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# **ORIGINAL ARTICLE**

# Gingival and alveolar ridge overgrowths: A histopathological evaluation from Saudi Arabia



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## KEYWORDS

Alveolar ridge; Gingiva; Incidence; Non-plaque-induced gingival disease; Lumps; Oral pathology **Abstract** *Background:* Focal tissue overgrowths on the gingiva and edentulous alveolar ridge are occasionally perplexing to periodontists, owing to the wide variety of differential diagnoses that may be responsible. As such, biopsy and microscopy are often required to establish a definitive diagnosis. The present study aimed to retrospectively evaluate focal gingival and alveolar ridge overgrowths at a single institution in Saudi Arabia.

*Materials and Methods:* Histopathology reports and slides from patients presenting to King Saud University Hospital between 1984 and 2016, particularly those with focal gingival enlargements other than those due to gingivitis and periodontitis, were collected and analyzed based on age, sex, and location.

*Results:* A total of 624 patient records were evaluated, with a mean age of 35 years (range, 1 week–91 years), peak incidence in the third decade of life, male-to-female ratio of 1:1.4, and a slightly higher prevalence of lesions in the mandible. The majority (88%) of the lesions were reactive or hyperplastic, followed by malignant (10%) and benign (2%) tumors. A total of 24 distinct histological entities were diagnosed across the three groups. The most common histologically diagnosed lesions were pyogenic granulomas (38%), fibromas (33%), peripheral ossifying fibromas (9%), squamous cell carcinomas (7%), peripheral giant cell granulomas (6%), neurofibromas (1%).

*Conclusion:* Similar to what has been reported by most previous studies, reactive hyperplastic lesions were the most prevalent focal overgrowths found in the gingival and alveolar mucosae. Carcinomas at these sites, however, may be an understated but significant clinical and epidemiological problem in Saudi Arabia. Gingival and alveolar ridge lumps can serve as a nexus for cooperation

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between periodontologists and oral pathologists to improve diagnosis, disease classification, and patient management.

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#### 1. Introduction

The gingival and edentulous alveolar ridge mucosae are primarily structured to adapt to the forces of mastication and oral friction (Kfir et al., 1980). In 1999, specific diseases and conditions of the gingiva were categorized into two broad groups: dental plaque-induced gingival conditions (DPIGC) and nonplaque-induced gingival diseases (NPIGD) (Caton et al., 2018). DPIGCs often do not require a histopathological examination, as they are treatable with effective oral hygiene, plaque elimination, and periodontal treatment (Kinane et al., 2017, Hirschfeld et al., 2019), although biopsies are sometimes requested when there is doubt about their nature (Armitage 2004). Conversely, as NPIGDs are not primarily caused by dental plaque, they typically do not resolve after plaque removal, although their severity may be affected by their interaction with residual plaque (Holmstrup et al., 2018). More often than not, these lesions require a biopsy and histological examination for diagnosis and proper management (Holmstrup et al., 2018).

Microscopic examination of biopsy specimens by oral pathologists provides a reliable way to diagnose and categorize gingival and alveolar ridge (GAR) lesions to ensure that appropriate management procedures are selected. Previous studies have focused on GAR mucosal lesions (Eversole and Rovin 1972, Anneroth and Sigurdson 1983, Barasch et al., 1995, Ababneh 2006, Zhang et al., 2007, Shamim et al., 2008, Buchner et al., 2010, Effiom et al., 2011, Carbone et al., 2012, Hunasgi et al., 2017, Alblowi and Binmadi 2018, Hernandez-Rios et al., 2018), although many were solely devoted to reactive lesions (Eversole and Rovin 1972, Anneroth and Sigurdson 1983, Zhang et al., 2007, Buchner et al., 2010, Effiom et al., 2011, Hunasgi et al., 2007, Buchner et al., 2010, Effiom et al., 2011, Hunasgi et al., 2017), a specific neoplasm only (Barasch et al., 1995), or a mixture of NPIGDs and DPIGCs (Carbone et al., 2012, Alblowi and Binmadi 2018).

The present study aimed to evaluate GAR mucosal overgrowth biopsy specimens submitted to our small university-based biopsy service to establish their prevalence and demographic characteristics in our area, compared with similar reports in relevant scientific literature, and to reevaluate the role of the oral pathologists in the diagnosis of these lesions.

## 2. Materials and methods

The present study was a retrospective review of histopathology reports and archived slides of patients with GAR overgrowths who visited the College of Dentistry, King Saud University, Riyadh, Saudi Arabia, between 1984 and 2016. The biopsy service primarily serves the employees of King Saud University, the general public residing near the facility, and patients on referral from distant regions. The cases included in the present study all had demographic data and retrievable histopathological slides or blocks available. To be included, documentation of the lesion having occurred in the gingiva or the alveolar ridge was required in the pathology reports. All cases not classifiable as overgrowths, such as gingivitis, ulcers of any type, and lesions presenting as macules, patches, or plaques, and including white, red, or pigmented lesions, were excluded. Patients with intraosseous tumors or cysts that extended into the gingival or alveolar mucosae were also excluded. The original hematoxylin-eosin stained slides prepared from paraffin-embedded biopsy samples were retrieved; however, if the original slides were not available, new slides were prepared from archived tissue blocks. None of the slides were deteriorated to the point that it affected the diagnosis. Each diagnosis was verified by both authors, and each case was classified as one of the following: 1) reactive hyperplasia or tumor-like lesion; 2) benign neoplasia; or 3) malignant neoplasia. Data were primarily analyzed as frequency distribution and chi-square statistics, where appropriate, using IBM SPSS version 23 (IBM Corp., Armonk, NY, USA), and are presented in tables or descriptively. An independent t-test was used to compare the mean values.

The present study was registered and approved by the College of Dentistry Research Center (CDRC); registration number, FR 0278.

## 3. Results

#### 3.1. General characteristics

From the 5,522 biopsy records reviewed, 624 cases (11%) met the inclusion criteria for the present study. Gingival lesions accounted for 86% of the cases, while alveolar ridge lesions accounted for 14% (Table 1). The mean age of the patients was 35 years (range, 1 week to 91 years), although there was a significant difference in the mean age based on the site of presentation (P < 0.001). Overall, 58% (n = 361) of the cases were of women (male-to-female ratio, 1:1.4). The peak age of incidence for both sexes was in the third decade of life; however, in the first six decades, there was a strong female predominance, followed by a negligible male predominance thereafter (Fig. 1a), resulting in a significant difference between the sexes in relation to age group (P = 0.002;  $\chi^2 = 26.159$ ). Lesions were more common in the mandible than in the maxilla (48% vs. 44%, respectively), and the majority of the lesions were reactive/hyperplastic (88%; Fig. 1b), followed by malignant (10%). Benign tumors constituted only 2% of all lesions. In terms of the frequency of individual lesions, the most common were pyogenic granulomas (PGs; 38% of all cases, Fig. 2a,b), fibromas (33%), peripheral ossifying fibromas (POFs; 9%, Fig. 2c,d), squamous cell carcinomas (SCCs; 7%), peripheral giant cell granulomas (PGCGs; 6%), neurofibromas, and non-Hodgkin lymphomas (1% each) (Table 2).

 Table 1
 General characteristics of Gingival and Alveolar Ridge Overgrowths.

General Characteristics*	Gingiva (%)	Alveolar Ridge (%)	Total (%)		
Type of Lesions					
Reactive/	<b>498</b> (79.8)	<b>50</b> (8.0)	<b>548</b> (87.8)		
Hyperplastic Lesions					
Benign tumors	5 (0.8)	<b>10</b> (1.6)	15 (2.4)		
Malignant tumors	30 (4.8)	31 (5.0)	61 (9.8)		
Total	535 (85.7)	89 (14.3)	<b>624</b> (100)		
Age (Mean; Range)	34 (1.5 - 91)	46 (0.02 - 91)	35 (0.02 -		
years	$32 \pm 16.4$	50 ± 19.8	91)		
Median; Standard			$34 \pm 17.4$		
deviation					
Sex (M: F)	218: 315	45: 46	263: 361		
	(41: 59)	(49.5:50.5)	(42:58)		
Location	× /	× /	. ,		
Maxilla	<b>243</b> (46)	<b>30</b> (33)	273 (44)		
Mandible	249 (47)	<b>53</b> (58)	302 (48)		
Both	2 (0.4)	<b>1</b> (1)	3 (0.5)		
Not stated	<b>39</b> (7)	7 (8)	<b>46</b> (7.5)		
Total	<b>533</b> (85)	<b>91</b> (15)	<b>624</b> (100)		

\* Percentages may not add up to, or may be over 100 in some cases because of rounding up of values.

#### 3.2. Reactive/Hyperplastic lesions

There were four types of lesions that were predominant among the reactive/hyperplastic group: PGs (43%), fibromas (40%), POFs (10%), and PGCGs (5%), accounting for 98% of the lesions in this group. The male-to-female ratio was 1:1.7 (39% to 61%), indicating a strong female predominance, and the mean age of the patients at presentation was 34 years. The prevalence of lesions in upper and lower jaws appeared to be similar, although 40 cases did not include recorded jaw locations. Further analysis of the four most common lesions in the reactive/hyperplastic group indicated that they constituted 86% of all lesions. The characteristic features of this group were conferred by these four lesions. The mean age of the patients with fibromas was significantly higher than that of the three others, i.e. PG, POF and PGCG (P = 0.039). PGs were more common in the maxilla, POFs had an almost equal occurrence in both jaws, and fibromas and PGCGs occurred slightly more in the mandible. It is not clear if the relative prevalence of lesions occurring in the jaws would have remained if the cases without recorded jaw locations had been properly documented (Table 2).

## 3.3. Benign tumors

Benign tumors were generally rare in the GAR mucosae (15 cases, 2% of the total lesions). The mean patient age at presentation was 29 years (range, 9 days to 81 years), with an almost equal sex predilection, and a slightly increased prevalence in the maxilla, likely due to the absolute maxillary predilection of congenital epulis (Table 2). Only neurofibromas and congenital epulis were fairly common in this group. The remaining five tumors together constituted five cases (33%). Peripheral odontogenic tumors, including peripheral ameloblastomas, peripheral calcifying epithelial odontogenic tumors, and peripheral odontogenic fibromas, were found to be rare, constituting 20% (3/15) of the benign tumor cases.

#### 3.4. Malignant tumors

Compared to benign tumors, malignant tumors were relatively more common (61 cases, 10% of the total lesions), and they were twice as common in men as women. The mean age at presentation was 53 years (range, 15–91 years), and more than two-thirds of the cases occurred in the mandible. This trend was well reflected by the number of SCC cases, which disproportionately predominated this group (72% of the cases, Fig. 3a–d). SCCs had a mean age of presentation of 61 years, were almost twice as common in men, and were approximately five times more common in the mandible than in the maxilla (Table 2). Non-Hodgkin lymphomas (NHLs; 10%) and rhab-

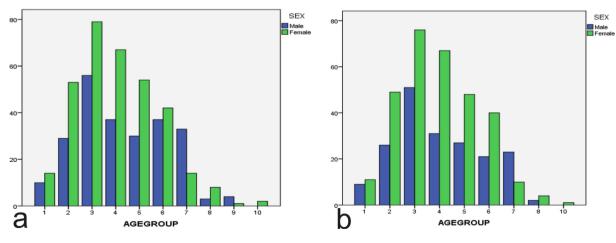
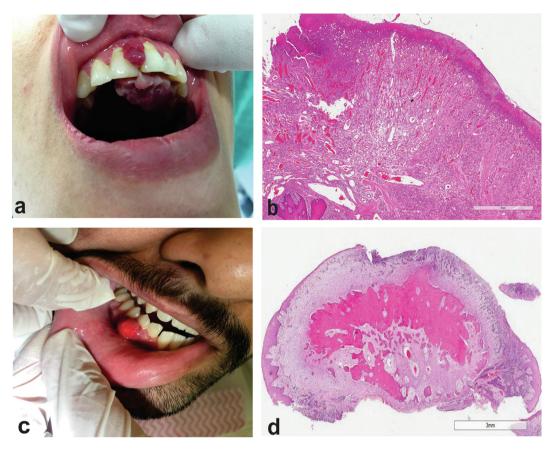


Fig. 1 a. Distribution of all lesions by age group versus sex. Strong female predilection in the first six decades of life; and b. distribution of the four most common hyperplastic lesions based on age and sex, mirroring the distribution of all lesions. Note: age groups are presented in decades (e.g., 1 = 0-9 years, 2 = 10-19 years, and so on.).



**Fig. 2** a,b. Pyogenic granuloma. A 22-year-old pregnant woman presenting with a relatively large, soft, ulcerated gingival overgrowth extending from the palatal to the labial surface of the upper central incisor teeth (a relatively large mass), for which microscopy showed pyogenic granuloma with ulceration; and c,d. Peripheral ossifying fibroma. An 18-year-old man with a red, soft-to-firm lesion on the right mandibular gingiva, particularly the facial surface of the canine and first premolar, for which histopathology was consistent with a peripheral ossifying fibroma as well as ulceration.

domyosarcomas (7%) were the only tumors that appeared to be fairly common in this group, as the remaining five malignant tumors accounted for only seven lesions (12%).

## 4. Discussion

The clinical differential or provisional diagnoses of lumps in the GAR are often diverse, and are occasionally incongruent with subsequent histology-based diagnoses, which usually range from hyperplastic lesions to benign and malignant tumors (Bello et al., 2022). The dual roles of the GAR as part of the oral mucosa and periodontium, along with the functional adaptation to frictional and pressure-related forces during mastication, are related to the variety of lesions encountered (Schroeder and Listgarten 1997).

The results of the present study showed that the vast majority of GAR overgrowths were reactive in nature, and four types of lesions (PGs, fibromas, POFs, and PGCGs) virtually dominated the prevalence of all other lesions. This finding is in accordance with almost every previous study on this subject. The most common lesion type in several studies was PG (Ababneh 2006, Shamim et al., 2008, Effiom et al., 2011, Alblowi and Binmadi 2018), while other reports found fibromas to be the most common of the four dominant lesions (Zhang et al., 2007, Buchner et al., 2010, Hernandez-Rios et al., 2018, Li et al., 2021). There may be a true difference in the prevalence of these four lesions based on specific geographical locations, or it may be related to the timing of presentation, as it has been suggested that long-standing PGs can mature into fibromas, which would explain the predominance of fibromas in some studies (Eversole and Rovin 1972). Therefore, it can be suggested that in populations with a higher prevalence of fibromas, late patient presentation resulted in PGs undergoing fibroplasia and presenting as fibromas. Fibromas are the most common reactive hyperplastic lesions encountered on the alveolar ridge, with a significantly higher mean age for fibromas than the other three lesion types. Edentulousness is often associated with increasing age, and the increased mean age of patients presenting with fibromas may therefore support hypotheses regarding ageand edentulousness-related fibrous proliferation.

Although hyperplastic lesions may occur at any age, most cases are seen in the third to fifth decades of life, alongside a definite female predilection. As has been well documented in the relevant literature, the effects of hormonal changes are significant in women in this age range, especially in cases of PG (Park et al., 2017), which constituted the most common lesion seen in the present study. A good example is the pronounced, aggressive-looking features of PGs during pregnancy (granuloma gravidarum) due to hormonal changes associated with

Table 2 Distribution of specific lesions according to age, sex and location on both gingiva and alveolar ridge.

	TOTAL	SEX MEAN AGE		LOCATION (Jaw)				
	(n = 624)	M (%) F	(%) F (%) (Range) years		Maxilla (%) Mandible (%) Both (%) Unknown (%)			
Reactive/Hyperplastic Lesions								
Pyogenic granuloma	236	<b>86</b> (36)	150 (64)	33 (4–79)	115 (49)	104 (44)	-	17 (7)
Fibroma	208	<b>87</b> (42)	121 (58)	36 (2–91)	<b>89</b> (43)	100 (48)	3 (1)	<b>16</b> (8)
Peripheral ossifying fibroma	56	19 (34)	37 (66)	31 (10-61)	<b>26</b> (47)	27 (48)	_	<b>3</b> (5)
Peripheral giant cell granuloma	38	16 (42)	<b>22</b> (58)	35 (7-65)	16 (42)	<b>20</b> (53)	_	<b>2</b> (5)
Squamous papilloma	4	<b>3</b> (75)	1 (25)	27 (10-45)	2 (50)	-	_	2 (50)
Traumatic neuroma	3	<b>2</b> (67)	1 (33)	41 (28-62)	1 (33)	<b>2</b> (67)	_	-
Nodular fasciitis	1	1 (100)	-	20	-	1 (100)	_	-
Verruciform xanthoma	1	1 (100)	_	40	1 (100)	-	-	-
Leiomyomatous hamartoma	1	1 (100)	-	1	1 (100)	-	_	-
	548	216 (39)	332 (61)	34 (1–91)	251 (46)	254 (47)	3 (0.01)	40 (7)
Benign Tumors								
Neurofibroma	6	4 (67)	<b>2</b> (33)	53 (20-81)	<b>2</b> (33)	<b>3</b> (50)	_	1 (17)
Congenital Epulis	4	1 (25)	<b>3</b> (75)	0.3 (0.02–1)	4 (100)	-	_	-
Myofibroma	1	-	1 (100)	12	-	1 (100)	_	-
Inflammatory myofibroblastic tumor	1	-	1 (100)	45	1 (100)	-	-	-
Peripheral ameloblastoma	1	1 (100)		65		1 (100)	_	-
Peripheral CEOT	1		1 (100)	27	1 (100)		-	-
Peripheral odontogenic fibroma	1	1 (100)	-	13	-	1 (100)	_	-
	15	7 (47)	8 (53)	29 (0.02-81)	8 (53)	6 (40)	_	1 (7)
Malignant Tumors								
Squamous cell carcinoma	44	<b>29</b> (66)	15 (34)	61 (32–91)	7 (16)	<b>34</b> (77)	-	<b>3</b> (7)
Non-Hodgkin lymphoma	6	<b>6</b> (100)	_	34 (16-50)	<b>2</b> (33)	<b>3</b> (50)	-	1 (17)
Rhabdomyosarcoma	4	<b>2</b> (50)	<b>2</b> (50)	21 (15-30)	<b>3</b> (75)	1 (25)	_	-
Malignant fibrous histiocytoma	2	1 (50)	1 (50)	35 (30-40)	1 (50)	1 (50)	-	-
Melanoma	2	-	<b>2</b> (100)	40	-	1 (50)	_	1 (50)
Verrucous carcinoma	1	1 (100)	-	50	-	1 (100)	_	-
Malignant peripheral nerve sheath tumor	1	_	1 (100)	19	-	1 (100)	_	-
Kaposi sarcoma	1	1 (100)	-	80	1 (100)	_	_	-
	61	40 (66)	21 (34)	53 (15–91)	14 (23)	42 (69)	-	5 (8)

pregnancy (Fig. 2a). The four common reactive lesion types have often been said to be expressions of the developmental stages of the same lesion (Eversole and Rovin 1972). While this may be readily apparent in PGs and fibromas, it would be less apparent in relation to POFs and PGCGs, where cells within the periodontal ligament with the capability of producing bone or cementum (Macleod and Soames 1987, Prasad et al., 2008), or mononuclear histiocytes differentiating into osteoclast-like giant cells (Aghbali et al., 2018), may possibly contribute to their histogenesis.

Based on the results of the present study, neoplasms seemed to be relatively rare on the gingiva, while the alveolar mucosa acted as a host for quite a few such lesions. Considering previous studies (Ababneh 2006, Shamim et al., 2008, Hernandez-Rios et al., 2018), neoplastic lesions accounted for 10-25% of the combined total lesions found at the two sites. One of the problems associated with the true prevalence of benign tumors in the gingiva is that the classification was not consistent across the various studies. Some studies categorized reactive entities, such as POFs, giant cell fibromas, fibromas, angiofibromas, and squamous papillomas, as benign tumors (Stablein and Silverglade 1985, Ababneh 2006, Shamim et al., 2008, Alblowi and Binmadi 2018, Hernandez-Rios et al., 2018), which may account for the relatively high prevalence reported in those studies. In the present study, any lesion in which the major pathology was a non-neoplastic hyperplasia of fibrous and/or epithelial tissue was classified as reactive. Moreover, some studies, with or without this ambiguity in classification, have reported more malignant than benign tumors (Li et al., 2021). Benign tumors were found to be twice as common in the alveolar versus the gingival mucosa. Interestingly, despite being individually rare, peripheral odontogenic tumors are a relatively significant cause of gingival overgrowth when considered as a single group. In general, because of the small number of benign tumors in the gingival and alveolar mucosae, it is difficult to make reliable statistical inferences.

Malignant tumors appeared to be evenly distributed between the GAR mucosae. SCC was by far the most common malignancy, with a mean age significantly higher than that seen with other malignancies, a mandibular predilection, and an increased prevalence in the alveolar versus the gingival mucosae (26 versus 18 cases, respectively). Our findings in the present study are supported by the results of several previously published studies (Shamim et al., 2008, Carbone et al., 2012, Kamath et al., 2013, Hernandez-Rios et al., 2018, Li et al., 2021). A more recent study (Li et al., 2021) actually found SCC to be the most common single gingival lesion in their large series (approximately 31% of all lesions), and reports from Asia suggested that SCC was significantly more common there than in the West (Shingaki et al., 2002, Mehrotra et al., 2003, Li et al., 2021), along with the mean



**Fig. 3** a. **Squamous cell carcinoma.** A 57-year-old man with a verrucopapillary lesion on the gingiva, related to the left lower molars (area with the circle); **b.** epithelial hyperplastic papillary lesion with pronounced hyperparakeratinization and elongated rete ridges; **c.** pushing border and chronic inflammation at the epithelial connective tissue interface; and **d.** invasive islands in a focal area in the connective tissue of the same lesion. The lesion was diagnosed as a squamous cell carcinoma arising from a verrucous carcinoma.

age at presentation being at least a decade younger (Shamim et al., 2008, Gupta et al., 2013). Earlier studies indicated an increasing incidence in females with an associated inverted male-to-female ratio (Barasch et al., 1995). This trend, however, has not been supported by more recent observations (Gomez et al., 2000, Fitzpatrick et al., 2012). Our findings on SCCs were generally in agreement with most previous studies, except for the aforementioned report (Li et al., 2021), which appears to be an outlier in regards to the prevalence of gingival SCCs. The results of the present study also showed that, in addition to SCCs, the GAR mucosae also host a variety of malignant neoplasms in comparison to benign ones, and that NHL and rhabdomyosarcoma should rank high among the differential diagnosis for malignant tumors when lumps are found at these sites.

The relationship between periodontology and oral pathology has been previously evaluated (Rich et al., 2017), highlighting how the two disciplines need to work together in order to diagnose and manage NPIGDs in a timely manner. While the classification of these diseases remains the duty of periodontists, the assistance of pathologists may be important in establishing the correct nomenclature, while removing outdated or unclear terms, and increasing the number of entities which can be included in the subclasses. This standardization will make it easier to compare the epidemiological features of the various types of lesions among numerous studies and enhance patient management.

#### 5. Conclusion

Overall, the GAR mucosal lumps observed by our biopsy service did not significantly differ from those observed in previous studies, and reactive lesions were by far the most common lumps encountered at these sites. While tumors are rather uncommon, SCCs might be epidemiologically important in Saudi Arabia as well as different areas of Asia compared to other parts of the world. Cooperation between periodontists and oral pathologists would be helpful in characterizing these lesions to improve epidemiological information and patient management.

#### **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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