

# Relative frequency of oral focal reactive overgrowths: An institutional retrospective study

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## Abstract

**Context:** Focal fibrous hyperplasia, peripheral ossifying fibroma, pyogenic granuloma, peripheral giant cell granuloma, giant cell fibroma and focal reactive overgrowth (FROGs) are one of the foremost numerous benign soft-tissue growths in the oral cavity. Chronic irritation or trauma is with identified as the causative aspect. It may develop up to few centimeters in diameter, pedunculated or sessile and may arise on the gingiva or buccal mucosa. Treatment involves surgical excision, and recurrences are infrequent.

**Aims:** The aim of this study was to assess the prevalence of FROGs of oral mucosa in an institutional setup.

**Subjects and Methods:** All the histopathologically diagnosed cases of FROGs within a period of 10 years (January 2008–December 2017) were retrieved from the archives of the Department of Oral Pathology. The information such as age, sex, site, anatomical side and its prevalence were recorded on customized case history performa.

**Statistical Analysis Used:** The significance of difference was assessed using the Chi-square test and Fisher's exact test.

**Results:** A total of 2849 cases were identified, of which 449 (15%) were FROGs. The most prevalent lesion amid them were focal fibrous hyperplasia (277, 62%), followed by pyogenic granuloma (92, 20%), whereas the least common was giant cell fibroma with 2 (0.5%) cases. All the FROGs were distributed among 21–40 years of age showing female predominance. The commonly affected site was the right buccal mucosa.

**Conclusions:** Nevertheless, information of the frequency and distribution of these lesions is favorable when establishing a diagnosis and treatment plan in clinical practice.

**Keywords:** Fibroma, hyperplasia, lobular capillary hemangioma, oral mucosa, pyogenic granuloma, tumor

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## INTRODUCTION

Oral mucosa is subjected persistently to external and internal stimuli that can lead to the development of the lesions known as focal reactive overgrowths (FROGs).

They occur in reaction to low-grade chronic irritation by dental plaque, calculus, food lodgment, faulty restoration, ill-fitting dental/oral appliances.<sup>[1]</sup> They manifest as a group of diseases which include focal fibrous hyperplasia (FFH), peripheral ossifying fibroma (POF),

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fibro-epithelial hyperplasia/polyp, peripheral giant cell granuloma (PGCG), pyogenic granuloma (PG), giant cell fibroma (GCF) and inflammatory gingival hyperplasia.<sup>[2]</sup> These proliferations clinically manifest as painless swellings with pedunculated or sessile base that contrast in color from light pink to red. The surface may be smooth, uneven or ulcerated. Histologically, fibrous tissues with a range of components such as multinucleated giant (MNG) cells, calcified materials or small vessel hyperplasia may be noted.<sup>[3]</sup> Surgical excision along with the removal of causative irritants remains the treatment of choice.<sup>[4]</sup>

Eversole and Rovin hypothesized to facilitate the different histological entities of inflammatory hyperplasia may possibly be due to connective tissue response to diverse intensities of mucosal irritation.<sup>[5]</sup> The differential diagnoses of FROGs are not easy due to their similarity in clinical appearance to that of neoplastic proliferation.<sup>[3]</sup> However, knowledge about the distribution of these lesions is very essential for prompt diagnosis and early intervention. Hence, this study intends to evaluate and compare the relative frequencies and the clinical aspects of oral mucosal FROGs in an institutional setup.

## SUBJECTS AND METHODS

A retrospective cross-sectional study was conducted on the hematoxylin- and eosin-stained formalin-fixed paraffin-embedded tissue sections of FROG retrieved from the archives of the Department of Oral and Maxillofacial Pathology, Institute of Dental Sciences, Bareilly, available from January 2008 to December 2017.

All the microscopic sections were examined by two pathologists. Most of the lesions could be readily classified into FFH, POF, PG, PGCG and GCF. However, some cases were intermediate

between FFH and PG, and then, they were categorized as PG if the endothelial and inflammatory components were prominent and FFH if the collagenous component was dominant. Cases of epulis fissuratum (denture-induced fibrous hyperplasia) were excluded from the study.

Clinical information relating to the type of lesion, age, gender, site and anatomical side was obtained from the submitted biopsy request forms and recorded and tabulated on customized data forms for all the lesions. Cases with incomplete data were reevaluated for the missing information. The significance of difference was assessed using the Chi-square test and Fisher's exact test.  $P < 0.05$  was considered statistically significant. Data were analyzed using the Statistical Package for the Statistical Package for the Social Sciences (SPSS) statistical software (IBM, Chicago, Illinois, USA, version 18).

## RESULTS

A total of 2849 cases during the period of 10 years were retrieved, of which 449 (16%) were found to be FROG. The most prevalent lesion among them was FFH, i.e., 277 (62%), followed by PG, i.e., 92 (20%), whereas the least common was GCF, i.e., 2 (0.5%) cases [Table 1]. They were mostly distributed among 21–40 years of age which showed a statistically significant difference [Table 2]. They showed a female predominance except in GCF [Table 3] with gingiva being the frequently affected site [Table 4]. On the whole, the right side was the most commonly affected side [Table 5].

## DISCUSSION

FROGs are a common lesion occurring in the oral cavity due to the increased frequency at which the tissues are

**Table 1: The master chart showing the prevalence of focal reactive overgrowths of oral mucosa since 2008 till 2017**

Year-wise distribution	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	Total (%)
Total cases	201	213	171	267	236	256	412	454	303	336	2849 (100)
Focal reactive overgrowths	39	37	30	24	22	40	78	65	32	82	449 (16)
Focal fibrous hyperplasia	28	33	16	13	15	25	59	46	6	36	277 (62)
Peripheral ossifying fibroma	3	2	10	8	1	3	0	6	8	4	45 (10)
Pyogenic granuloma	3	2	4	2	4	7	9	11	12	38	92 (20)
Peripheral giant cell granuloma	5	0	0	1	0	5	10	2	6	4	33 (7.5)
Giant cell fibroma	0	0	0	0	2	0	0	0	0	0	2 (0.5)

**Table 2: Age-wise distribution of focal reactive overgrowths of oral mucosa**

Focal reactive overgrowths	Age group (years)				P
	0-20 (%)	21-40 (%)	41-60 (%)	61-80 (%)	
Focal fibrous hyperplasia	55 (20)	127 (46)	59 (21)	36 (13)	<0.001 (significant)
Peripheral ossifying fibroma	19 (42)	21 (47)	3 (7)	2 (4)	<0.001 (significant)
Pyogenic granuloma	33 (36)	40 (43)	17 (19)	2 (2)	<0.001 (significant)
Peripheral giant cell granuloma	3 (10)	21 (64)	5 (16)	4 (13)	<0.001 (significant)
Giant cell fibroma	-	1 (50)	1 (50)	-	-
Total	110 (24)	210 (47)	85 (19)	44 (10)	

injured. The literature, when reviewed, showed reactive lesions occurring in various incidences [Table 6]. Chronic trauma can bring about inflammation leading to granulation tissue with endothelial cell proliferation, chronic inflammatory cells and soon after fibroblasts proliferate and noticeable as an overgrowth called reactive hyperplasia.<sup>[6]</sup> Irritation fibroma, oral leukoplakia and OSCCs mostly showed an increased expression of matrix metalloproteinase (MMP)-2 and MMP-9 in the epithelium and connective tissue compared with normal mucosa. There was a significant difference in the epithelial expression of MMP-2 and MMP-9 between irritation fibroma and oral leukoplakia.<sup>[7]</sup>

In the present study, FFH was the most common lesion encountered when compared to all the other reactive overgrowths of the oral cavity, and similar results have been recorded by Kfir *et al.*,<sup>[8]</sup> Buchner *et al.*,<sup>[9]</sup> Reddy *et al.*<sup>[6]</sup> and Kadeh *et al.*<sup>[10]</sup> Histologically, it shows hyperplastic fibrous tissue with varying degrees of collagenization.<sup>[11]</sup> Some time secondary to orthodontic treatment they appear paler in color and bulky, in comparison to inflammatory induced outgrowth which are red and flimsy.<sup>[12]</sup> Mucoperiosteal raised flaps help to excise lesion satisfactorily followed by debridement and curettage of the underlying bone and adjacent tooth root surface.<sup>[13]</sup>

In the present study, PG was the second most common lesion encountered after FFH which was in accordance with the study by Peralles *et al.*<sup>[14]</sup> Contrastingly, Stablein and Silverglade,<sup>[15]</sup> Zarei *et al.*,<sup>[16]</sup> Effiom *et al.*<sup>[4]</sup> and Kashyap *et al.*<sup>[11]</sup> concluded PG as the first most common lesion followed by FFH. PG comprises a variety of terminologies such as benign vascular tumor, pregnancy tumor and vascular epulis.<sup>[17]</sup> The major etiological factors are the occurrence of plaque, calculus and pregnancy.<sup>[18]</sup>

**Table 3: Gender-wise distribution of focal reactive overgrowths of oral mucosa**

Focal reactive overgrowths	Male (%)	Female (%)	P
Focal fibrous hyperplasia	132 (48)	145 (52)	0.6714 (nonsignificant)
Peripheral ossifying fibroma	17 (38)	28 (62)	<0.001 (significant)
Pyogenic granuloma	13 (39)	20 (61)	<0.001 (significant)
Peripheral giant cell granuloma	31 (34)	61 (66)	<0.001 (significant)
Giant cell fibroma	2 (100)	0 (0)	-
Total	195 (43)	254 (57)	

**Table 4: Site-wise distribution of focal reactive overgrowths of oral mucosa**

Focal reactive overgrowths	Site				P
	Buccal mucosa (%)	Gingiva (%)	Palate (%)	Total (%)	
Fibroma	61 (22)	188 (68)	28 (10)	277 (100)	0.001*
Peripheral ossifying fibroma	0 (0)	24 (53)	21 (47)	45 (100)	0.002*
Peripheral giant cell granuloma	0 (0)	30 (90)	3 (10)	33 (100)	0.336#
Pyogenic granuloma	8 (9)	75 (82)	9 (9)	92 (100)	0.088#
Giant cell fibroma	0	2 (100)	0	2 (100)	-

\*Denoted for significant value, #Denoted for non-significant value

**Table 5: Side-wise distribution of focal reactive overgrowths of oral mucosa**

Focal reactive overgrowth	Anatomical side				P
	Left (%)	Right (%)	Midline (%)	Total (%)	
Fibroma	61 (22)	188 (68)	28 (10)	277 (100)	<0.001 (significant)
Peripheral ossifying fibroma	5 (11)	16 (36)	24 (53)	45 (100)	0.0023 (significant)
Pyogenic granuloma	29 (32)	40 (43)	23 (25)	92 (100)	0.0889 (nonsignificant)
Peripheral giant cell granuloma	9 (27)	9 (27)	15 (46)	33 (100)	0.3362 (nonsignificant)
Giant cell fibroma	2 (100)	0	0	2 (100)	-

**Table 6: Literature review showing year-wise distribution of focal reactive overgrowths of oral mucosa**

Authors	Year	Study duration	Study period (years)	Sample size (%)	Lesions				
					FFH (%)	POF (%)	PG (%)	PGCG (%)	GCF (%)
Kfir <i>et al.</i>	1980	1968-1978	11	741 (64)	414 (56)*	78 (11)	199 (27)	50 (7) <sup>+</sup>	-
Stablein <i>et al.</i>	1985	1978-1983	6	460 (55)	163 (35)	74 (16)	197 (43)*	26 (6) <sup>+</sup>	-
Zarei <i>et al.</i>	2007	2000-2005	5	111 (32)	21 (19)	18 (16) <sup>+</sup>	40 (36)*	32 (29)	-
Buchner <i>et al.</i>	2010	1989-2008	20	1675 (7)	532 (32)*	341 (29)	488 (29)	314 (19) <sup>+</sup>	-
Effiom <i>et al.</i>	2011	1970-2008	38	314 (6)	61 (19)	64 (20)	179 (57)*	10 (3) <sup>+</sup>	-
Naderi <i>et al.</i>	2012	1988-2005	17	1276 (61)	288 (14) <sup>+</sup>	-	365 (18)	623 (30)*	-
Reddy <i>et al.</i>	2012	2001-2010	10	209 (13)	120 (57)*	37 (18)	39 (19)	13 (6) <sup>+</sup>	-
Kadeh <i>et al.</i>	2015	2006-2012	7	154 (34)	91 (20)*	11 (12) <sup>+</sup>	37 (41)	15 (17)	-
Kashyap <i>et al.</i>	2018	1.5 years	1.5	67%	35%	18%	42%*	10%*	-
Present study	2018	2008-2017	10	449 (15)	277 (62)	45 (10)	92 (20)	33 (7.5)	2 (0.5)

\*The most common lesion, <sup>+</sup>The least common lesion. FFH: Focal fibrous hyperplasia, POF: Peripheral ossifying fibroma, PGCG: Peripheral giant cell granuloma, PG: Pyogenic granuloma, GDF: Giant cell fibroma

Recently, it is also known as lobular capillary hemangioma due to the existence of well-circumscribed and discrete lobular arrangement, with central large vessels and peripheral aggregates of well-formed capillaries. These make tissues of gingiva further vulnerable to chronic inflammation secondary to plaque and calculus.<sup>[19]</sup> If left untreated, over time it undergoes fibrous maturation with ossification and develops into POF.<sup>[8]</sup> The hemorrhagic nature of the lesion poses obscurity during treatment; consequently, laser is recommended above scalpel resulting in less significant recurrence rates. The higher recurrence rate is contributed by poor oral hygiene, hormones, deep-seated lesions and existence of local irritants. Excision of PG for the period of pregnancy is indicated in the first trimester and must be avoided in the other two trimesters unless it causes purposeful destruction.<sup>[20]</sup>

In the present study, POF was the third most common FROG encountered. Parallel studies done by Zarei *et al.*<sup>[16]</sup> and Kadeh *et al.*<sup>[10]</sup> showed that POF was the least common lesion noted. The POF initiates from the undifferentiated mesenchymal cells of periodontal ligament (PDL), and allied causative agents are local irritants. The existence of oxytalan fibers within POF supports its source from PDL.<sup>[20]</sup> Clinically, POF presents as a sessile or pedunculated mass with discrepancy in the color ranging from erythematous to usual pink. A certain diagnosis of POF is made by histopathology, which comprises atrophic epithelium and dense connective tissue stroma with fibroblastic proliferation and least vascular formation. Concentrated chronic inflammatory cell infiltrates through foci of the cementum/dystrophic calcifications are apparent.<sup>[11]</sup>

In the present study, PGCG was the least frequently encountered FROG after GCF. Similarly, Kfir *et al.*,<sup>[8]</sup> Stablein and Silverglade,<sup>[15]</sup> Buchner *et al.*,<sup>[9]</sup> Effiom *et al.*,<sup>[4]</sup> Reddy *et al.*<sup>[6]</sup> and Kashyap *et al.*<sup>[11]</sup> also reported the same. Contrastingly, Naderi *et al.*<sup>[3]</sup> showed it as the most frequently arising lesion. PGCG is known to occur from the cells of PDL or periosteum of bone. The precise etiology is unidentified. Probable factors well-thought-out are chronic irritation, tooth extractions, xerostomia and hormones.<sup>[21]</sup> Definite parameters regarding this lesion such as its etiology, recurrent nature, proliferative potential and derivative roots of MNG cells and mononuclear stromal cells remain incomprehensible.<sup>[22]</sup> Cells of stroma are well-thought-out to be the proliferative section and are associated with the clinical behavior of lesion.<sup>[23]</sup> PGCG consists of abundant MNG cell and fibrocellular stroma. The source of giant cell is notorious and predictable to be originated from phagocytosis, osteoclasts, foreign body and endothelial blood cells. CD68 immunohistochemical positivity suggests

that the MNG cells are derived from monocyte/macrophage lineage.<sup>[24]</sup> The management comprises the elimination and inhibition of essential etiological factors with abolition of the whole base of the lesion.<sup>[20]</sup>

GCF was the least commonly encountered lesion in the present study, and it occurs in the age group between 21 and 60 years. Contrastingly, this lesion was not reported with any of the other parallel studies. The GCF was earliest known as an entity between fibrous hyperplastic soft-tissue lesions by Weathers and Callihan in 1974.<sup>[25]</sup> It was named for its MNG cells, which are usually large, stellate shaped with mono/multinuclear fibroblasts.<sup>[26]</sup> According to Sabarinath *et al.*,<sup>[25]</sup> it ranges between 4 and 17 mm in maximum dimension and predominance in the patients among 6–67 years of age. These giant cells were most numerous in the connective tissue beneath the epithelium.<sup>[2]</sup>

## CONCLUSIONS

The present study indicates some differences in the age, gender and site distribution among the reactive hyperplastic lesions. Although these lesions can be differentiated based on the clinical and histological appearance, these are the variations of a single entity which may be influenced by the irritant, duration of the lesion or possible hormonal changes. Proper diagnosis, prevention and treatment of these lesions are of utmost important due to the occurrence and similar presentations of neoplastic growths though the incidence is rare. Hence, close postoperative follow-up is required as some of the lesions may exhibit recurrence.

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## Conflicts of interest

There are no conflicts of interest.

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