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An updated clinical and epidemiological profile of the adenomatoid odontogenic tumour: a collaborative retrospective study

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BACKGROUND: Adenomatoid odontogenic tumour (AOT) is a benign odontogenic jaw lesion. The aim of this study was to update the biological profile of AOT.

MATERIAL AND METHODS: Cases published in the literature and cases in files of co-authors were included.

RESULTS: 550 new cases were retrieved, and of a total of 1082 cases analysed, 87.2% were found in the second and third decades. The M:F ratio was 1:1.9. 70.8% were of the follicular variant (extrafollicular: 26.9%, peripheral: 2.3%). 64.3% occurred in the maxilla. 60% of follicular AOTs were associated with unerupted canines. Nineteen cases of AOT (2.8%, M:F ratio was 1:1.4) were associated with embedded third molars. Twenty-two peripheral AOTs (2.3%, M:F ratio was 1:5.3) were recorded. The relative frequency (RF) of AOT ranged between 0.6% and 38.5%, revealing a considerably wider AOT/RF range than hitherto reported (2.2–7.1%).

CONCLUSIONS: This updated review based on the largest number of AOT cases ever presented, confirms the distinctive, although not pathognomonic clinicopathological profile of the AOT, its worldwide occurrence, and its consistently benign behaviour.

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Keywords: adenomatoid odontogenic tumour; epidemiology; relative frequency

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Introduction

The adenomatoid odontogenic tumour (AOT) is a unique lesion of the maxillofacial skeleton (centrally located), or in the soft tissue (gingiva) overlying tooth-bearing areas or alveolar mucosa in edentulous regions (peripherally located). By some authors it is regarded as a true benign, non-aggressive non-invasive neoplasm and by others as a developmental hamartomatous odontogenic growth (1).

The distinctive clinicopathological AOT features have repeatedly been profiled and updated through the years 1991–2004 (2–8). The present group of authors

representing 12 institutions and/or centres of Oral and Maxillofacial Pathology agreed to produce yet another update coinciding with the appearance of the new and totally revised WHO Classification of Head and Neck Tumours (9).

Aim

The aims of this retrospective multicentre study were to:

A retrieve data from a worldwide literature survey of reported AOT cases *not* included and analysed in the most recent review article by Philipsen and Reichart (6), as well as cases reported from 1999 to the end of 2005;

B collect and analyse data from AOT cases not hitherto published (originating from private files and sources in the above-mentioned centres in Argentina, Brazil, Guatemala, India, Japan, Malaysia, Mexico, Nigeria, China, Peru, South Africa and Thailand) and

C collect and analyse data from AOT cases published in the Chinese and Japanese languages.

For cases to be accepted as representing an AOT, a demonstration of biological and histomorphological features that match the present concept as it is interpreted in the most recent WHO classification (9) had to be presented.

Material and methods

The new and not previously analysed AOT cases which form part of the total number of analysed cases in the present updated profile, stem from three sources (see Aim of study above): A (49 cases), B (273 cases) and C (228), in total 550 cases.

Table 1 AOT (M + F) by age groups [*n* (%)]

Age groups (years)	*1999-article (6; n = 532)*	*Present study (n = 1082)*
0–9	26 (4.9)	46 (4.2)
10–19	365 (68.6)	707 (65.3)
20–29	103 (19.4)	237 (21.9)
30+	38 (7.1)	92 (8.5)

Table 2 AOTs by gender [*n* (%)]

Gender	*1999-article (6; n = 532)*	*Present study (n = 1082)*
Males	185 (34.8)	371 (34.4)
Females	347 (65.2)	711 (65.6)
M:F ratio	1:1.9	1:1.9

The material on which the final analyses produced in the present update are based (see Results and Discussion below as well as Tables 1–4) comprises the data published previously [Philipsen and Reichart (6)] to which the 550 new cases mentioned above are added as follows:

1 AOTs by age groups: $n = 532$ (according to data retrieved from Fig. 2 in 1999-article (6) + 550, giving a total of 1082 cases);

2 AOTs by gender: $n = 532$ (according to data retrieved from Fig. 2 in 1999-article (6) + 550, giving a total of 1082 cases);

3 AOT variants by gender: $n = 412$ (according to data retrieved from Table 2 in 1999-article (6) + 550, giving a total of 962 cases) and

Table 3 AOT variants by gender, *n* (%) [A + B]

	Variants			
	Follicular	*Extrafollicular*	*Peripheral*	*Row total*
Males	233 (24.2) [100 + 133]	87 (9.0) [35 + 52]	3 (0.3) [1 + 2]	323 (33.6) [136 + 187]
Females	448 (46.6) [192 + 256]	172 (17.9) [67 + 105]	19 (2.0) [17 + 2]	639 (66.4) [276 + 363]
Column total	681 (70.8) [292 + 389]	259 (26.9) [102 + 157]	22 (2.3) [18 + 4]	962 (100.0) [412 + 550]

n: number of AOT cases; in soft brackets: row and column percentage, respectively; in sharp brackets: A – number of cases retrieved from Table 2 in the 1999-article [Philipsen and Reichart (6)], B – number of AOT cases in the respective groups retrieved from the three sources of new data mentioned previously under Material and Methods section (in total 550 cases).

Table 4 AOT variants by location, *n* (%) [A + B]

	Variants			
	Follicular	*Extrafollicular*	*Peripheral*	*Row total*
Maxilla	450 (46.8) [202 + 248]	149 (15.5) [63 + 86]	19 (2.0) [16 + 3]	618 (64.3) [281 + 337]
Mandible	232 (24.1) [91 + 141]	108 (11.2) [37 + 71]	3 (0.3) [2 + 1]	343 (35.7) [130 + 213]
Total	682 (70.9) [293 + 389]	257 (26.7) [100 + 157]	22 (2.3) [18 + 4]	961 (100.0) [411 + 550]

n: number of AOT cases; in soft brackets: row and column percentage, respectively; in sharp brackets: A – number of cases retrieved from Table 3 in the 1999-article [Philipsen and Reichart (6)], B – number of AOT cases in the respective groups retrieved from the three sources of new data mentioned previously under Material and Methods section (in total 550 cases).

4 AOT variants by locations: $n = 411$ (according to data retrieved from Table 3 in 1999-article (6) + 550, giving a total of 961 cases).

Results and discussion

As a 'by-product' of reviewing the literature on AOT, it became evident that a search for the first identifiable case has in fact not been settled. Over the years credit has been given to authors like Steensland (10), Dreybladt (11), James and Forbes (12), L'Esperance (13) and Stafne (14) for reporting the earliest AOT case. However, the cases reported by the first four of the abovementioned authors *do not* qualify as bona fide cases of AOT. Stafne (14), on the other hand, must be recognized as the first author who considered the AOT as an *entity* although this author did not propose a specific term for it, but reported his series of three AOTs under the title 'Epithelial tumours associated with developmental cysts of maxilla'. Our meticulous literature survey quite clearly discloses that the first case demonstrating irrefutable proof of an AOT, is the one reported from Norway by Harbitz (15) in 1915 as a 'cystic adamantoma' in the left mandible of a 14-year-old girl.

Demographic features

Distribution of AOTs by age groups

Table 1 shows more than a doubling of the total number of AOTs based on case reports from 1999 (6; $n = 532$) to end of 2005 (present study, $n = 1082$). The difference in number of cases in each age group expressed in percentage is negligible with a very slight decrease in the second decade (in the order of 3.3%) and a slight increase in the third decade (2.5%). The vast majority of AOTs is still to be found in the second and third decades [88.0% (1999) vs. 87.2% (present study)]. Figure 1 clearly illustrates the characteristic distribution of AOTs by age groups and gender.

Distribution of AOTs by gender

The figures in Table 2 indicate that the M:F ratio has remained unchanged (1:1.9) when comparing data from Philipsen and Reichart (6; $n = 532$) and the present study ($n = 1082$). Even when data from the 1991 report (2) are taken into account, the last 15 years with an increase of 685 new cases have not influenced the gender ratio.

Distribution of AOTs by gender and variants

It was suggested by Philipsen et al. (2) and further elaborated on a year later (3) that the three clinical and radiographical AOT variants could – according to their intraosseous or extraosseous locations – appropriately be named as (i) follicular (or pericoronal), (ii) extrafollicular (or extracoronal) and (iii) peripheral (or extraosseous/gingival) AOT types. Of 962 AOTs (Table 3) 681 cases or 70.8% were of the follicular type of which almost half the number being females. The extrafollicular type accounted for 26.9% again with a M:F ratio of (close to) 1:2. The rare peripheral variant (2.3%) shows a remarkable M:F ratio of 1:6.3.

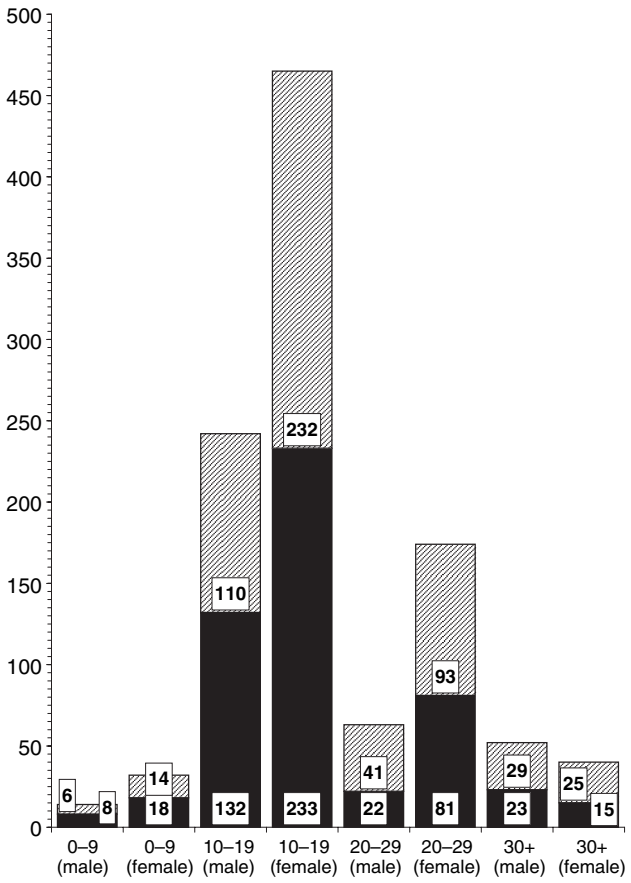

Figure 1 Distribution of AOT cases according to age groups and gender as published by Philipsen and Reichart (6; $n = 532$, black columns) and cases of the present study ($n = 1082$, hatched).

Distribution of AOTs by location and variants

Table 4 discloses that 64.3% of all AOT variants occur in the maxilla of which 62.3% are intraosseously located. In the mandible the corresponding figures are: 35.7% and 35.3% indicating that the peripheral variant is very rarely encountered in the mandible (0.3%). Comparing these data with those reported in the 1999-article (6) reveals only very minor differences, the general trend remaining unchanged.

Follicular AOT associated with unerupted third molars

Among unerupted permanent teeth associated with a follicular AOT, the third molar is very rarely involved. Philipsen and Reichart (6) reported that eight molars (six maxillary and two mandibular) were associated with 341 follicular AOT cases (2.3%). In the present updated profile a similar analysis disclosed that the total number of reported AOT/third molar cases has increased to 19 (11 maxillary and eight mandibular) cases out of 682 follicular AOTs (2.8%; Table 5) which indicates a rather steady trend. The mean age of these cases (males + females) of 20.3 years is well beyond the 16.5 years characteristic of the mean age of 'classical' follicular AOT/permanent canine cases (2). This difference may be accounted for by the later biological development of third molars compared with canines. Further, and

Table 5 Follicular AOTs associated with embedded third molars

Reference	*Gender*	*Age*	*Embedded third molar*[a]
Ghosh (32)	M	18	28
Miles (33)	M	18	38
Nagai et al.[b] (34)	F	24	38
Takeda et al.[b] (35)	M	20	38
Ozaki et al.[b] (36)	M	26	48
Rao et al. (37)	M	53	28
Ando et al.[b] (38)	F	23	18
Okada et al. (39)	F	27	18
Nakahata et al.[b] (40)	F	22	28
Layton (41)	F	19	18
Philipsen et al. (3)	F	20	28
Morita et al.[b] (42)	F	17	48
Yoshino et al.[b] (43)	M	22	28
Fujiki et al.[b] (44)	F	17	28
Naito et al.[b] (45)	F	20	28
Takahashi et al. (46)	M	22	28
Kawada et al.[b] (47)	F	17	38
Sato et al. (48)	F	20	48
Takata et al.[c]	M	27	48

[a]The FDI two-digit system of designating teeth is used throughout the tabulated data.
[b]Cases from the Japanese literature, retrieved and verified through the kindness of Dr Ogawa (co-author), Hiroshima University Hospital, Japan.
[c]From the files of Dr Takata (co-author), Hiroshima University, Hiroshima, Japan.

Table 6 Peripheral AOTs reported or from private files

Reference	*Gender*	*Age (years)*[a]	*Site*[b]	*Bone loss*
Gorlin and Chaudhry (49)	F	16	12, 11 or 21, 22	n.i.
Abrams et al. (50)	M	9	11	n.i.
	F	11	21	no
	F	13	31, 41	no
Berghagen et al. (51)	F	19	22	Slight
Yazdi and Nowparast (52)	F	16	11, 12	Slight
Courtney and Kerr (53)	n.i.	n.i.	11, 12 or 21, 22	No
Lorber and Lennartz (54)	F	12	21	Slight
Swinson (55)	F	16	23	Slight
Eriksson and Dahl (56)	F	9	21	Bone pocket
Takeda and Kudo (57)	F	17	21, 22	Bone pocket
Philipsen et al. (3)	F	16	21	Bone pocket
Imai et al. (58)	M	7	Ant. max.[c]	n.i.
Montes-Ledesma et al. (59)	F	21	21	n.i.
Unal et al. (60)	F	4[d]	51	No
Kearns and Smith (61)	F	3	73	No
Mosqueda-Taylor et al.[e]	F	14	21	n.i.
Hazarey[f]	F	17	11, 21	n.i.
Carlos-Bregni R[g]	M	15	11, 21	n.i.
	F	17	31–32	n.i.

[a]At the time of operation.
[b]Indicated by adjacent tooth/teeth.
[c]Adjacent tooth not identified.
[d]Lesion observed by parents from the age of 2.
[e]From the private files of Dr Mosqueda-Taylor, Mexico (co-author).
[f]From the private files of Dr Hazarey, India (co-author).
[g]From the private files of Dr Carlos-Bregni, Guatemala (co-author).
n.i., no information available.

possibly of greater significance, is that tooth impaction and associated tumour development are likely to be diagnosed later in life when located in the posterior rather than in the anterior jaw regions. The M:F ratio (1:1.4) for follicular AOT/third molar cases is somewhat lower than that for follicular AOT/canine cases (1:1.9). Maxillary third molars are associated with AOTs more often than with the corresponding mandibular molar by a factor of 1.5.

Extraosseous (peripheral) AOT variant

The peripheral or 'epulis' variant occurs by far with the lowest frequency of the three AOT types. Table 6 shows the 22 reported as well as unpublished cases (from private files of co-authors). It is noteworthy that the gender distribution of 19 peripheral AOTs (gender and age not recorded in three cases) shows a remarkable M:F ratio of 1:5.3. All cases were located in the gingival soft tissue adjacent to a permanent tooth in the maxillary (19 cases) or mandibular (three cases) incisor/canine region. The mean age of 19 peripheral AOTs (age range: 3–21) was 13.3 years which is the lowest mean age value recorded for any AOT variant.

Unusual odontogenic lesions with adenomatoid structures

Adenoameloblastic odontoma/adenoid ameloblastoma with dentinoid induction/AOT with dentinogenesis/adenomatoid dentinoma/ adenomatoid odontogenic hamartoma

During the recent 10–12 years a few cases have appeared in the English-language literature (16–23) showing odontogenic lesions composed of hard dental tissues (dentin and/or enamel) and odontogenic epithelium forming duct-like structures. However, these lesions present histopathological and clinical features different from those of the classical AOT, and oral pathologists should keep the above lesions in mind to avoid misdiagnosis with AOT. It is the view of the present authors – as well as that of Rick (1) – that it is wise to refrain from creating new entities until distinctive clinicopathological parameters are established and have been confirmed.

Multifocal AOT

A very unusual case was reported by Larsson et al. (24) in which a 12-year-old girl developed a dozen separate radiolucent lesions over a 5-year period. They were removed surgically along with about 20 associated tooth germs and multiple and unerupted malformed teeth. The excised lesions resembled AOT to a certain degree microscopically and were of the extrafollicular rather than the follicular variant. This extremely rare lesion remains very difficult to evaluate.

Recent studies on radiological features of AOT

Based on radiographic findings, differentiating AOTs from dentigerous cysts, periapical cysts, calcifying cystic odontogenic tumours [previously termed calcifying odontogenic cysts (COCs)], CEOTs, keratocystic odontogenic tumours [KCOTs; previously termed odontogenic keratocysts (OKC; 9)] and ameloblastomas may

Table 7 AOT/RFs by author and geographical regions

Geographical region [author(s), (country)]	*Number of odontogenic tumours/number of AOTs*	*Relative frequency of AOT (%)*
Europe		
(1) Happonen et al. (62) (Finland)	319*/5	1.6
*2 melanotic neuroectodermal tumours of infancy and 9 unclassified odontogenic tumours excluded; 159 odontogenic keratocysts included		
(2) Prein et al. (63) (Switzerland)	232*/5	2.2
*German-Austrian-Swiss register for tumours of the facial skeleton (highly selected material), Basel, Switzerland		
*One dens in dente, and 55 odontogenic cysts excluded		
(3) Günhan et al. (64) (Turkey)	409/11	2.7
(4) Mothes et al. (65) (Germany)	318/6	1.9
(5) Stupulkowska (66) (Poland)	112*/2	1.8
*52 cases of central giant cell granuloma excluded		
(6) Tamme et al. (67) (Estonia)	75/1	1.3
(7) Olgac et al. (68) (Turkey)	515*/11	2.1
*One gigantiform cementoma and one cemento-osseous dysplasia not included		
(8) Jones and Franklin (69) (UK)	267*/10	3.7
Patients aged 16 and below		
*25 dens in dente and 22 'other' excluded; 71 odontogenic keratocysts included		
(9) Jones and Franklin (70) (UK)	903*/6	0.7
Patients aged 17 and older		
*19 odontomes – 'other and dens in dente' excluded; 591 odontogenic keratocysts included		
Middle East		
(10) Maaita (71) (Amman, Jordan)	58/1	1.7
(11) Al-Khateeb et al. (72) (Irbid, Jordan)	23*/1	4.3
Patients aged 19 years and below		
*1 cementifying fibroma excluded		
North America		
(12) Regezi et al. (73) (USA)	641*/22	3.4
*11 cementifying fibromas and 54 periapical cementifying dysplasias excluded		
(13) Bhaskar (74) (USA)	426*/14	3.3
*3 melanotic neuroectodermal tumours of infancy excluded		
(14) Daley et al. (75) (Canada)	780*/14	1.8
*Local (southern Ontario) and distant referrals and 335 odontogenic keratocysts included		
(15) Mosqueda-Taylor et al. (28) (Mexico)	349/25	7.2
(16) Ogunsalo (76) (Jamaica)	85*/3	3.5
*10 odontomas and 5 odontogenic keratocysts included		
South America		
(17) Keszler et al. (77) (Argentina)	76*/5	5.3
Patients aged 15 years and below		
*One case of melanotic neuroectodermal tumour of infancy excluded; 12 odontogenic keratocysts included		
(18) Sousa et al. (78) (Brazil)	187*/10	5.3
Patients aged 14 years and below		
*26 odontogenic keratocysts included		
(19) Ochsenius et al. (79) (Chile)	362/24	6.6
(20) Orellana et al. (80) (Venezuela)	205/10	4.8
Patients aged 18 years and below		
(21) Fernandes et al. (81) (Brazil)	340/13	3.8
Asia		
(22) Ishikawa (82) (Japan)	162/1	0.6
(23) Hiraide (83) (Japan)	109/1	0.9
(24) Khanna and Khanna (84) (India)	46*/5	10.9
7 cases of cementifying and cemento-ossifying fibromas excluded		
(25) Sirichitra (85) (Thailand)	280/9	3.2
(26) Wang and Su (86) (China)	973/41	4.2
(27) Wu et al. (87) (China)	183/10	5.5
(28) Wu and Chan (88) (Hong Kong, China)	68*/3	4.4
9 cementifying fibromas, 2 periapical cemental dysplasias and 3 gigantiform cementomas excluded		
(29) Zhu and Wang (89) (China)	66/4	6.1
(30) Zhou (90) (China)	330/22	6.7
(31) Yun-Chen et al. (91) (China)	100/5	5.0
(32) Mendis and MacDonald (92) (Sri Lanka)	244*/21	8.6
*Odontomas excluded by authors		
(33) Sato et al. (93) (Japan)	79/1	1.3
Patients aged 15 years and below		
(34) Lu et al. (94) (China)	759/63	8.3

Table 7 Continued

Geographical region [author(s), (country)]	*Number of odontogenic tumours/number of AOTs*	*Relative frequency of AOT (%)*
(35) Chen et al. (95) (Taiwan)	69*/1	1.4
Patients aged 15 years and below		
*5 cases of cementifying fibroma excluded		
(36) Zhen et al. (96) (China)	55/2	3.6
(37) Wang et al. (97) (China)	89/7	7.9
(38) Dhanuthai (98) (Thailand)	1020*/57	5.6
*Includes data from (24) and Sirichitra (85)		
(39) Sato et al. (48) (Japan)	559/10	1.8
(40) Hazarey (India)	199*/32	16.1
*Unpublished data, supplied by co-author		
Africa		
(41) Mosadomi (30) (Nigeria)	29/2	6.9
(42) Mosadomi (99) (Nigeria)	31/2	6.5
(43) Sawyer et al. (100) (Nigeria)	863*/5	0.6
*14 odontogenic keratocysts included		
(44) Subbuswamy and Shamia (101) (Nigeria)	35/5	14.3
(45) Sawyer# (102) (Nigeria)	116*/8	6.9
#The author makes no reference to his article above (43) published 5 years earlier, why duplication of data are likely		
*One case of calcifying odontogenic cyst included, 2 cases of periapical cemental dysplasia and 4 cases of central cementifying fibroma excluded		
(46) Ajagbe et al. (103) (Nigeria)	198/13	6.6
(47) Taiwo er al. (104) (Nigeria)	20/3	15.0
(48) Asamoa et al. (105) (Nigeria)	13/5	38.5
Patients aged 14 years and below		
(49) Odukoya (106) (Nigeria)	289/18	6.2
(50) Arotiba et al. (107) (Nigeria)	107/13	12.1
(51) Arotiba (108) (Nigeria)	31/5	16.1
(52) Arotiba et al. (109) (Nigeria)	128/16	12.5
(53) Arotiba et al. (110) (Nigeria)	?/ 57*	n.a.
*The total number of odontogenic tumours of which 57 cases were diagnosed as AOTs cannot be deducted from this publication, why AOT/RF cannot be given		
(54) Adebayo et al. (111) (Nigeria)	78/7	9.0
Patients aged 18 years and below		
(55) Simon et al. (112) (Tanzania)	220*/2	0.9
*7 odontogenic keratocysts included		
(56) Ajayi et al. (113) (Nigeria)	92/18	19.6
Patients aged 19 years and below		
(57) Ladeinde et al. (114) (Nigeria)	319/24	7.5
(58) Simon et al. (115) (Tanzania)	116*/1	0.9
*A 4-year prospective study		
(59) Adebayo et al. (116) (Nigeria)	324*/9	2.8
*Revised figures (personal communication)		
(60) Aregbesola et al. (117) (Nigeria)	20/2	10.0
Patients aged 19 and below		

pose diagnostic problems. As an aid in diagnosis, a useful radiographic feature is the presence of calcified material within the radiolucent background of the follicular AOT, in particular. Dare et al. (25) proved that the intra-oral periapical radiograph is superior to panoramic radiography when it comes to perception of the flocculent pattern of the intralesional radiopacities of discrete calcified deposits. Recently, Konouchi et al. (26) and Asaumi et al. (27) studied the use of MRI in the radiographic differential diagnosis of AOT. Although both articles demonstrated that the MRI features of AOT were characteristic, it seems too early to decide when it is feasible to involve MRI or DCE-MRI imaging particularly considering the cost-effective aspects.

Relative frequency of AOT

The relative frequency (RF) of an odontogenic tumour can be defined as the ratio between the number of odontogenic tumours of the series in question and the total number of odontogenic tumours under study – expressed in percentage.

It has been generally reported that the RF of the AOT corresponds to 2.2–7.1% (2, 6, 28). However, a thorough worldwide literature survey discloses a much wider AOT/RF range. The AOT/RF figures shown in Table 7 which are based on 60 publications worldwide is the most comprehensive collection of AOT/RF data presented so far. According to the survey compiled from reports published between 1975 and end of 2005, the AOT/RFs vary from 0.6% to 38.5%.

If distribution according to geographical location of AOT cases is analysed, it clearly shows that certain countries with special emphasis on the 17 reports from Nigeria (of 19 from the African continent) have produced a rather large 'input' to the AOT/RF subject. No less than five Nigerian institutions and centres have

supplied the data but the vast range in reported AOT/RF (0.6–38.5%) seems to indicate that a closer co-operation between the institutions especially within the field of tumour diagnosis would be beneficial. Hopefully, the new and totally revised edition of the WHO Classification of Head and Neck Tumours (including odontogenic tumours; 9) will become available on a worldwide scale. It should, however, be stressed that considering the demographic facts about Nigeria, true geographical differences may explain the remarkable RF range. The apparently high RF of certain odontogenic tumour including AOT and especially prevalent in African countries has been credited to a 'harvesting phenomenon', a theory introduced by Anand et al. (29) and supported by Mosadomi (30) from Nigeria. These authors explained that 'untreated tumours, which grow slowly and seldom threaten life, accumulate for lack of doctors to treat them; hence a pool of untreated cases conveys an erroneous impression of prevalence when a centre becomes available where these tumours can be treated'.

Several publications reporting on paediatric oral lesions, including odontogenic tumours use a variety of age ranges for the patients analysed: 0/14, 0/15, 0/18 and 0/20 years old; this makes direct comparisons difficult and open to misinterpretation, and it is highly recommended to introduce a standard age range when reporting on odontogenic as well as non-odontogenic oral and maxillofacial lesions in paediatric (children and adolescent) populations.

It should be stressed that some of the publications presented in Table 7 (entry 1, 8, 9, 14, 16, 17, 18, 43 and 55), the authors have included data on cases of OKCs retrieved during their study. However, OKCs are now, according to the recently published WHO classification of odontogenic tumours (9) to be regarded as a benign cystic odontogenic tumour (KCOT). As a consequence these data have been included in the RF figure presented in Table 7. Adding the KCOTs to the odontogenic tumours make in some instances a marked impact on the AOT/RF figure.

It is likely that it will take some more years to accumulate reliable data on AOT/RF. The hitherto commonly accepted AOT/RF estimate (2.2–7.1%) is however, today hardly tenable as these figures are based on mere 12 observations (6).

Contributions from authors

Table 8 summarizes data which were contributed by the co-authors of this study.

Future research on AOT and case reporting

The AOT is a unique, intriguing odontogenic tumour that has been subjected to series of biological profile studies since the late 1960s/early 1970s. Although the number of cases for analyses has steadily increased – in the present multicentre study having reached close to 1100 observations (data on age and gender) – the trend as regards distribution by age, gender, location and AOT-subtypes has shown quite a remarkable consistency, not forgetting that the benign biological behaviour of AOT has never been questioned.

However, there still remain unanswered questions especially regarding some aetiological, ethnical and pathogenetic aspects. Molecular pathology has only recently entered the field of odontogenic tumours (31),

Table 8 Cases of AOTs contributed by co-authors (private files), and cases retrieved from the literature including Japanese and Chinese publications

	Gender		*Location*		*Type of AOT*			
Contributor	*M*	*F*	*Maxilla*	*Mandible*	*Follicular*	*Extrafollicular*	*Peripheral*	*Total*
1	11	19	22	8	25	5	0	30
2	1	2	2	1	2	1	0	3
3	2	7	3	6	4	5	0	9
4	9	9	13	5	17	1	0	18
5	4	10	8	6	8	4	2	14
6	16	28	27	17	33	11	2	44
7A	6	4	4	6	7	3	0	10
7B[a]	53	140	103	90	141	52	0	193
8	11	25	27	9	29	7	0	36
9	10	22	22	10	21	10	1	32
10	5	3	7	1	8	0	0	8
11[a]	13	22	23	12	25	10	0	35
12	24	43	45	22	37	30	0	67
13	2	0	2	0	0	2	0	2
Subtotal	167	334	308	193	357	141	3	501
–[b]	20	29	29	20	32	16	1	49
Total	187	363	337	213	389	157	4	550

Contributions 1, 2, 3, 4, 5, 6, 7A, 8, 9, 10, 12, 13 (273 cases) all originate from co-authors' private files.
[a]Contributions 7B and 11 (228 cases) are retrieved from the Japanese and Chinese literature with the kind assistance of Drs I. Ogawa (Hiroshima, Japan) and X. Zhang (Beijing, China; 34–36, 38, 40, 42–45, 47, 58, 83, 86, 87, 89, 90, 96, 97, 118).
[b]Covers 49 cases from the world literature not included in the review by Philipsen and Reichart (6), and further retrieved from 1999 to end of 2005 (58, 118–150).

and has only sporadically been applied when it comes to studies of the AOT. We totally agree with Rick (1) when he stated that 'we eagerly await the result of in situ hybridization, DNA microarray analysis, gene rearrangement studies, and other developing molecular biology techniques to solve the remaining mysteries'.

Based on the present study we recommend to:

1 *dis*continue reporting 'classical' follicular AOT/permanent canines as these cases are not likely to add significantly to our present knowledge base;
2 continue reporting well-documented cases of the *follicular AOT when associated with second and third molars*. Further, the extrafollicular variant (with indication of the exact location [see Fig. 1 in Philipsen and Reichart (6)], and in particular the peripheral variant;
3 continue reporting *unusual or* 'rare' histomorphological features, immunohistochemical findings and – as alluded to the above – results of applying molecular biological techniques;
4 continue reporting the poorly understood *possible ethnic (geographical?) differences* in the biological behaviour of AOTs and
5 continue search for documented cases of *tumour recurrence*.

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