Odontogenic Cysts: A 10-Year Retrospective Study in an Iranian Population

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Abstract

***Objectives*:** The purpose of this study was to determine the frequency of all odontogenic cysts (OCs) along with age range, gender distribution, and the site of involvement over a 10-year period (March 2001 to March 2011) and to compare these data with findings from other surveys.

***Methods*:** The archives of departments of oral and maxillofacial pathology from Shahid Beheshti and Tehran University of Medical Sciences were retrieved and analyzed for demographic data such as age, gender, location and histopathological diagnosis of OCs.

***Results*:** Of the 8,563 biopsy samples that were received, 1,518 (17.7%) were diagnosed as OCs. Radicular cyst was the most common diagnosis (33.2%), followed by dentigerous cysts (24.1%), and odontogenic keratocysts (18.6%). OC occurred 59.3%, 40.6% in male and female respectively. Mandibular involvement was 62.4% while in maxilla was 37.6%.

***Conclusion*:** Our study provided demographic data on a large series in Iran, a Southwest Asian country. In our study, radicular cysts, the most common OC, had a lower frequency compared to that reported in most other studies. On the other hand, calcifying OCs seem to be more prevalent in the Iranian population compared to other populations male to female to female ratio was 1.45:1.

***Key Words*:** Cysts; Jaw; Iran

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Introduction

Odontogenic cysts are a group of diverse entities consisting of commonly incidentally diagnosed lesions such as radicular cysts (RCs) and dentigerous cysts (DCs)(1-3), and rare complicated lesions such as calcifying odontogenic cysts (COCs) and glandular odontogenic cyst (GOCs)(3,4). While all OCs, inflammatory and developmental, develop from tooth forming epithelium (2,3) or their residues (5) such as epithelial rest of Malassez , dental lamina, or enamel organ (6), their behaviors differ noticeably. Moreover, neoplastic proliferation in the epithelial lining of an odontogenic cyst, or in association with it, has created a long-standing discussion in the literature and there are many reports, which illustrate OCs accompanying odontogenic and non-odontogenic tumors (7-10). Therefore, collecting accurate data about their clinical and histopathological features can help us improve our understanding of these complicated lesions. While there are many informative studies about the incidence of OCs in different regions of the world (3,6,11-13), there are limited data about the prevalence of OCs in West Asian countries (2, 14). Therefore, the aim of this study was to determine the incidence of OCs in Iran and comparing that with findings from other investigations.

Methods

This was a retrospective study of OCs. Medical records from Departments of Oral and Maxillofacial Pathology of Shahid Beheshti (SBMU) and Tehran University of Medical Sciences (TUMS), for the time period between March 2001 and March 2011, were reviewed. We included medical records of patients with histopathological diagnosis of OC. Medical records of patients with missing data were excluded. A total of 8,563 specimens were received from both departments (4,239 from SBMU and 4,324 from TUMS); 1,518 (17.7%) of which, were diagnosed with OC. Demographic data and clinical information for each individual, including age, gender, site of involvement, and histopathological diagnosis were recorded. Age was categorized into decades, while site of involvement was divided into the following categories: anterior, premolar, and molar regions in the maxilla and the mandible. The data were analyzed using SPSS software (version 11.5)(SPSS Inc., IL, USA). Statistical significance was determined using the Chi-square test.

Results

Of the 1,518 cases diagnosed with OCs, 29 (1.9%) had missing information and were excluded. The mean age of the remaining 1,489 cases was 31.5 (±15.8) years, ranging from 5 to 86 years. The highest incidence of OCs was in the third decade (Table 1). Eight hundred and ninety-nine cases occurred in men and 615 in women (male to female ratio of 1.45:1). Four cases were missing information regarding gender. The mean age of men and women was estimated to be 32 and 31 years, respectively. Data regarding site of lesion were available for 1,490 cases: 930 (62.4%) lesions were located in the mandible while 560 (37.6%) were in the maxilla. Table 1 summarizes the rank order distribution of OCs by frequency for all ages in men and women.

Table 1- Distribution of odontogenic cysts according to the frequency, gender and age

Diagnosis	No.of case (%)	No.of male (%)	No.of female (%)	M : F ratio	Age range	Age (± SD) years
Radicular cyst	506 (33.2)	282 (56)	221 (44)	1.27:1	5-86	32.8 (14.5)
Dentigerous cyst	366 (24.1)	237 (65)	128 (35)	1.85:1	6-66	24.1 (14)
Odontogenic keratocyst	282 (18.6)	163 (58)	119 (42)	1.37:1	9-84	33.5 (15.5)
Residual cyst	88 (5.8)	57 (65)	31 (35)	1.38:1	11-84	42.7 (16)
Calcifying odontogenic cyst	22 (1.5)	16 (73)	6 (27)	2.66:1	8-82	34.3 (20.6)
Buccal bifurcation cyst	16 (1.1)	8 (50)	8 (50)	1	8-86	32.3 (18.3)
Total	1280	763	519			

Radicular cyst was the most common form of OC with 506 cases (33.2%) and occurred in 282 (56%) men and 221 (44%) women (Table 1). Three cases were missing information regarding patient's gender. Male to female ratio was 1.27:1. Dentigerous cyst

was the second most common cyst with 366 (24.1%) cases and mean age of 24.7 years. Patient gender was known in 365 cases with male to female ratio of 1.85:1. Two hundred and sixty seven lesions (73%) were located in the mandible while 99 (27%) lesions were in the maxilla. The lower molar region accounted for 45% of the cases (n=183) followed by the lower premolar region with 19.1% (n=70) of the cases.

Comparing RC and DC, Chi-square test showed a significant correlation between lesion type and patient gender (P=0.018); DC occurred in 34.8% of the men and 27.2% of the women; whereas RC occurred in 41% of the men and 48% of the women.

Odontogenic keratocyst (keratinizing odontogenic tumor = KOT) were found in 282 cases (18.6%). The male to female ratio was 1.37:1. Two hundred and four lesions occurred in the mandible (73%) compared with 76 lesions in the maxilla (27%). Among the 280 cases with available information for site of presentation, the most common site of involvement was mandibular molar region with 160 cases (48%). The mean age at the time of diagnosis was 33.5 years. Peak incidence (30%) was in the third decade, followed by the second and the fourth decades (20% and 19%, respectively).

In some cases, cystic lesions involved more than one site and this caused some confusion about the exact site of presentation.

Most DCs were diagnosed in the second decade (29%) while most odontogenic keratocysts (OKCs) and RCs were diagnosed in the third decade (30% and 31.6%, respectively). Chi-square test showed a significant difference in frequent locations among three cysts (P<0.001). Our results showed that DCs and OKCs most frequently involved mandibular molar regions (43.4% and 38.3% respectively); whereas, RCs most frequently occurred in the anterior maxillary region (52%).

All 88 cases of residual cysts (mean age at the time of diagnosis 42.7 years) were surgically resected in fourth and fifth decades of life (20%)(Table 1). Fifty-seven cases occurred in men and 31 cases in women (male to female ratio of 1.38:1). Fifty-eight cases occurred in the mandible and 30 cases involved the maxilla. Mandibular molar region was the most common site of residual cysts (57 cases).

There were 22 cases of COCs with a mean age of 34 years at the time of diagnosis and peak incidence in the second decade. There were 16 cases in men and 6 cases in women. The most common sites for COCs were the lower molar and premolar area (57%).

The remaining cysts included 16 (1.07%) Buccal bifurcation cysts (paradental cyst), 14 (0.94%) lateral periodontal cysts (LPC), 13 (0.87%) glandular odontogenic cysts (GOC), 6 (0.4%) orthokeratinized odontogenic cysts (OOC), and two (0.13%) gingival cysts (GC)(Tables 2 and 3). Two hundred and nine cases were not classified due to difficulties in differentiating between truly inflammatory cysts versus secondary inflamed developmental cysts. This is particularly problematic when there are insufficient clinical information.

Table 2- Distribution of rare odontogenic cysts according to the frequency, gender and age

Diagnosis	No.of case N(%)	No.of male	No.of female	M : F ratio	Mean age (+ SD) years
LPC	14 (0.9)	9	5	1.8	34.2(17)
GOC	13(0.8)	9	4	2.2	39.7(9)
OOC	6(0.4)	3	3	1	3603(15.4)
GC	2(0.1)	0	2	0.5	52.5(34.4)

Table 3- Distribution of rare odontogenic cysts according to the site

Diagnosis	No.of case	Mand ant.	Mand premolar	Mand molar	Maxilla ant.	Maxilla premolar	Maxilla molar
LPC	14	2	6	2	3	1	1
GOC	13	6	3	3	3	2	1
OOC	6	2	1	2	1	1	1
GC	2	-	1	-	1	-	-

Discussion

While OCs are well-known oral and maxillofacial lesions, there are some disagreements about their histogenesis, classification, and true incidence. Most of the available data in the literature are from diagnostic biopsies, which are received by oral pathology services and result in some controversy. The first problem is related to the interests and specialty of the clinicians (oral surgeons, periodontists, endodontists, or general practitioners) who provide the biopsy samples. The second bias is related to the specimens, which are not sent to the pathology services. This occurs especially in cases of RCs and DCs. The third source of controversy is the lack of general agreement about classification and nature of cystic neoplasms such as unicystic ameloblastoma, KOTs, and COCs. This makes it difficult to completely revise old archives based on new entities. In our opinion, controversy is mainly due to the authors not reporting the source of their data. Some investigators have collected their data from all patients who had been referred to oral surgery clinics (4,6,13), oral and maxillofacial hospitals, or diagnostic departments (2,15), while the data in some other articles were collected from the records of oral pathology departments (1,3,5,11,12,16). Our study falls in the second category and as previously mentioned, we reviewed the records of oral and maxillofacial pathology departments of two major universities in Tehran, Iran.

In our study, the incidence of OCs was 17.7%, which was similar to the incidence of OC in Canada (17.12%)(12), but was higher than that reported in the UK (12.8%)(3), and Brazil (10.45% and 9.94%) (5). This suggests that there are no geographic differences in the incidence of OCs. However, the incidence of OC was much higher in studies that were performed in clinical departments; it was 31.5% in Turkey (2) and 33.8% in Spain (6). This discrepancy might be related to the different sources of data (clinical vs. pathology) that were used in different studies. In the present study, odontogenic cysts occurred more commonly in men compared to women (1.45:1) and this finding was consistent with that of other studies (1,3,4).

Radicular cysts were the most common type of OCs reported in all studies. However,

their incidence varies between different studies. They accounted for 33.2% of total OCs in our study, which was consistent with the findings of the study by Ledesma-Montes *et al*,(11) in 20001 which reported an incidence of 33.8% in Mexican Population. The incidence of RCs in other investigations varied between 50.2% (1,6), 52.3% (3,5), 52.8% (13), 53.5% (4), and 54.7% (2). We suppose the lower incidence of RC in our study and that of Ledesma-Montes *et al*,(11) in 2000 might be due to clinicians and surgeons not submitting the specimens to pathology lab. On the other hand, RC had a similar incidence in different populations based on socio-economic status (1,2-6,13). Even though RC is related to dental caries and pulp necrosis, the internal tendency of an individual tooth (or patient) is the main etiological factor for developing RC. The male to female ratio in our study (1.27:1) was higher than that reported by a study in the UK (1.06:1)(3), while it was lower than the ratio reported by a study from India (1.81:1)(1). In our study, most RCs were diagnosed in the third decade, with the mean age of 32.8 years, which was consistent with findings from other studies. Most lesions were found in the anterior maxillary region (52%), which was in accord with findings from other studies (3,6,11). This may be due to greater degree of care and attention that is given to the anterior maxillary teeth (2) and also related to pulp necrosis of anterior teeth following composite restorations with no symptoms.

Dentigerous cysts were the second most common form of OCs in our study (24.1%). This was similar to the findings from previous studies in India, Turkey, France, Spain, Canada and Germany (1,2,4,6,12,13), in which the incidence of dentigerous cysts ranged from 21.3 to 26.6%. However, the incidence of dentigerous cysts in UK was 18.1% (3) and 30.7% in Latin American (5) were different from those reported in the aforementioned studies. This discrepancy may be due to the total number of OCs in different studies, greater sample sizes, and lower percentage of DCs. The mean age in our study (24.1 year) was similar to that reported by studies in Asia (1,2) and Latin American countries (5); however, it was different from the values reported by studies from the UK (3), France (4), and South Africa (13).

After the World Health Organization published a new edition of histological classification of odontogenic tumors (17) and OKC was recognized as a tumor, OKC was omitted from some studies of OCs but not all. This inconsistency affects the results of studies of OCs and tumors, especially the incidence of OCs compared with other odontogenic and non-odontogenic oral lesions. However, as we mentioned above, there is a lot of variability in the incidence of OCs. In the investigations, which included OKC as a type of OC, the incidence of OCs varied from 3.51% to 21.62% (2,3,11,12,14,16). However, the incidence of OCs in articles that excluded OKCs ranged from 9.94% to 33.8% (5,6). Therefore, it seems that many interventional factors affect the incidence of OCs, mainly due to the three reasons that were mentioned above.

The incidence of OKC in our study was 18.6%, which was similar to that reported by Ledesma – Montes *et al*. (18.7%) in the Mexican population (11). The incidence of

OKC varies from 3.3% to 27.6% in studies from different regions of the world (2,3,4,6,12,14,16,18). This large variation is not related to sample size, the country, or ethnic factor. Moreover, some authors assessed the incidence of OKC among developmental OCs; however not in all OCs (14). Another source of controversy is the lack of general agreement about excluding OOCs from parakeratinized OKCs. Surprisingly, there are few investigations, which report OOCs as a form of OC (4,16). Another bias is suggested in comparing this discrepancy with lower difference in incidence of DC in various investigations (18.1% to 30.7%). Inflammatory OKCs, which mostly arise in follicular cells, may be misdiagnosed as inflammatory DCs, especially if they are completely inflamed. Last bias is related to missing incisional and excisional biopsy reports in all studies. In our study, OKCs were the third most common OCs, which was consistent with most, but not all other studies (3,4,11-13,16). The male to female ratio in our study (1.37) was similar to those in studies from the UK (1.27)(3) and Iran (1.26)(16), but different from those reported in other studies (1.53-1.89) (1,4,11,14). Interestingly, only in one study from Turkey there was an inverse male to female ratio (1:1.1) (2). In our study, most lesions were diagnosed in the third decade (30%). This was similar to findings reported by Ledesma-Montes *et al*,(11) in Mexico (2000), Khosravi *et al*,(16) in 2013 Ramachandra *et al*,(1) in India, with peak incidence in the second and third decades. In contrast, in studies by Jones, *et al*. (3)(2006) from the UK and Açikgöz *et al*,(2) in 2012 and Tekkesin *et al*,(14) in 2012 from Turkey most lesions were diagnosed in the sixth decade of life and those show mean age from 36.1 to 40 years old (4,13,14,19). In our study, the most frequent affected region of the jaw was the mandible, with 72.85% of the cases occurring in this region. This was consistent with Myoung *et al*. (20)(2001) findings, which reported 76.5% of their cases were in the mandible. However, in the study by Ramachandra *et al*,(1) in 2001 only 61.81% of the lesions were located in the mandible. Other studies with different sample sizes reported frequencies ranging from 65% (15) to 83.45% (4). Mandibular molar region was the most common site in all studies and this was consistent with our findings (54.14%). However, there is some controversy in different studies due to extension of OKCs from one side of a quadrant to anterior and/or posterior regions. Some studies have mentioned this factor (3,16) while others did not mention it. Perhaps this is due to incomplete clinical and radiographic data.

Residual cysts, which are retained radicular cysts after tooth extraction, accounted for 5.8% of the lesions in our sample. In this aspect our study was similar to studies from the UK and France (3,4), but different from another study from Iran (12.98%)(16). The mean age at the time of diagnosis was 42.7 years, which was similar to that reported in a study by Tekkesin *et al*,(14) in 2012 but different from other studies, which reported values ranging from 29 to 51 years (3,4,16). In our study, residual cysts were more predominant in men and the mandible was the most common site for these lesions. These findings were consistent with findings from other studies (3,4,14,16).

Calcifying odontogenic cysts are rare, interesting entities that may evolve to malignant tumors, classified by the World Health Organization as odontogenic tumors in 2005 (ghost cell odontogenic tumor)(17). Therefore, in most articles published after 2005, these lesions were not classified as OCs. The incidence of COCs in our study was 1.5%, which is similar to that reported by Khosravi *et al*,(16) in Iran (1.31%) and higher than those reported in studies from the UK (3) and Turkey (14). Another study from Iran estimated the rate of COC to be 2% (21). These findings support the theory that COC may be more common in Iran than other countries, particularly those in Europe (3,4,6).

The term paradental cyst (PC) was first proposed by Craig (22) in 1976 as a specific inflammatory OC, reported in 49 cases. When a partly erupted tooth develops pericoronitis (3) and causes inflammation in the residue of dental follicle around the unerupted part of the tooth crown, proliferation of epithelial lining of the follicle results in cyst formation (3). The incidence rate of buccal bifurcation cyst varies from 0.2% (14) to 20.8% (6)(1.1% in the current study). However, most studies reported an incidence rate of about 0.5% (3,5,12,16), which may be due to the lack of submitting tissue to the laboratory upon tooth extraction. This hypothesis is supported by the lack of any reports of PCs in many studies of OCs. While most studies reported that PCs occurred more frequently in men, in our study men and women were equally affected. Most PCs involved the mandible and were diagnosed most commonly in the third decade of life, which were consistent with the findings from other studies (3,5,16), with the exception of one study, which reported the peak incidence of PCs in the fourth decade (14).

There were no primordial cysts in our study. This is due to the fact that diagnosis of primordial cysts is based on clinical and radiographic findings and all primordial cysts are histologically classified as OKCs.

Lateral periodontal cysts and glandular odontogenic cysts had an incidence rate of less than 1% (0.9% and 0.8%, respectively) while orthokeratinized odontogenic cysts had an incidence of 0.4% and gingival cysts had an incidence of 0.1% (Table 2). Among the mentioned cysts, GOCs are important as they demonstrate aggressive behavior and challenging histopathological features. There are specific criteria consisting of mucin-spilled space, mucous cells, and ciliated cells (23), which are seen in some other OCs. Moreover, plaque-like epithelial whorls or shears observed in GOCs (24) are also seen in LPCs and botryoid odontogenic cysts (BOCs), the latter showing clinical behavior similar to that of GOCs, which makes diagnosis difficult. In fact, the term sialo-odontogenic cyst was proposed in order to describe the lesions that showed histological features of both BOCs and mucoepidermoid tumors (25).

This may also explain why BOCs are not reported in many studies. Indeed, LPCs and their multilocular counterpart, BOCs, are more frequently observed in North- and South American countries (0.98% to 2.1%)(5,11,12,25,26) than in Europe and Asian countries (0.1% to 0.9% incidence rate).

In two studies from Libya (18) and Spain (6) the incidence rate of LPCs was 1.5 and 1.6, respectively. Several studies from Asian countries did not report any cases of LPCs or BOCs (1,15).

Conclusion

The distribution of different types of OCs in Iran was similar to that reported in other studies. However, some forms of OCs were less common in our study compared to studies from other countries.

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