



# Odontogenic Tumors: A 13-year Retrospective Study of 395 Cases in a South Indian Teaching Institute of Kerala

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## ABSTRACT

**Objective:** The aim of the present study was to determine the epidemiology and clinicopathological presentation of odontogenic tumors (OTs) seen in a Government Teaching Institute from Kozhikode district of Kerala (South India), over a period of 13 years and to compare the data obtained with previous reports published in literature from different world population.

**Study design:** Records of the Oral Pathology and Microbiology, Government Dental College, Kozhikode (Kerala, South India), were analyzed during a period of 13 years and reclassified according to World Health Organization (WHO) 2005 Classification.

**Results:** A total of 6.08% of odontogenic tumors were reported out of which (96.7%) were benign and (3.3%) were malignant. Keratocystic odontogenic tumor (35.9%) was the most frequent type, followed by ameloblastoma (25.9%), calcifying cystic odontogenic tumor (10.6%), and odontoma (8.9%). The mean age was 32.69 ± 17.27, and males were more commonly affected.

**Conclusion:** A marked geographic and demographic variation was observed in the relative frequency of various odontogenic tumors in the South Indian population which stresses upon the influence of genetic and/or environmental (epigenetic) factors on tumor pathogenesis.

**Keywords:** Classification, Odontogenic tumors, South India.

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## INTRODUCTION

Odontogenic tumors (OTs) are heterogeneous group of lesions which are derived from odontogenic apparatus

comprised of odontogenic epithelium, ectomesenchyme and/or mesenchymal elements. These tumors may be generated at any stage in the life of an individual.<sup>1</sup> Once considered relatively rare, recent literature shows increased frequency of these tumors in different parts of the world. In 2005, the classification of OT was reviewed and updated with some changes. Odontogenic keratocyst (OKC) is now considered as keratocystic odontogenic tumor (KCOT); furthermore, bone-related lesions and melanotic neuroectodermal tumor of infancy have also been included under the category of benign tumors. However, odontogenic origin of these lesions is still doubtful. The update has produced an increase in the frequency and prevalence of OTs. Most of the previous studies still adhere to the 1992 World Health Organization (WHO) Classification. Recently, published studies from different parts of the world have adopted this updated WHO classification, but data from South-East Asia is still minimal in the literature.

India and China are home for about half of the world's population. There is limited information available in English literature on the prevalence of OTs in Indian sub-continent. Okada et al (2007) reported 226 cases from Sri Lanka, Sriram et al (2008) reported 250 OTs from a teaching institute of Mumbai (India) and Gupta et al (2010) analyzed 489 cases in Dravidian population from South India.<sup>2-4</sup> But the data of these studies was analyzed according to WHO 1992 classification. More recent Indian reports by Varkhede et al, Mullapudi et al and Gill et al presented their data according to the updated WHO classification.<sup>5-7</sup>

The aim of the present study was to determine the epidemiology and clinicopathological presentation of OTs seen in a Government Teaching Institute from Kozhikode district of Kerala (South India) over a period of 13 years and to compare the data obtained with previous reports published in literature from different world population.

## MATERIALS AND METHODS

Data from 6,496 samples of oral biopsies was retrieved from the archival files of Department of Oral Pathology and Microbiology, Government Dental College, Kozhikode (Kerala, South India), over a period of 13 years (January 2001-December 2013). Of these 6,496 cases, 395 cases of OTs were used in the present study after reassessing the diagnosis adapted from latest WHO

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Classification (2005). Slides without histopathologic criteria for definitive diagnosis of OT and cases without slides and paraffin-embedded tumor specimens were excluded. Data were analyzed for age, gender, site, radiographic features, symptoms and histological type. Recurrent tumors were considered as one individual case. Two cases were diagnosed as hybrid lesion of ameloblastoma; however, no such entity is specified in WHO 2005 classification. These cases clinically and radiographically resembled ameloblastoma-solid multicystic (SMA) and were managed by wider surgical excision akin to SMA. Thus, we preferred to include these lesions in SMA class. The maxilla and mandible were divided into six segments each as follows:

1. *Segment 1:* Involved 18 to 14 including maxillary tuberosity region
2. *Segment 2:* Involved 13 to 23
3. *Segment 3:* Involved 24 to 28 including maxillary tuberosity region
4. *Segment 4:* Involved 38 to 34 including angle and ramus region
5. *Segment 5:* Involved 33 to 43
6. *Segment 6:* Involved 44 to 48 including angle and ramus region.

Those lesions involving two or more areas were assigned to the region closest to the center of the lesion.

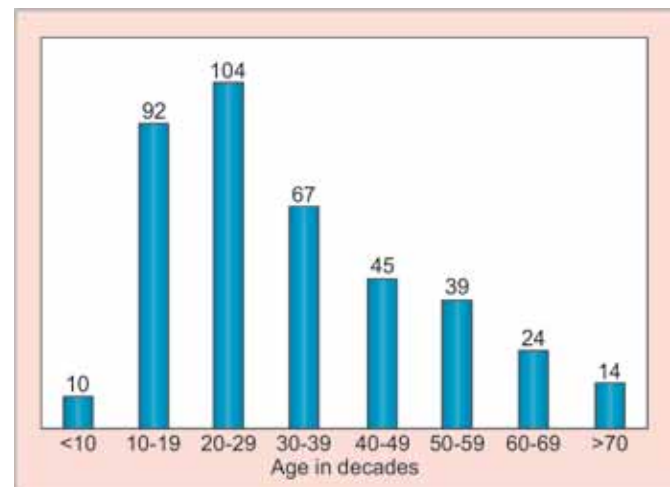
In addition, we explored the English literature on odontogenic tumors between 2005 and 2013. Results of the present study were compared with the series that followed 2005 WHO classification. Finally, a database was generated using the SPSS (v 13.0) statistics software; statistical analysis was done using Chi-square test. p-value below 0.05 was considered statistically significant.

**RESULTS**

The relative frequency of odontogenic tumors was 6.08% (395 cases of 6,496 oral biopsies). In the present series,

97.5% were intraosseous tumors and remaining 2.5% were extraosseous. A single case of peripheral CEOT and nine peripheral odontogenic fibromas were seen. Three hundred and eighty-two (96.7%) were benign and 13 (3.3%) cases were malignant. These tumors affected individual of all age groups from 5 years to 88 years (mean 32.69 ± 17.27). 66.6% cases were distributed in 2nd to 4th decade with a peak incidence in 3rd decade. Age distribution of OTs in decades of life is shown in Graph 1. Table 1 shows distribution of individual lesions in decades of life (years). The frequency and gender distribution of all the tumors is shown in Table 2. Male predominance was seen with male to female ratio of 1.4:1 (229 males and 166 females). Keratocystic odontogenic tumor (35.9%) was the most frequent tumor followed by ameloblastoma (25.9%), CCOT (10.6%) and odontome (8.9%).

Table 3 shows distribution of OTs by site of occurrence. Mandible (280 cases) was affected more commonly than maxilla (115) with a ratio of 2.43:1. A total of 70.6% cases affected the posterior segment of the jaws as compared to 29.4% cases affecting the anterior segment of the jaws. Among 102 cases of ameloblastoma, 73 (71.6%) were solid



**Graph 1:** Age distribution of OTs in decades of life

**Table 1:** Distribution of individual lesions in decades of life (years)

	Abbreviation	<10	10-19	20-29	30-39	40-49	50-59	60-69	>70	Total
Ameloblastic carcinoma	AC	0	0	0	1	0	2	1	0	4
Primary intraosseous carcinoma	PIOC	0	0	1	0	1	2	2	3	9
Ameloblastoma	AMEL	0	12	32	19	19	10	6	4	102
Calcifying epithelial odontogenic tumor	CEOT	0	0	2	2	1	1	0	0	6
Adenomatoid odontogenic tumor	AOT	0	12	4	3	0	1	0	0	20
Keratocystic odontogenic tumor	KCOT	1	23	44	29	16	12	11	6	142
Ameloblastic fibroma	AF	2	6	1	1	0	0	0	0	10
Ameloblastic fibro-odontoma	AFO	0	1	1	0	0	0	0	0	2
Odontoma	OD	5	19	7	2	1	1	0	0	35
Calcifying cystic odontogenic tumor	CCOT	1	12	7	7	5	7	3	0	42
Odontogenic fibroma	OF	1	6	1	2	1	2	1	0	14
Myxoma	MX	0	1	1	1	1	1	0	1	6
Cementoblastoma	CB	0	0	3	0	0	0	0	0	3
<b>Total</b>		<b>10</b>	<b>92</b>	<b>104</b>	<b>67</b>	<b>45</b>	<b>39</b>	<b>24</b>	<b>14</b>	<b>395</b>

**Table 2:** Distribution of frequency and gender with mean age of individual lesion

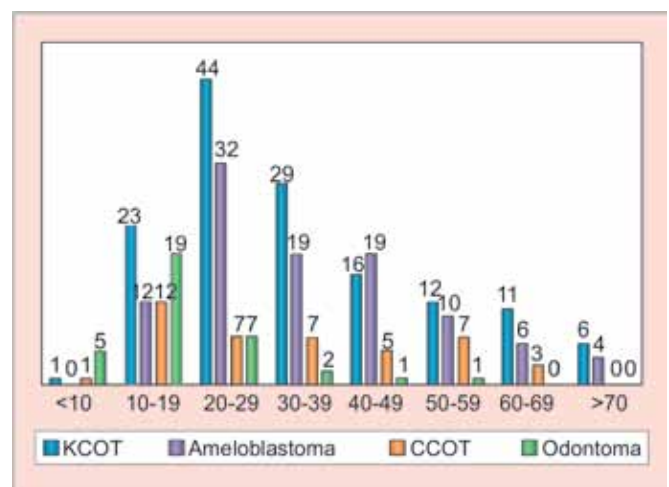
	Total		Gender			Mean age (in years)
	Number	%	Male (M)	Female (F)	M:F	
AC	4	1.0	2	2	1:1	51.25
PIOC	9	2.3	4	5	0.8:1	60.56
AMEL	102	25.9	60	42	1.43:1	36.02
CEOT	6	1.5	4	2	2:1	37.00
AOT	20	5.1	7	13	0.5:1	21.40
KCOT	142	35.9	98	44	2.2:1	34.31
AF	10	2.5	7	3	2.3:1	17.00
AFO	2	0.5	1	1	1:1	22.00
OD	35	8.9	16	19	0.8:1	18.03
CCOT	42	10.6	23	19	1.2:1	33.20
OF	14	3.5	3	11	0.3:1	28.68
MX	6	1.5	2	4	0.5:1	42.00
CB	3	0.8	2	1	2:1	26.67

**Table 3:** Distribution of individual lesion by site of occurrence

	Maxilla			Mandible			Total
	Segment 1 (involved 18-14 including maxillary tuberosity region)	Segment 2 (involved 13-23)	Segment 3 (involved 24-28 including maxillary tuberosity region)	Segment 4 (involved 38-34 including angle and ramus region)	Segment 5 (involved 33-43)	Segment 6 (involved 44-48 including angle and ramus region)	
AC	0	0	0	1	1	2	4
PIOC	0	0	1	2	2	4	9
SMA	4	0	5	27	12	25	73
UA	0	2	0	9	4	9	24
DA	0	2	0	0	3	0	5
KCOT	17	12	12	41	18	42	142
CEOT	1	2	1	1	0	1	6
AOT	1	8	1	1	6	3	20
AF	1	1	0	4	3	1	10
AFO	0	0	2	0	0	0	2
CCOT	8	6	1	16	2	9	42
OD	3	11	3	6	9	3	35
OF	0	6	0	4	3	1	14
MX	0	0	2	0	3	1	6
CB	0	0	2	0	0	1	3
Total	35	50	30	112	66	102	395

multicystic type, 24 (23.5%) were unicystic and five cases (4.9%) were diagnosed as desmoplastic variant. Solid multicystic ameloblastoma were further subclassified according to the predominant histological pattern that was present. Follicular variant constituted (47 cases, 64.4%) was most common followed by plexiform type (15 cases, 20.54%), granular cell type (6 cases, 8.22%) and acanthomatous type (5 cases, 6.84%). All the tumors mainly affected posterior segments except adenomatoid odontogenic tumor (AOT), odontogenic fibroma and odontoma which were more common in anterior segments.

Graph 2 shows age distribution of four most frequent OTs. Keratocystic odontogenic tumor was the most frequent tumor, which affected males more commonly than females. The peak incidence was seen



**Graph 2:** Age distribution of four most frequent OTs



in the 3rd decade. Around 71.1% cases were seen in the mandible and posterior region was more commonly affected. Ameloblastoma was the 2nd common tumor with gender, age and site distribution similar to KCOT. Calcifying cystic odontogenic tumor (CCOT) and odontome affected 2nd decade of life. Slight female predilection was seen for odontoma (0.8:1).

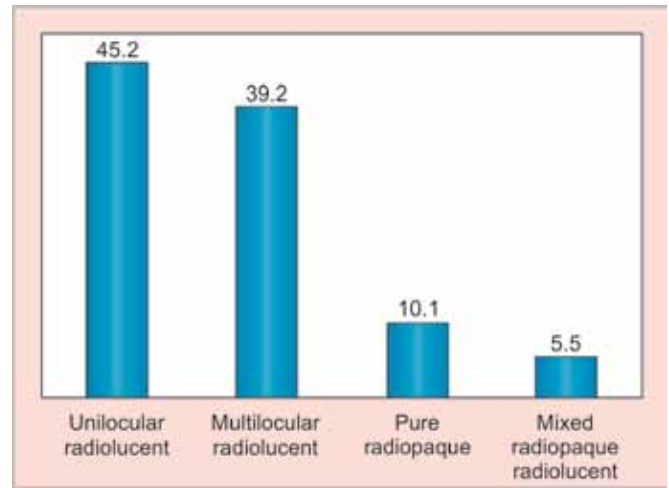
Among 13 malignant tumors, four cases of ameloblastic carcinoma were seen while primary intraosseous carcinoma constituted remaining nine cases. All the malignant tumors were mainly seen in the mandible and were predominantly seen after 6th decade.

Radiographic presentation is shown in Graph 3. Around 96.9% cases showed well-defined borders on radiograph and rest 3.1% had ill-defined borders. Expansion of cortical plates was noticed in 79.7% of the cases. 92.2% of ameloblastomas showed buccal and lingual cortical expansion. Comparatively, 78.2% of KCOT and 71.4% of CCOT showed expansion of cortical plates clinically. However, only 42.8% of odontomas showed expansion.

The most common symptom was painless swelling (65.1%) followed by painful swelling (14.7%), pain (9.6%), noneruption of teeth (5.8%). Only 4.8% of cases were asymptomatic (cases discovered incidentally).

**DISCUSSION**

Literature search showed numerous published reports on the frequency and incidence of odontogenic tumors



**Graph 3:** Radiographic presentation of odontogenic tumors

from different parts of the world. Whilst some papers followed 1992 WHO classification, others considered updated and revised 2005 WHO classification. As already mentioned, this update has caused a drastic change in the relative frequency of odontogenic tumors. We have followed WHO 2005 classification to present our data and excluded bone related lesions since none of the previously published reports included these lesions. Including these lesions would have produced a major bias in comparison. Furthermore, their odontogenic origin is still controversial.

Table 4 shows the relative percentage of OT from published data from different parts of the world,

**Table 4:** Frequency of odontogenic tumors from different parts of the world

	Jing 2007 <sup>16</sup>	Avelar 2008 <sup>14</sup>	Luo 2009 <sup>9</sup>	Tawfik 2010 <sup>11</sup>	Gaitan-Cepeda 2010 <sup>15</sup>	Mulla-pudi 2011 <sup>5</sup>	Osterne 2011 (non-specified 1.62) <sup>17</sup>	Var-khede 2011 <sup>6</sup>	Gill 2011 <sup>7</sup>	Rez-vani 2011 <sup>31</sup>	Senel 2012 <sup>8</sup>	Da-Costa 2012 <sup>10</sup>	Lawal 2013 <sup>18</sup>	Servato 2013 <sup>13</sup>	John-son 2013 <sup>12</sup>	Our Study
AMEL	40.3	23.7	36.52	41.5	19.3	71.4	29.19	40.83	47.4	30.5	12.7	29.8	65.4	20.0	11.8	25.9
SOT	0.2	0.4	—	—	—	—	—	0.83	—	—	—	—	0.4	—	—	—
CEOT	0.6	2.0	0.46	3.7	1.4	7.1	0.54	0.83	1.4	6.8	3.4	2.0	1.1	0.8	—	1.5
AOT	4.1	5.4	2.06	3.7	1.4	8.5	0.54	5.83	7.7	2.54	—	1.0	2.3	1.3	—	5.1
KCOT	35.8	30.00	38.73	19.5	38.9	—	28.11	37.5	23.4	42.4	17.4	32.3	4.1	31.7	74.2	35.9
AF/AFO	1.2	1.7	0.99	2.4	—	1.4	2.16	0.83	1.0	1.7	—	2.0	4.1	—	2.1	2.5
AFO	0.2	0.4	0.92	—	—	—	—	—	—	0.8	—	1.0	0.4	—	1.1	0.5
OD	4.7	22.1	6.11	13.4	30.8	4.3	19.46	11.67	5.3	9.32	41.8	18.4	—	31.7	5.4	8.9
OA	0.1	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
CCOT	2.2	6.3	1.99	—	—	—	3.78	0.83	7.6	1.7	—	2.0	1.5	3.8	5.4	10.6
DGCT	0.5	—	0.38	—	—	—	—	—	—	—	—	0.5	—	0.4	—	—
OF	0.3	—	1.60	—	1.4	2.8	3.78	—	—	—	4.6	—	1.9	2.1	—	3.5
MX	4.6	6.3	2.60	8.5	5.8	4.3	7.03	—	3.3	2.54	9.3	4.5	14.7	4.6	—	1.5
CB	2.0	1.7	1.68	3.7	—	—	3.78	0.83	2.9	1.7	3.4	1.0	—	1.7	—	0.8
AC	1.6	—	1.3	—	—	—	—	—	—	—	1.1	3.5	1.1	1.3	—	1.0
PIOC	0.9	—	3.74	2.4	—	—	—	—	—	—	4.6	0.5	2.6	0.4	—	2.3
MA	—	—	—	1.2	—	—	—	—	—	—	—	—	—	—	—	—
CCOC	0.1	—	0.61	—	—	—	—	—	—	—	—	0.5	—	0.4	—	—
GCOC	0.3	—	0.23	—	—	—	—	—	—	—	—	—	—	—	—	—
AFS	0.1	—	0.08	—	—	—	—	—	—	—	1.1	1.0	0.4	—	—	—

classified according to 2005 WHO edition. The conclusions (regarding frequency and incidence) drawn from this extensive literature search were as follows:

- Benign odontogenic tumors are more common than malignant OTs in all parts of the world.
- Ameloblastoma, KCOT, odontoma, CCOT, AOT and myxoma are among the most common tumors.
- SOT, AFO, OA and DGCT are relatively rare lesion and need further documentation.
- Calcifying epithelial odontogenic tumor (CEOT) is relatively uncommon with highest incidence in a South Indian and Iranian population.

Overall frequency of OTs in our report was 6.08% which is comparatively higher than the published reports. Somewhat similar frequency of OTs was seen in Maharashtrian (India, 5.78%) and Turkish (7.38%) population.<sup>6,8</sup> There was an overall male preponderance for OTs in Indian, North Chinese, Brazilian, Egyptian and Australian population.<sup>5-7,9-12</sup> Our findings, in regard to gender predilection, are similar to aforementioned reports. However, a female predilection is seen in a few published reports.<sup>17</sup> In the present series, 96.7% tumors were benign and malignant tumors accounted for remaining 3.3% of the OTs. This is similar to the findings of Tawfik et al, Jing et al, Luo et al, Lawal et al and Servato et al. Only a few reports have stressed upon the symptomatology of odontogenic tumors. In the report published by Servato et al, swelling was the most common symptom followed by pain with swelling and pain.<sup>13</sup> Ninety-three cases in their series were asymptomatic.<sup>13</sup> In another study of 238 odontogenic tumors, Avelar et al showed that 75.6% of cases were asymptomatic.<sup>14</sup> Contrary to this, 95.2% of 395 cases in our series presented with one or the other symptom with painless swelling being the most common followed by painful swelling, pain and noneruption of teeth similar to Servato et al.

Keratocystic odontogenic tumor was the commonest tumor in our study akin to the published data of Luo et al, Da costa et al, Jonson et al, Avelar et al and Gaitan-Cepeda et al.<sup>9,10,12,14,15</sup> In contrary, ameloblastoma was found to be the most common odontogenic tumors in reports from other parts of the world.<sup>5-7,11,16-18</sup> One hundred and one of 142 KCOT cases affected mandible and vast majority affected the posterior region including angle and ramus region. A male predilection was seen and most of the tumors were seen in 3rd decade. The term OKC is now replaced by KCOT. The reasons for this belief include its clinical behavior, with a high recurrence rate after simple enucleation, the histological appearance, and, more recently, the presence of tumor markers, specifically proliferating cell nuclear antigen (PCNA), Ki67, BCE 2 sequence of the enzyme dihydrolipoyl acetyltransferase,

matrix metalloproteinase (MMP) 2 and 9, and p53.<sup>19</sup> Cottom et al suggested that subepithelial hyalinization of the underlying connective tissue capsule, superepithelial splitting and basal mitotic figures can also be considered as predictors of higher recurrence rate in KCOT.<sup>20</sup>

In contrast to other Indian reports where ameloblastoma was the most common odontogenic tumor, its frequency was lesser than KCOT in our series.<sup>5-7</sup> There was a peak incidence in the 3rd decade of life with males being more commonly affected than females. Posterior mandible was the most preferred site. Solid multicystic ameloblastoma outnumbered unicystic and desmoplastic variants. Follicular ameloblastoma was the most common histological type. These findings are in accordance with the previous literature.<sup>21</sup> In an extensive review of 3,677 cases of ameloblastoma, Reichart et al reported the average age of initial diagnosis in industrialized countries to be 39.1 years compared with 27.7 years from developing countries and hypothesized that persons from developing countries develop ameloblastoma 10 to 15 years earlier than in industrialized countries.<sup>22</sup> Dodge proposed that this variation among countries may be due to the accelerated aging process in developing countries owing to poor nutrition and healthcare.<sup>23</sup> But in the present study, the mean age of occurrence was 36.02 years being closer to industrialized countries. According to the large sample Surveys on Household Consumer Expenditure conducted by the National Sample Survey Office (NSSO) of the Ministry of Statistics and Programme Implementation, only 7.5% of Kerala population is under poverty line (results published on 20th June 2013).<sup>24</sup> A better living standard owing to low poverty in respective population may cause preponderance of ameloblastoma in 4th decade in contrast to the usual occurrence in 3rd decade in developing country. However, the results cannot be generalized unless more reports are published from other parts of Kerala and also from other Indian states with low poverty rate, such as Goa (5.09%), Himachal Pradesh (8.06%), Punjab (8.26%) and Sikkim (8.19%).

Calcifying cystic odontogenic tumor is a rare benign cystic neoplasm of odontogenic origin, characterized by an ameloblastoma-like epithelium with ghost cells that may calcify. This was the third most frequent tumor in our data which is in agreement with a single report from Australia.<sup>12</sup> A peak incidence was seen in 2nd decade with a male predilection. Akin to the other KCOT and Ameloblastoma, CCOT most commonly affected posterior mandible. In contrary the reports from elsewhere shows no gender and site predilection.<sup>1</sup>

Odontoma is considered to be a tumor-like malformation (hamartoma) of dental tissues rather than a true odontogenic neoplasm and this tumor accounted for the



fourth most common tumor. In the present study, this tumor arose mainly in young people, with a mean age of 18.03 years and female patients were affected more than male patients, which is in agreement with reports from Australia, Egypt, China, Brazil, whereas Ladeinde et al reported no sex predilection in their study from Nigeria.<sup>11-13,16,25</sup> In the present study, odontomas were found in the anterior regions of both jaws, maxilla being more commonly affected. In general, the posterior segments of the jaw are preferred site for complex odontoma (irregular masses) and compound odontoma (resembling teeth) affects anterior parts of the jaw.<sup>1</sup> In our study, all the complex odontoma occurring in the posterior segments were large, bulbous and molariform, however, the dental tissues were arranged in a disorganized manner. The predominance of molariform odontoma in the posterior segments and incisoriform odontoma in the anterior segments can be explained in regard to difference in dental patterning, because domains of Barx-1 and Dlx-1/2 expression overlap in the mesenchyme of presumptive molar region, whereas domains of Msx-1, Msx-2, and Alx-3 overlaps in presumptive incisor mesenchyme.<sup>26</sup> Thus, resemblance and site preference of respective odontoma may correspond to the normal dental patterning although defective and abortive. The relative less number of odontoma in the present series may be attributed to the fact that odontoma are usually asymptomatic and the patients do not seek medical assistance. Furthermore, some cases may be lost to ENT specialists and also all the excised specimen are not submitted for histopathological examination.

Adenomatoid odontogenic tumor with a maxillary predilection and female preponderance was similar to a previous finding by Okada et al, Arotiba et al and Mohamed et al.<sup>3,27,28</sup> In contrast, Gill et al showed no gender difference.<sup>7</sup> The youngest patient was 10 years old and only a single patient had the tumor in 6th decade which resulted in higher mean age of 21.4 years since mean is sensitive to extreme values (median 16.5 years). The overall frequency of AOT was 5.1% in the present series similar to the reports of Varkhede and Avelar.<sup>6,14</sup> Mohamed et al retrospectively analyzed 33 cases from South African population and found 61% of cases affecting maxilla.<sup>28</sup> In contrary to this, we found an equal distribution; however, anterior segments were more commonly affected. This preponderance for anterior portions of the jaw is similar to previously published data.<sup>11</sup>

The frequency of other benign lesions was comparatively less to draw any conclusion. Similar low frequency was seen in the report published by Gupta et al.<sup>2</sup> We found only 10 peripheral lesions during a period of 13 years and all except one were peripheral odontogenic

fibroma. Only a single case of peripheral calcifying epithelial odontogenic tumor was reported.

There were 13 malignant odontogenic tumors (3.3%). Of these, nine were PIOC (2.3%) and four AC (1%). A single diagnosed and published case of central mucocystic carcinoma from the institution has not been included since we are presenting our data strictly according to WHO 2005 classification.<sup>29</sup> The malignant tumors showed marked predilection for mandible (one case occurred in maxilla). In contrast to benign tumors, malignant tumors were seen in elderly patients (mean 57.7 years). These findings are in agreement with Chai-suparat R et al.<sup>30</sup> Ameloblastic carcinomas were equally distributed in males and females. Primary intraosseous carcinomas showed slight predilection for females.

## CONCLUSION

A marked geographic and demographic variation was observed in the relative frequency of various odontogenic tumors. In contrast to other Indian population, *viz* Maharashtrian, Gujarati and another Dravidian population (linguistically Telugu), where ameloblastoma was the most common tumor; KCOT constituted the commonest OT in present 'Dravidian population'—linguistically (Malayalam), ethnically and geographically different, stressing upon the influence of genetic and/or environmental (epigenetic) factors on tumor pathogenesis.

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