Original Article

Prevalence Of Reactive Lesions of The Oral Cavity in Educational Hospitals and Institutions in Cairo (Cross Sectional Study)

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ABSTRACT

Introduction: Reactive lesions (RLs) of the oral cavity are non-neoplastic tumor-like hyperplasia that are often a response to persistent inflammation induced by different types of low-grade irritations. They are relatively common and have a clinical appearance similar to neoplastic proliferations. The purpose of this study was to evaluate the prevalence of reactive lesions based on WHO's head and neck tumor classification (2022) and the previous classifications in the literature over a period of 10 years in Cairo's educational hospitals and institutions and to compare the results with findings in the literature.

Materials and Methods: Data of reactive lesions diagnosed between 2011 and 2020 were collected from the files of the Cairo's educational hospitals and institutions. Furthermore, stratification of age, gender and site affection of each individual lesion will be performed. The data were recorded, then analyzed using SPSS software.

Results: Reactive lesions of the oral cavity constituted 10% of all the 21420 registered oral and maxillofacial biopsies. A total of 2142 cases of RLs were collected and reviewed. Of these, irritational fibroma was the common (40.7%) followed by pyogenic granuloma (27%). The gingiva was the most common site, while the anterior part of maxilla was the most frequently affected location. Females were commonly affected than males with ratio (1.8:1). The highest occurrence of reactive lesions was found with patients in the third and fourth decades.

Conclusions: There were some similarities as well as differences between our results and those of preceding studies involving different populations. we observed an obvious geographic variation in the relative frequencies of various reactive lesions in Cairo governorate. The corresponding prevalence of RLs in various nations can be retrospectively analyzed to improve knowledge of RLs, which is crucial for pathologists and oral and maxillofacial surgeons.

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Key Words: Epidemiology; oral cavity; oral pathology; prevalence; reactive lesions.

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INTRODUCTION

The tissues of the oral and maxillofacial area are constantly exposed to an abundance of inflammatory stimuli, which can be of bacterial, viral, physical, chemical, or immunological origin. Chronic/prolonged, low-grade inflammatory stimuli or recurrent irritation can induce an enhanced repair response in oral tissues, leading to the incidence of non-neoplastic, hyperplastic lesions, referred to as reactive lesions (RLs)^[1,3].

Reactive lesions differ in color, appearance, and volume from normal oral mucosa. The clinical features of these lesions can vary in various populations and ethnicity, indicating unique environmental factors and distinct lifestyles^[2]. Reactive lesions are widespread proliferations in the skeletal and soft tissues of the orofacial area that can be exophytic masses^[4].

According to WHO's head and neck tumor classification (2022) and the previous classifications in

the literature, we suggest to categorized RLs clinically into four groups: the first group of Verrucous/papillary swellings including Verruca vulgaris, Condyloma acuminatum, Heck's disease and Verruciform xanthoma, the second group of Red to purple swellings that are highly vascular, in which hemorrhage is an important clinical and histological feature involving Pyogenic granuloma, Pregnancy tumour, Epulis granulomatosum and Peripheral giant cell granuloma, the third group of Mucosal-colored swellings with connective tissue predominantly consisting of collagen fibers containing Peripheral ossifying fibroma, Irritational fibroma, Denture fissuratum and Inflammatory papillary hyperplasia, and the last group of other that has variable clinical appearance including Traumatic ulcerative granuloma with stromal eosinophilia, Traumatic neuroma, Myositis ossificans, Masseter muscle hypertrophy and Necrotizing sialometaplasia^[4-6].

To the best of our knowledge, there aren't many research that describe the prevalence of RLs in various regions of

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Egypt in the literature. Because of this, the purpose of this study was to investigate the prevalence of various reactive lesions in the Cairo governorate using the most recent WHO classification of head and neck tumors (2022) and the previous classifications in the literature.

MATERIAL AND METHODS

Data for this retrospective cross-sectional study was obtained from the reports of patients diagnosed histopathologically with reactive lesions between January 2011 to December 2020. Cases were reviewed from the archives of the Cairo's educational hospitals and institutions, as follows: Oral and Maxillofacial Pathology Department, Faculty of Dentistry, Cairo University; General Pathology Department, Faculty of Medicine, Cairo University; Oral Pathology Department, Faculty of Dentistry, Ain Shams University; General Pathology Department, Faculty of Medicine (Eldemerdash Hospital), Ain Shams University; El-Sayed Galal Hospital, Al-Azhar University and Ahmed Maher Teaching Hospital. These reactive lesions were assessed for age, gender and site.

Ethics This study was approved by the Research Ethical Committee at Faculty of Dentistry, Cairo University (number: 1 6 21). Permission was obtained from Cairo's educational hospitals and institutions to access the database used for this study.

Statistics

Qualitative data were presented as frequencies and percentages. Chi-square test was used for comparisons regarding qualitative variables. Time series analysis was performed to determine the trend of reactive lesions prevalence as well as to predict prevalence of reactive lesions for ten years period after the study. The significance level was set at $P \leq 0.05$. Statistical analysis was achieved with IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.

RESULTS

Between January 2011 and December 2020, there were

21420 oral and maxillofacial biopsies that were registered. Only 2142 (10%) was reactive lesions after exclusion of missing histopathology data from biopsy records and incomplete medical records. The most common RLs group was mucosal coloured lesions (51.6%) followed by red to purple swellings (46.7%), then other lesions (0.9%). The verrucous papillary lesions were the least group (0.8%). Irritational fibroma was the most common type (40.7%) followed by pyogenic granuloma (27%), Peripheral giant cell granuloma (15.6%) and Peripheral ossifying fibroma (8.9%). The least common types were condyloma acuminatum and verruciform xanthoma with equal prevalence (0.05%).

Most of the patients were in the second and fourth decade of life (37.53y). Approximately one fifth of the participants aged less than 20 years old, one third aged 21-40 years old, one third of participants aged 41-60 years old and only 6.8% aged over 60 years old while 3.9% of participants' age was not available (Table 1).

The present study showed the predominance of female's gender with 1386 cases (64.8%) than males with 754 cases (35.2%) (Table 2).

The most common site was gingiva (52.4%) followed by buccal mucosa (15.1%) while maxillary tuberosity and mental foramen were the least common sites (0.1% for each site, respectively). The most affected region of the tongue was the lateral border followed by dorsum then tip while ventral surface was the least commonly affected region. Lower lip has higher affection with reactive lesions than upper lip. Anterior maxilla was the most commonly affected anatomic location as in (Table 3).

Time series analysis showed that there is no specific trend for increase or decrease in the prevalence of RLs in the study centers in the last ten years. However, a decrease in prevalence of lesions was observed from 2018 to 2019 and 2019 to 2020. The lowest prevalence was observed in 2020 while the highest prevalence was observed in 2018.

Table 1: Distribution and Mean age of different types of RLs

Tumor Type	N	0-20	21-40	41-60	>60	NA	Mean
Irritational fibroma	872	103(14.2y)	321(32.8)	363(49.7y)	48(66.6 y)	37	39.8y
Pyogenic granuloma	579	142(13.4y)	218(31 y)	160(50y)	32(66.5y)	27	34y
Peripheral giant cell granuloma	334	79(9.9 y)	94(33 y)	117(51.2y)	35(67.3y)	9	37.6y
Peripheral ossifying fibroma	191	48(13.7)	68(31.7 y)	61(49.7y)	10(66.5y)	4	34.8y
Epulis granulomatosum	49	6(11)	19(33 y)	18(50.2)	4(66.5)	2	39.6y
Denture fissuratum	37	0	3(35)	21(51.6)	10(68.1 y)	3	55y
Pregnancy tumour	30	2(18.5)	27(29.7)	1(42)	0	0	29.3y
Traumatic eosinophilic granuloma	14	1(4)	3(33)	6(55)	4(66.3y)	0	49.9y
Verruca vulgaris	12	2(8.5)	8(29.8)	1(57)	1(67y)	0	31.6y
Lobular Capillary Hemangioma	8	4(12.5y)	3(30.3y)	1(43y)	0	0	23y
Inflammatory papillary hyperplasia	7	1(5y)	0	4(51.5)	2(61y)	0	47.6y
Traumatic neuroma	5	0	1(35y)	3(45.7)	0	1	43y
Heck's disease	2	0	1(40y)	1(45 y)	0	0	42.5y
Condyloma acuminatum	1	0	1(22y)	0	0	0	22y
Verruciform xanthoma	1	0	1(28y)	0	0	0	28y
Grand Total	2142	146	388	768	757	83	37.53

NA: not available.

Table 2: the prevalence rate of RLs according to gender

Tumor type	N	Female	Male	Female: Male Ratio
Irritational fibroma	872	548(62.8%)	322(36.9%)	1.7:1
Pyogenic granuloma	579	387(66.8%)	192(33.2%)	2.1:1
Peripheral giant cell granuloma	334	209(62.6%)	125(37.4%)	1.7:1
Peripheral ossifying fibroma	191	132(69.1%)	59(30.9%)	2.2:1
Epulis granulomatosum	49	36(73.5%)	13(26.5%)	2.8:1
Denture fissuratum	37	23(62.2%)	14(37.8%)	1.6:1
Pregnancy tumour	30	30(100%)	0(0%)	NA
Traumatic eosinophilic granuloma	14	5(35.7%)	9(64.3%)	0.6:1
Verruca vulgaris	12	3(25%)	9(75%)	0.3:1
Lobular Capillary Hemangioma	8	4(50%)	4(50%)	01:01
Inflammatory papillary hyperplasia	7	4(57.1%)	3(42.9%)	1.3:1
Traumatic neuroma	5	3(60%)	2(40%)	1.5:1
Heck's disease	2	0(0%)	2(100%)	NA
Condyloma acuminatum	1	1(100%)	0(0%)	NA
Verruciform xanthoma	1	1(100%)	0(0%)	NA
Grand Total	2142	1386(64.7%)	754(35.2%)	1.8:1

NA: not available.

Table 3: Maxillary to mandibular ratio of different types of RLs

Tumor type	N	Maxilla	Mandible	NA	Maxillary: Mandibular ratio
Irritational fibroma	872	163	137	572	1.2:1
Pyogenic granuloma	579	241	190	148	1.3:1
Peripheral giant cell granuloma	334	113	204	17	0.6:1
Peripheral ossifying fibroma	191	98	86	7	1.1:1
Epulis granulomatosum	49	26	21	2	1.2:1
Denture fissuratum	37	19	7	11	2.7:1
Pregnancy tumor	30	14	9	7	1.6:1
Traumatic eosinophilic granuloma	14	1	1	12	1:1
Verruca vulgaris	12	3	1	8	3:1
Lobular Capillary Hemangioma	8	1	2	5	0.5:1
Inflammatory papillary hyperplasia	7	2	0	5	NA
Traumatic neuroma	5	0	3	2	NA
Heck's disease	2	0	0	2	NA
Condyloma acuminatum	1	0	0	1	NA
Verruciform xanthoma	1	0	1	0	NA
Grand Total	2142	681	662	799	1.1:1

NA: not available.

DISCUSSION

Reactive lesions of the oral cavity have large prevalence rates, variable patterns of involvement^[7]. Epidemiologic studies are crucial for learning about the incidence and severity of RLs in a particular population, but they are rarely published internationally and the outcomes of such research can be very inconsistent^[8]. The differences in age, gender, histopathological diagnosis, and anatomic location in comparison with other studies are primarily owing to different classifications and terminology of lesions and the number of cases^[9,10].

The incidence of RLs (10%) in the current study was nearly similar to the studies conducted in Nigeria (14.2%) (3), India (10.7%)^[11] and Kuwait (13.9%)^[12]. However, other studies conducted in Saudi Arabia (20.1%)^[13], Brazil (22.25%)^[14], Iran (34.6%)^[15], and Nepal (67.56%)^[16] showed a higher incidence of RLs. The differences in RLs distribution could be due to the genetic, regional, and oral hygiene measure variances across the various research groups. The prevalence of RLs by year in the present study showed a decrease in the incidence of RLs from 2018 to 2020. This period correlated with the emergence of the COVID-19 epidemic that resulted in the closure of several institutes and the focusing and directing the hospitals and medical staff toward fighting Corona.

Additionally, the average age of RLs in our study was found to be between the second and fourth decade (37.5 years) similar to studies from Nigeria^[3], Saudi Arabia^[13], Iran^[15], India^[17] and Portugal^[18]. This might be because the middle age population is commonly subjected to prolonged, low-grade inflammatory stimuli, trauma, or

recurrent irritation that is considered the main predisposing factors for most RLs.

In terms of gender, the literature indicates that RLs have a greater impact on female patients than on male patients^[11,12,13,15,19], as in our study that showed a female predominance (64.8%), with F: M of ratio 1.8:1. Only two studies showed a higher predominance of males^[20,21]. The female predominance coincides with the literature and ensures the role of hormonal imbalance, stress, and chronic irritation in an increased risk of RLs, also the fact that female patients are keener on detecting and reporting changes in their oral cavity.

The most affected site by the RLs in the present study was the gingiva, followed by the buccal mucosa, in accordance with most studies^[3,20,21,22]. The higher affection of gingiva and buccal mucosa may be due to that these regions are the most common areas subjected to trauma, irritation, and several sources of direct and indirect infection. Furthermore, the anterior maxilla (28.81%) and posterior mandible (28.73%) were the most affected sites respectively. These data were consistent with Kashyap B *et al.*,^[7]; Poudel *P*^[16] and Babu B & Hallikeri K,^[23].

The most prevalent RLs in our study was irritational fibroma, which is consistent with the majority of the earlier reported research in Saudi Arabia^[13], Brazil^[14], India^[17], Portugal^[18] and Chile^[19] and followed by pyogenic granuloma, peripheral giant cell granuloma, and peripheral ossifying fibroma.

Irritational fibroma (IF) is the most common RLs in our study with 872 cases (40.7%) which is consistent and in agreement with the findings in prior studies in

Nigeria^[3], Iran^[15], and India^[17] and in contrast to the studies conducted in Nigeria (15.4%)^[3], Kuwait (30%)^[12], Saudi Arabia (26.5%)^[13], Brazil (72%)^[14], Iran (13.93%) ^[15], Chile (71.1%)^[19], and Portugal (82.6%)^[18]. Regarding gender, IF occur more frequently in females (female: male ratio 1.7:1), in accordance with the findings of other studies^[9,10,12,16,20]. Although some authors reported a male predilection^[4,7,21,23]. Mishra, A., & Pandey, R. K.,^[24] showed that gender predominance is not specific.

Furthermore, our study revealed that the high affection of IF was between the third and fourth decades with a mean age of onset 39.8 years, similar to those reported in other studies^[17,23,25]. While some studies showed the predominance of IF in old age group after the fourth decade of life^[3,4,13,14,20,24]. The age difference in IF between nations may be caused by variations in oral health, as well as the frequency and duration of exposure to various types of irritation.

The most common site was buccal mucosa (31.7%) followed by gum (29.7%) then labial mucosa (10.8%), lateral border of the tongue (8.7%), and tip of the tongue (3.3%) similar to the results of some studies^[20,21,24,26], On the other side, Soyele, O. O. *et al.*,^[3]; Lakkam, B. D. *et al.*,^[9] and Dutra, K. L. *et al.*,^[14] revealed that the gingiva is most common site. Moreover, the anterior maxilla (31%) was the most severely affected area supporting the body of published literature^[17,23].

Surprisingly, the second most common RLs was pyogenic granuloma (PG) (27%) similar to studies in Saudi Arabia^[13], Iran^[15] and India^[17]. Whereas PG has a higher prevalence rate in Nigeria^[3], Kuwait^[12], Iran^[15], and Nepal^[16]. In our study, the peak age of PG incidence occurred between the second and fourth decades (34y), which is consistent with studies^[9,12,20,25,23]. Also, our results showed a female prevalence of PG (66.8%), this was concurrent with several studies^[3,7,9,10,12,16,20,23,25]. Hormonal changes, trauma, and stress are common in middle-aged females, so they were prone to the occurrence of PG.

The most common site of PG is gingiva (70.1%), especially interdental papilla (16.5%) followed by labial mucosa (6.2%) and buccal mucosa (5.9%) similar to most of the studies^[3, 9,14,12,20,21]. PG commonly occured in the anterior part of maxilla which is consistent with several reports^[16,25].

Peripheral giant cell granuloma (PGCG) was recorded as the third commonest RL (15.6%) in the current series in conformity with several studies^[7,8,22], while two studies in Iran found PGCG to be the most prevalent RLs representing (27.6%)^[20] and (30.12%)^[21] respectively. PGCG in the current study occurs mostly in middle-aged individuals with a mean age of 37.6 similar to the literature^[9,20,27], some studies showed the predominance in old age over 60 years old^[26,25], while other studies revealed the prevalence in younger age less than 20 years old^[14,23]. Regarding gender, our result observed that female predilection (62.6%) of PGCG, which are in concurrent with studies^[3,9,20,21,23,26,25,27].

The most common site was gingiva followed by alveolar ridge^[3,9,12,14,20,21,27]. The mandible showed high predilection for PGCG in this study in similarity to numerous studies^[3,7,16,23,27], only one study showed equal jaw distribution^[25].

Peripheral ossifying fibroma (POF) comes as the fourth prevalent RL (8.9%) in this study in agreement with studies from Saudi Arabia^[13]. India^[11] and Croatia^[28].

Additionally, POF had a female prevalence in our study parallel to the literature^[3,20,9,25,29] and in contrast to studies demonstrated by Naderi, N. J. *et al.*,^[21] and Kashyap B. *et al.*,^[7]. The average age of POF was 34.8 years in similarity with several studies^[9,12,13], whereas some reports revealed a higher incidence in younger age^[3,21,23,25,28,29] and others found the older age predominance^[7,20].

The gingiva is the most impacted region of POF in the present study, then the alveolar ridge^[3,12,14,19,21,29], the Anterior maxilla was the favoured POF location similar to most studies^[3,23,7], and in contrast to some reports^[3,25,29].

The last two lesions of mucosal-coloured swellings that revealed a lower prevalence rate; were denture fissuratum and inflammatory papillary hyperplasia. Denture fissuratum in our series showed a prevalence rate (1.7%) similar to studies in India^[6], Iran^[15], and Portugal^[18], while the prevalence of palatal papillomatosis (0.3%) was parallel to the studies in Iran^[15], and India^[17]. While Alhindi NA. *et al.*^[13] showed different occurrence rates of (5.7%).

On the other hand, in this study, the group of other reactive lesions showed a significantly lower incidence rate such as traumatic eosinophilic granuloma (0.7%) and traumatic neuroma (0.2%).

Lastly, the group of Verrucous Papillary Lesions (VPLs), in our study, has the least prevalence rate (0.8%). Verruca vulgaris had a low frequency of (0.6%), then heck's

disease had a lower incidence (0.1%), as the study done in Sweden, the prevalence in the general Caucasian population was observed to be $(0.11\%)^{[30]}$. While condyloma acuminatum (0.05%) and verruciform xanthoma (0.05%) were the least prevalent verrucous lesions.

Despite the presence of several articles in this field, inadequate epidemiological studies on RLs have been reported. Nevertheless, such studies are essential to clarify the frequency and characteristics of RLs in different inhabitants, including the Egyptian people.

CONCLUSIONS

Between our study and earlier research from other countries, several similarities and differences were found. The differences in the relative frequency of reactive lesions seen among the various series, including the current study, may be partially attributed to underlying cultural variations between various geographic areas, as well as to various aspects of the study design, the determination of which would require additional research.

Comprehensive knowledge about the prevalence of RLs can be useful for diagnosing and treating patients.

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Ahmed Metwally wrote the manuscript and was responsible for data collection and entry. Awatef Draz and Hatem Amer supervised the project and were responsible for data curation and edited the manuscript for English language. All authors reviewed the final draft and approved it

CONFLICT OF INTERESTS

There are no conflicts of interest.

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الملخص العربي

إنتشار الآفات التفاعلية داخل تجويف الفم في المستشفيات والمؤسسات التعليمية في التشار الآفات التعليمية القاهرة (دراسة مقطعية)

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المقدمة: الهدف من هذه الدراسة هو تقييم انتشار الآفات التفاعلية داخل تجويف الفم المشخصة في المستشفيات و المؤسسات التعليمية بالقاهرة ومقارنة النتائج مع البيانات المسجلة بالدر اسات السابقة حول العالم.

المواد والطرق: تم جمع بيانات الآفات التفاعلية التي تم تشخيصها بين ٢٠١١ و ٢٠٢٠ من ملفات المرضى المقيدين في قسم أمراض الفم والوجه والفكين - كلية طب الأسنان - قسم علم الأمراض جامعة القاهرة، كلية الطب - جامعة القاهرة، قسم أمراض الفم - كلية طب الأسنان - جامعة عين شمس، كلية الطب - جامعة عين شمس، قسم أمراض الفم - كلية الطب - جامعة الأزهر، قسم أمراض الفم كلية طب الأسنان (بنات) - جامعة الأزهر، كلية الطب - (للبنات) جامعة الأزهر، قسم علم الأمراض مستشفى الزهراء - قسم أمراض الفم (بنين) كلية طب الأسنان - جامعة الأزهر، قسم علم الأمراض كلية الطب (بنين) - جامعة الأزهر، قسم علم الأمراض مستشفى الحسين - جامعة الأزهر، قسم علم الأمراض مستشفى السيد جلال – جامعة الأزهر ومستشفى أحمد ماهر التعليمي.

النتائج: أوضحت الإحصائيات أن من إجمالي ٢١٤٢ خزعة من الفم والوجه والفكين تم تشخيص ٢١٤٢ آفة فقط من الناحية النسيجية كالآفات التفاعلية ،والأغلبية عبارة عن آفات ملونة مخاطية بينما الآفات الحليمية الثؤلولية وغيرها من الأفات شكلت نسبه ضئيلة. تأثرت الإناث بشكل أكبر من الذكور. كان معظم المرضى في العقد الثالث والرابع من العمر ٣٧,٥ سنة. اللثة هي المكان الأكثر تأثرا. كان الفك العلوي الأمامي هو الموقع الأكثر إصابة ، يليه الفك السفلي الخلفي والفك العلوي الخلفي والفك العلوي الخافي والفك المهيج كان أكثر الآفات التفاعلية شيوعاً يليه الورم الحبيبي القيحي كالآفة الشائعة الثانية.

الاستنتاج: في هذه الدراسة ، لاحظنا تباينًا جغرافيًا ملحوظًا في الحدوث النسبية لمختلف الأفات التفاعلية في مدينة القاهرة مقارنة بالنتائج الموجودة في الدراسات العالمية السابقة.