mucosa showed predominance of neoplastic lesions. The two disciplines of dentistry (oral pathology and periodontics) must work together to formulate a functional classification for a definitive diagnosis and an effective treatment plan.

Keywords: Alveolar mucosa, Biopsied lesions, Demographics, Frequency distribution, Gingiva

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Introduction

Periodontium, the supporting structure that envelops the necks of the teeth and covers the alveolar processes of the jaws, includes the gingiva, which is made up of free and attached gingiva. Conversely, the tissue that extends past the mucogingival junction is known as the alveolar mucosa. It is red, freely attached, and nonkeratinized [1-3]. Both gingiva and the alveolar mucosa are subjected to the same chronic mechanical irritants, but their compositions and histological characteristics differ [4]. In addition to being regularly inflamed in plaque-induced conditions such as gingivitis and periodontitis, they are also at risk for several nonplaque-induced illnesses that may manifest as both neoplastic and nonneoplastic lesions [1, 2].

Plaque-induced lesions usually disappear after appropriate treatment, but plaque-free lesions, such as pyogenic granuloma (PG), fibroma, and peripheral ossifying fibroma (POF), which are generally reactive, persist [1, 3]. These lesions primarily arise in the periodontal tissues, and most of them are directly associated with chronic local irritation caused by poor oral hygiene and subsequent accumulation of biofilm and calculus. Ill-fitting restorations, occlusal trauma, prosthetic and orthodontic appliances, iatrogenic, and some specific systemic factors (such as

pregnancy-induced hormonal changes) could also be some of the causative factors [5]. The neoplastic lesions occur clinically as autonomous growths originating from epithelial or mesenchymal tissues of the gingiva and/or from the adjacent soft or hard tissues. Previous studies suggest that the prevalence of nonneoplastic lesions outweighs that of the neoplastic lesions [6-9].

The primary detection of a lesion or disease is usually done visually by observing the subtle changes in color, size, shape, and consistency [4]. While clinical and radiographic assessment could prove useful, the confirmatory diagnosis can only be made after their microscopic analysis following the biopsy. Although previous studies have compiled the demographic data, frequency, and distribution of various gingival biopsied lesions, no study has published the epidemiologic data of gingival and alveolar mucosal biopsied lesions in India.

The current investigation aimed to determine the frequency distribution of biopsied lesions of the gingiva and alveolar mucosa at a tertiary care dental teaching institute diagnosed in the past 13 years and to compare the categories, frequencies, and age distribution of lesions at these two sites.

Materials and Methods

The present cross-sectional and observational study was performed on the cases that were reported over 13 years (January 2011–August 2023). The protocol was waived by the institutional review committee for human subjects as the case records of patients available in the department were checked along with their corresponding slides.

From a total of 5068 diagnosed cases, biopsies of the gingiva (302) and alveolar mucosa (70) were segregated for further analysis. The demographic data (age, gender), site, and type of lesion were recorded in each case along with other dental records (clinical signs or symptoms or radiographic findings, if any) and medical history (long-term drug history or any systemic disease). Biopsies of the gingiva and alveolar mucosa of all age groups and genders whose biopsy requisition forms and histopathological reports included all relevant details were included in the study. Edentulous patients, those with missing clinical records and biopsies from the alveolar ridge or a region other than gingiva or alveolar mucosa were excluded.

The histopathological slides in each case were blindly re-evaluated by an experienced oral pathologist under a brightfield research microscope to confirm the diagnosis. The gingival biopsies were classified based on the classification of nonplaque-induced gingival diseases and conditions published in 2017 by Holmstrup *et al.* [10]. The tabulated data were subjected to statistical analysis using Microsoft Excel 2019 computer software, and mean values were calculated.

Results and Discussion

Of the 5068 diagnosed oral lesions, 302 (5.95%) gingival and 70 (1.38%) alveolar mucosal biopsies met the eligibility criteria and were included in the study. The detailed categorization and demographic details of gingival and alveolar mucosal biopsies are tabulated in **Tables 1–3**.

Table 1. Details of the gingival biopsies for their frequency distribution and demographic data

Category	Subcategory	FD	Male:female ratio	Mean age (years)	Max:mand: both	Ant: Post
Genetic/developmental disorders		-	-	-	-	-
Specific infections	Bacterial origin	-	-	-	-	-
	Viral origin squamous papilloma	1	0:1	52	0:1:0	1:0
	Fungal	-	-	-	-	-
Inflammatory and immune conditions and lesions	Hypersensitivity reactions plasma cell gingivitis	13	2:11	30.9	9:4:0	10:3
	Autoimmune diseases of skin and mucous membranes pemphigus vulgaris	3	0:3	15	1:0:2	0:3
	Granulomatous inflammatory conditions (orofacial granulomatosis)	-	-	-	-	-
Reactive processes Epulides	Fibrous epulis (fibroma)	7	2:5	31.9	3:4:0	3:4
	FEH	50	19:31	32.7	33:14:3	31:19

	Inflammatory epithelial hyperplasia	63	17:46	39.7	15:12:6	24:9
	Calcifying fibroblastic granuloma (POF)	67	22:45	28.8	42:25:0	38:29
	PG (vascular epulis)	96	26:70	36.5	56:40:0	49:47
	PGCG (or central)	9	0:9	35.3	2:7:0	1:8
Neoplasms	Premalignant	-	-	-	-	-
	Malignant squamous cell carcinoma	10	4:6	43.5	2:8:0	3:7
	Non-Hodgkin's lymphoma	1	0:1	58	1:0:0	1:0
Endocrine, nutritional, and metabolic diseases	Vitamin deficiencies	-	-	-	-	-
Traumatic lesions	Physical/mechanical insults	-	-	-	-	-
	Chemical (toxic) insults	-	-	-	-	-
	Thermal insults	-	-	-	-	-
Gingival pigmentation	Gingival pigmentation/melanoplakia	1	0:1	40	1:0:0	1:0
Diseases which did not fall in classification	Langerhans cell histiocytosis	1	0:1	47	1:0:0	1:0
	Foreign body granuloma	1	0:1	48	0:1:0	0:1
	Nonspecific granulomatosis	1	0:1	39.3	0:1:0	0:1
	Small round cell tumor	1	0:1	52	0:1:0	0:1
	Chronic inflammatory lesion	1	0:1	36	1:0:0	1:0
	Verrucous keratoma	1	1:0	45	0:1:0	0:1
	Malignant melanoma	1	1:0	36	1:0:0	1:0

FD: Frequency distribution; Max :Maxilla; Mand: Mandible; Ant: Anterior; Post: Posterior; POF: Peripheral ossifying fibroma; FEH: Fibroepithelial hyperplasia; PGCG: Peripheral giant cell granuloma; PG: Pyogenic granuloma

Table 2. Details of the alveolar mucosal biopsies for their frequency distribution and demographic data

Category	FD	Male:female ratio	Mean age (years)	Max:mand:both	Ant:post
Well differentiated squamous cell carcinoma	41	27:14	49.8	32:9:0	17:24
Moderately differentiated squamous cell carcinoma	20	12:8	43.3	8:12:0	5:15
Poorly differentiated squamous cell carcinoma	4	2:2	61	4:0:0	0:4
Adenoid cystic carcinoma	1	1:1	55	2:0:0	0:2
PG	1	0:1	25	1:0:0	0:1
Malignant salivary gland tumor	2	2:0	62.5	0:2:0	1:1

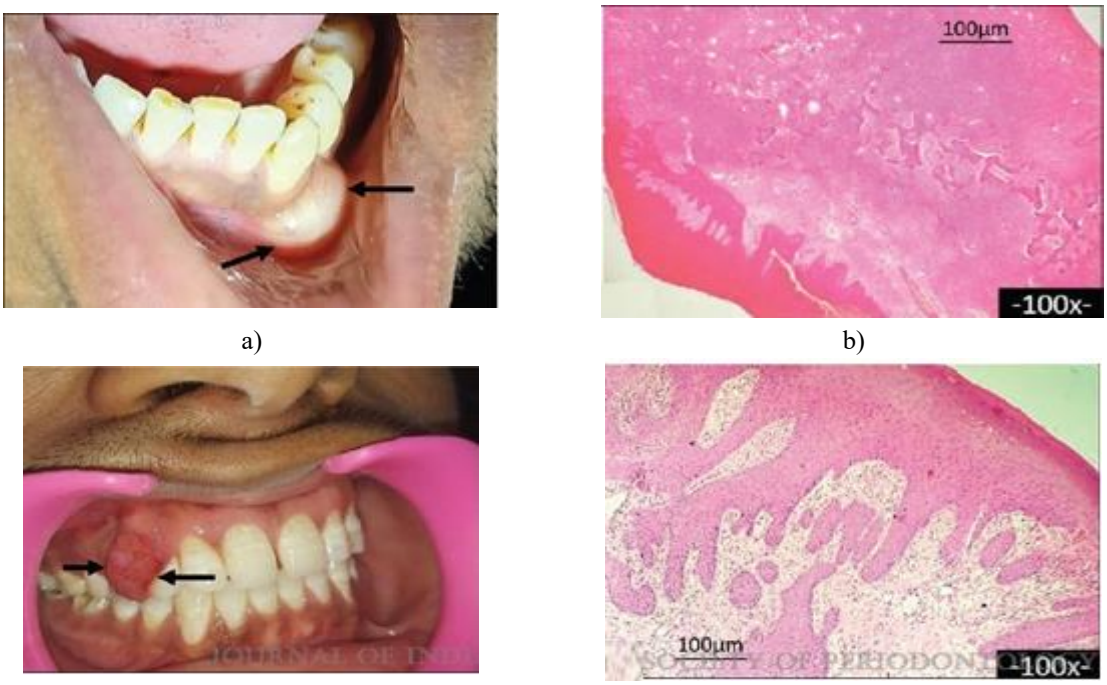
FD: Frequency distribution; Max: Maxilla; Mand: Mandible; Ant: Anterior; Post: Posterior; PG: Pyogenic granuloma.

Table 3. General characteristics of gingival and alveolar mucosal lesions

General characteristics	Gingiva	Alveolar mucosa	Total
Total	302	70	372
Type of lesions			
Specific infections	1	-	1
Inflammatory and immune conditions and lesions	16	-	16
Reactive processes	262	1	263
Neoplasms	11	69	80
Gingival pigmentation	1	-	1
Diseases which did not fall in classification	11	-	11
Mean age (years)	38.7	50.4	44.55
Sex (male:female)	98:204	44:26	142:230
Location			
Maxilla	169	47	216
Mandible	118	23	141
Both	15	0	15
Anterior	168	23	191
Posterior	134	47	181

The average age of the gingival biopsy cases was 38.7 years, which ranged from 2 to 94 years. The youngest patient was diagnosed with fibroepithelial hyperplasia (FEH) **(Figure 1)**, while the oldest had PG. Female dominance (67.54%) was observed, while males accounted for 32.45% of all cases. The lesions were more

commonly reported in the maxilla (169/55.96%), followed by the mandible (118/39.07%), while the involvement of both jaws was 15/4.96%. Of these, 58.01% were found in the anterior and 41.98% in the posterior region of the jaws. Gingival biopsied lesions were divided into five categories, with reactive lesions being the most common (86.75%), followed by inflammatory and immune conditions and lesions (5.29%), neoplasms (3.64%), gingival pigmentation (0.33%), and specific infections (0.33%). Some lesions did not fit into any of the above categories (3.64%).



a) b)

c) d)

Figure 1. (a) A pink sessile nodule in the anterior aspect of left lower canine and premolar in a 24-year-old male, (b) Histopathology of peripheral ossifying fibroma with flecks of osteoid tissue in the connective tissue stroma along with overlying hyperplastic epithelium (H and E, ×100), (c) A red proliferative sessile growth in the anterior aspect of right upper canine and premolar in a 16-year-old male, (d) Histopathology of fibroepithelial hyperplasia with hyperplastic keratinized epithelium with associated fibrous connective tissue stroma (H and E, ×100)

Reactive lesions were further divided into six subcategories with most cases being diagnosed as PG (31.78%) reported more in females, followed by POF (22.18%) **(Figure 1)**, FEH (16.55%), inflammatory epithelial hyperplasia (10.92%), peripheral giant cell granuloma (PGCG) (2.98%), and fibrous epulis (2.31%). There were two subtypes of inflammatory and immune disorders and lesions, with plasma cell gingivitis (4.30%) being more common in hypersensitivity reactions, followed by pemphigus vulgaris (0.99%) in autoimmune skin and mucous membranes. In the neoplasm category, oral squamous cell carcinoma (OSCC) (3.31%) was frequently reported, followed by non-Hodgkin lymphoma (0.33%). A single case of squamous papilloma (0.33%) was assigned to the category of specific infections.

The gingival lesions that did not fit into any of the categories listed in Holmstrup's *et al*. classification [10] were chronic inflammatory lesions (0.99%), nonspecific granulomatosis (0.99%), Langerhans cell histiocytosis (0.33%), foreign body granuloma (0.33%), small round cell tumor (0.33%), verrucous carcinoma (0.33%), and malignant melanoma (0.33%).

On the other hand, the average age of occurrence of alveolar mucosal biopsies was 50.4 years, which ranged from 17 to 72 years. Both 17-year-old and 72-year-old patients were diagnosed with well-differentiated and poorly differentiated OSCC. The alveolar mucosal biopsy results showed a male dominance with 62.85% of cases while females were 37.14%.

Similar to gingival biopsies, the maxillary jaw was affected in 67.14% of cases, and the mandible in 32.85% of cases in the alveolar mucosa. The majority of them occurred in the posterior (67.14%) while only 32.85% of cases were noted in the anterior part of jaws. Well-differentiated OSCC was the most frequently diagnosed lesion

amongst the alveolar mucosa biopsies, constituting 58.57%, followed by moderately differentiated (28.57%) and poorly differentiated OSCC (5.71%). Around 2.85% of cases were reported as adenoid cystic carcinoma and malignant salivary gland tumor. Unlike the gingival biopsies, only a single case of PG was noted.

The present study was a preliminary attempt to analyze the biopsied gingival and alveolar mucosal lesions in an Indian subpopulation. Various countries have investigated the incidence and distribution of gingival lesions over different periods [1, 6-9, 11, 12]; however, only a few studies report the frequency distribution of lesions on both gingiva and the alveolar mucosa [4, 9, 13].

The current study reported the average age of occurrence for 302 gingival biopsies as 38.7 years, which was similar to some past studies [3, 11], while a younger age group (20–29 years) was also reported to be affected in the previous literature [6, 7, 14, 15]. The current study showed a female dominance (67.54%), which was consistent with many retrospective studies [6-8, 14, 16].

Five categories of nonplaque-induced gingival lesions were noted, and the most common category was reactive lesions (86.75%). The results were similar to almost all the previous studies on this subject with variable frequency. The most common lesion in this category was PG, followed by POF and FEH. Several studies in the past reported PG as the most common [1, 3, 6, 7, 9, 11], while others quoted fibroma as the most common lesion in this category [12, 17-19]. These variable results could be due to the time when the patient reports to clinics, as long-standing PG matures into fibroma. Due to the delayed patient presentation, PG might have developed fibroplasia and eventually developed into a fibroma [9, 20].

PGs occurred at a mean age of 36.5 years with female dominance, similar to previous studies [7, 9, 13, 15]. The literature suggests that the hormonal changes (in adolescence, pregnancy, effects of oral contraceptive pill, or hormone replacement therapy) in women, along with thin and more sensitive gingiva in this age group, could be probable causes of high occurrence of PG in women [9, 11, 21, 22].

The anterior maxilla has been stated as the most common anatomical location for PG, POF, and FEH, followed by the anterior mandible [13, 23]. similar to the present study results. This could be explained by reduced saliva concentration and altered tooth position in this region, making it difficult to maintain oral hygiene [13, 24]. Overall, the reactive lesions occurred more frequently in the maxilla (57.63%) than the mandible (38.93%), with similar incidence in the anterior and posterior jaw.

POF was the second most common lesion and accounted for 25.57% of all reported reactive lesions, with female dominance and anterior maxilla predilection. The results were consistent with few past studies [12, 17, 25], while some quoted dissimilar results [7, 14]. These differences could be attributed to the categorization of POF as benign lesions in the gingival biopsies [11].

PGCG has been frequently observed in the mandible of women, and the current study met with the same response [7, 8]. However, a study by Motamedi *et al.* [26]. stated its prevalence was similar for both genders. Although there was no anatomical difference between PGCG, FEH, POF, and PG, there might be certain local factors that influence how different tissues react to irritant stimuli [13].

In the category of inflammatory and immune conditions and lesions, 5.29% of cases were plasma cell gingivitis with an average age of 30.9 years and complete female incidence. These findings were consistent with past studies [1, 3, 16]. The majority of lesions occurred in the upper jaw (62.5%) and affected the anterior part more (62.5%) than the posterior area (37.5%). Pemphigus vulgaris showed the highest frequency within autoimmune diseases of skin and mucous membranes with female predominance, which was consistent with previous studies [11, 14, 16]. Pemphigoid cases have also been reported [4, 14] but no case was found in the present study.

Malignant neoplasms followed inflammatory and immune conditions and lesions (3.64%), with OSCC cases (3.31%) exceeding the number of lymphomas (0.33%). Most studies found a prevalence rate of around 2%–8% for gingival malignancies [6, 8, 11, 16]. The outlier data were presented in a study by Li *et al*. [19], in which 33.14% of cases were malignancies. As previously reported, the gingiva was the third most common site for OSCC after the floor of the mouth and tongue [27]. OSCC was the most common malignant neoplasm reported in the present and previous studies [3, 6-8, 11, 14, 16, 18, 19]. It is the most common oral cancer that is often associated with smoking. However, this connection was less pronounced in the gingiva. In contrast to this study, males are more commonly affected with OSCC [8, 11, 16, 18]. Similar to the results of the current study, the number of OSCC cases was extremely low in all of the studies, and the mandible was where cancer was most frequently reported.

In comparison to the past studies, the present study did not find even a single case of a benign neoplastic lesion on the gingiva [6, 7, 18]. One of the difficulties associated with the actual prevalence of benign tumors in the

gingiva is the use of different classification systems by various studies. In some studies, POF, fibroma, squamous papilloma, angiofibroma, and giant cell fibromas were classified as benign tumors [3, 4, 6, 7, 18], which has likely led to an increased prevalence of benign tumors.

The rarest lesions were gingival pigmentation and specific infections, with only one case reported of each. In contrast to other infections [9, 16] that exhibit a male and maxillary jaw preponderance, one instance of squamous papilloma implicated the anterior mandible in a 52-year-old female. Consistent with a prior study, gingival pigmentation was observed in the anterior maxilla of a 40-year-old female [14].

Gingival and alveolar mucosal biopsies showed a marked difference in the results **(Table 3)**. In contrast to gingival patients, males (62.85%) were affected more than females. Both were found to have a certain degree of similarity, which often affected the posterior portion of the jaw. In a single case, a reactive lesion was found in the alveolar mucosa, which was reported as PG in the maxilla of a female. However, the reactive lesions of the alveolar mucosa cannot be compared with gingival cases due to the disparity between the frequency of their occurrence at both sites.

Malignant tumors have been reported on both the gingival and alveolar mucosa. Based on the current study findings, neoplasms in the gingiva appeared to be relatively rare (3.64%), while the alveolar mucosa had an overwhelming number of cases (98.58%). This may most likely be because the two tissues – one lining the mucosa and the other masticatory – are exposed to similar mechanical stress in the oral cavity, but they differ in their connective tissue organization and epithelial turnover rate [4]. In light of previous studies [6, 7, 18], neoplastic lesions accounted for 10%–25% of the combined total lesions at both sites. OSCC is by far the most common malignancy with a mean age of onset in the fifth and sixth decades, but it had a different incidence at both locations. In OSCC of the alveolar mucosa cases, there was a male and maxillary jaw predilection, which was opposite to that found in gingival biopsied lesions. In addition to OSCC, adenoid cystic carcinomas and malignant salivary gland tumors in the alveolar mucosa were also reported in this study, while non-Hodgkin lymphoma, small round cell tumor, verrucous carcinoma, and malignant melanoma occurred in the gingiva.

The reciprocal relationship between oral pathology and periodontology has already been investigated [28], highlighting the need for the two disciplines to work in sync to formulate a definitive diagnosis and effective treatment of gingival and alveolar mucosal lesions at the earliest. Although classifying such lesions remains the responsibility of periodontists, an oral pathologist could help formulate the correct nomenclature by withdrawing the outdated terms and placing the lesions in wider subheadings [9].

Conclusion

The present study highlights the high prevalence of gingival and alveolar mucosal lesions in oral tissue biopsies. A marked contrast was also observed in the results of the two tissue biopsies. In contrast to gingival lesions, alveolar mucosal biopsies resulted in neoplastic lesions with a predominant male prevalence, which most commonly affected the lower jaw. The difference could be attributed to the different nature of these tissues (epithelium and its thickness, degree of keratinization, vascularity, approximation to the bone). These results could help update data on the frequency distribution of these lesions in the Indian subpopulation and aid general practitioners and periodontists in identifying the most common lesions and formulating their treatment plan. The use of standard terminology and its further classification will help facilitate the comparison of epidemiological data from different studies and improve patient management. Future multicenter nationwide studies are the order of the day to collect data from across the country to know in depth the epidemiology, characteristics, and frequency distribution of these lesions.

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