REVIEW

Editorial Process: Submission:05/31/2022 Acceptance:11/24/2022

Prevalence and Epidemiological Profile of Ameloblastoma in India: A Systematic Review and Meta-Analyses

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Abstract

Introduction: Ameloblastoma is regarded as the second most prevalent odontogenic tumor in the light of its prevalence, clinical characteristics, greater incidence of tumor recurrence, and therapeutic challenges. The aim of this systematic review was to establish the prevalence of ameloblastoma in the Indian subcontinent and to establish a national epidemiologic profile for these lesions. **Material and Methods:** A systematic review was undertaken based on the PRISMA guidelines in search of epidemiologic studies concerning odontogenic tumors and ameloblastoma that are listed by PubMed, EBSCO, and Google Scholar embracing the period from January 2010 to December 2021, to evaluate the prevalence rate in India. A total of 277 publications were retrieved, of which 27 articles were selected, based on the World Health Organization classification of odontogenic tumors. **Results:** The affected individuals were on average in the third decade of life, with a higher male predominance. The majority of the tumors were multilocular radiolucencies in the posterior mandible, with follicular and plexiform histopathological features. The most common type of malignant lesion is ameloblastic carcinoma. Over 60% of follicular ameloblastoma recurred more frequently than the other types of ameloblastoma. The random effect model shows overall point estimate of 4.83 with 95% confidence interval (4.44 -5.26). **Conclusion:** The systematic study indicates a slight male predisposition to ameloblastoma, with a peak incidence in the third decade of life and the mandible as the preferred anatomical site. The solid/multicystic ameloblastoma is the most prevalent histopathologic pattern. More epidemiological research on the prevalence rate of ameloblastoma is required, particularly in India, in an effort to accurately determine the national epidemiological profile of ameloblastoma.

Keywords: Ameloblastoma- WHO classification- odontogenic tumor- recurrence- ameloblastic carcinoma

Asian Pac J Cancer Prev, **23 (11)**, 3601-3610

Introduction

Ameloblastoma is among the most invasive odontogenic tumors (OT) in many nations around the world. It is a localized malignant tumor developing from odontogenic epithelium without the presence of odontogenic ectomesenchyme, with about 70% of cases enduring malignant transformation and up to 2% of cases disseminating to other sites (Effiom et al., 2018; Hendra et al., 2020). It accounts for nearly 1% of all oral tumors, 13-58% of all OT, and is far more common in developing countries with a high risk of recurrence (Chae et al., 2015; Intapa, 2017). It is more prevalent among young individuals in their third decade of life, with a propensity for the posterior mandible (Chawla et al., 2013). It can potentially cause bone destruction, with well-defined multilocular radiolucencies encircled by cortical bone sclerosis, notably in solid ameloblastoma. It is worthy to note that the vast majority of ameloblastoma studies conducted in India revealed a substantial male predisposition (Anila et al., 2021; Bhattacharjee et al., 2016).

Though the etiology of ameloblastoma is uncertain, it could be linked to localized trauma, inflammation, nutritional imbalances, mutations, and/or molecular aberrations involving many signalling pathways. The enamel organ, remnants of odontogenic epithelium, and

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the lining of an odontogenic cyst have all been related to the development of ameloblastoma (Hendra et al., 2020). Recent hypotheses suggest that genetic and molecular abnormalities account for varying aggressive tendencies and the likelihood of metastasis (Ruslin et al., 2018). It is a slow-growing, invasive tumor that is usually unilateral and manifests as asymptomatic facial asymmetries as the lesion progresses (Chae et al., 2015; Wright et al., 2014). In developing nations, it frequently manifests with significantly enlarged lesions before seeking medical attention owing to naivety and inadequate health resources (Hendra et al., 2020).

According to the World Health Organization (WHO), ameloblastoma was categorized into benign and malignant forms based on its biological characteristics. The clinical types includes conventional, unicystic and peripheral/ extraosseous. The malignant ameloblastoma encompasses metastasizing ameloblastoma, primary ameloblastic carcinoma, secondary intraosseous ameloblastic carcinoma, and secondary peripheral ameloblastic carcinoma (Hendra et al., 2020) (Santos T et al., 2020). The nomenclature of ameloblastoma was reclassified in the fourth edition of WHO (2017) based on genetic studies (Gupta et al., 2010; Wright et al., 2017).

Despite the fact that many retrospective research studies had been published in Asia, the United States, Africa, and Europe, well-documented studies on ameloblastoma in Indian populations are sparse (Effiom et al., 2018; Page M et al., 2021). The aim of this study was to evaluate the prevalence of ameloblastoma in India through a systematic review and Meta analysis of the articles published between 2010 and 2021 as well as to provide a national epidemiological profile of ameloblastoma based on available studies conducted in India in terms of gender and age distribution, tumor location and types, histopathologic and radiological appearance.

Materials and Methods

Registration and Protocol

This protocol has been registered on the International Platform of Registered Systematic Review and Meta-analysis Protocols (INPLASY registration number: INPLASY202260048; INPLASY DOI number: 10.37766/ inplasy2022.6.0048 Available at: https://inplasy.com) and was carried out using PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) (Page et al., 2021)..

Eligibility criteria

The studies that evaluated the prevalence rate of ameloblastoma, published from January 2010 to December 2021 following the WHO classification of OT were included in the review. The search was limited to full-text English-language and human studies in India. Exclusion criteria include case reports, animal studies, in-vitro studies, guest editorials and review articles.

Information sources and searching strategy

A comprehensive search of databases (PubMed, EBSCO, and Google Scholar) was conducted for articles published from January 2010 to December 2021, with the combination of medical subject heading (MeSH) terms "odontogenic tumor", "odontogenic lesions", "ameloblastoma incidence", "epidemiology", "WHO classification", "ameloblastoma recurrence", "ameloblastoma prevalence", using the Boolean operators "AND" and "OR". A literature search for the studies conducted in India that were published during this period was conducted. In addition, manual searches were performed to find other eligible articles that were not available in the electronic databases.

Study selection, data collection, and data items

The selection procedure was conducted by two independent reviewers who were blinded to each other. The appropriateness of the relevant articles was appraised by the reviewers. If there was any disagreement between them, the consensus was reached through discussion. The first step consists of screening in which the authors screen the titles and abstracts from the search results and eliminated the studies that did not elaborate on the prevalence of ameloblastoma in India. The authors reviewed the full-text manuscripts in the second stage and excluded studies that did not fulfil the inclusion criteria. Studies without any full-text available or data that was incomplete or unclear were excluded.

The following data for each study were retrieved from the selected studies and tabulated: author, year of publication, region of study, gender and age distribution, prevalence rate, tumor location and types, the histopathologic and radiological patterns, tumor recurrence and malignant transformation. Meta-analysis can be carried out on the transformed proportions using increase of variance as a study weight. Transformation was performed using logit method l=ln (P/1-P) where P is the prevalence/proportion, thereby it treats small and large values symmetrically. The back transformation to a proportion is done using p= exp(l)/exp(l)+1

Results

Study selection

The search technique generated a total of 277 articles from all databases and other sources, of which 168 were eliminated after screening for duplication. After reading the titles and abstracts, 49 articles were removed, and the full-text articles of the remaining 60 studies were independently appraised for eligibility by two authors. Thirty-three articles were excluded then, as they did not fit our inclusion criteria. For the final review, a total of 27 studies were considered (Ahire et al., 2018; Anila et al., 2021; Bansal et al., 2015; Bhagwat et al., 2017; Deepa et al., 2016; Deepthi et al., 2016; Ebenezer et al., 2010; Gill et al., 2011; Gotur et al., 2017; Kadashetti et al., 2014; Kaur et al., 2021; Kiruthika et al., 2021; Krishnapillai et al., 2010; Mehngi et al., 2018; Mullapudi et al., 2011; Nalabolu et al., 2017; Nazir et al., 2019; Page et al., 2021; Pandiar et al., 2015; Parashar et al., 2018; Saxena et al., 2012; Selvamani et al., 2014; Sharma et al., 2017; Singhal et al., 2013; Syed et al., 2019; Varkhede et al., 2011) [, #2038]. Figure 1 illustrates the study sequence.

Table 1. Risk of Bias for Included Studies Using the National Institute of Health (NIH) Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies

Studies included	Was the research question or objective in this paper clearly stated?	Was the study population clearly specified and defined?	Was the participation rate of eligible persons atleast 50%?	Were all the subjects selected or recruited from the same or similar populations?	Was a sample size justification, power description, or variance and effect estimates provided?	For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured? outcome(s) being measured?	Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed? exposure and outcome if it existed?	For exposures that can vary in amount or level, did the study examine different levels of the exposure? exposure?	Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all participants participants? implemented consistently across all participants?	Was the exposure(s) assessed more than once over time?	Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Were the outcome assessors blinded to the exposure status of participants?	Was loss to follow-up after baseline 20% or less?	Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	Summary Quality
Chawla et al., 2013	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Gupta and Ponniah, 2010	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Singh et al., 2020	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Singhal et al., 2013	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Mullapudi et al., 2011	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Pandiar et al., 2015	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Selvamani et al., 2014	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Kaur et al., 2021	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Gotur et al., 2017	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Gill et al., 2011	Y	N	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Poor
Syed et al., 2019	Y	N	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Poor
Nalabolu et al., 2017	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Varkhede et al., 2011	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Parashar et al., 2018	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Deepthi et al., 2016	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Krishnapillai et al., 2010	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Kadashetti et al., 2014	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Bhagwat et al., 2017	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Mehngi et al., 2018	Y	N	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Poor
Nazir et al., 2019	Y	N	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Poor
Saxeena et al., 2012	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Bansal et al., 2015	Y	N	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Poor
Ebenezer et al., 2011	Y	N	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Poor
Ahire et al., 2018	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Kiruthika et al., 2021	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Deepa et al., 2016	Y	Y	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Fair
Sharma et al., 2017	Y	N	NA	Y	N	NA	NA	NA	Y	N	Y	NA	NA	NA	Poor

Summary Quality: Poor (0–4 out of 14 questions), Fair (5–10 out of 14 questions), or Good (11–14 out of 14 questions); NA, Not applicable; Y, Yes; N, No

Quality assessment of the risk of bias within studies

The quality assessment was based on the criteria of the National Institute of Health (NIH) quality assessment tool for observational cohort and cross-sectional studies (Cadavid et al., 2019). Each study is being critically appraised based on the reported details and consideration of the concepts for minimizing bias and rated as good, fair and poor. According to the NIH quality evaluation tool, seven studies were of poor quality, while the remaining twenty studies were of fair quality in this present review

(Table 1).

Synthesis of results

Meat-analysis was performed for the included studies. RevMan 5.4 software served as the statistical platform for computing tests and associated graphical results. We transformed the prevalence estimate using logit method. Results are presented after back transformation. The test of the heterogenicity for the included studies were analyzed using Tau square with a p value of >0.001 and I^2 is 98%. The studies were considered heterogenous and hence random effect model was used. The random effect model shows overall point estimate of 4.83 with 95% confidence interval. (4.44 -5.26) The main outcome of meta-analysis is Forest plot, a graphical display as shown in the figure on the forest plot , 95% confidence intervals of all studies were entirely on the positive side of zero and it does not overlap 1, hence there is statistical significance at the individual study level. Similarly, 95% confidence interval of the overall estimate does not overlap 1 and there is statistical significance at the meta-analysis level (Figure 2).

National epidemiological profile of Ameloblastoma

Prevalence rate

The review included twenty-seven retrospective studies on the prevalence rate of ameloblastoma from various states in India. The prevalence of ameloblastoma in different parts of India ranged from 14.02% to 71.4% of the odontogenic tumour (Ahire et al., 2018; Pandiar et al., 2015).

Gender and age distribution

The age distribution in the current review ranged from 0 to 88 years (Table 2). Though the tumor afflicted people of all ages, the second and third decades were determined to have the highest incidence. but benign lesions showed a wide variation (Gotur et al., 2017). While all of the included studies indicated a significant male predominance, Kadahsetti et al., (2014) reported a four-fold male predilection (Bhagwat et al., 2017). However, Singhal et al., (2013). in the Puducherry populations found a female inclination of 1:1.3, Deepthi et al. in South Kerala observed a ratio of 1:1.13 (Parashar et al., 2018), Kiruthika et al., (2021) and Deepa et al., (2016) established a female preponderance of 1:1.4 in Tamil Nadu and Karnataka populations.

Anatomic site of the tumor

Tumors of the mandible outweighed tumors of the maxilla in all of the included studies. The body of the mandible, ramus, and the angle region are the most common anatomic site reported. Selvmani et al., (2014)

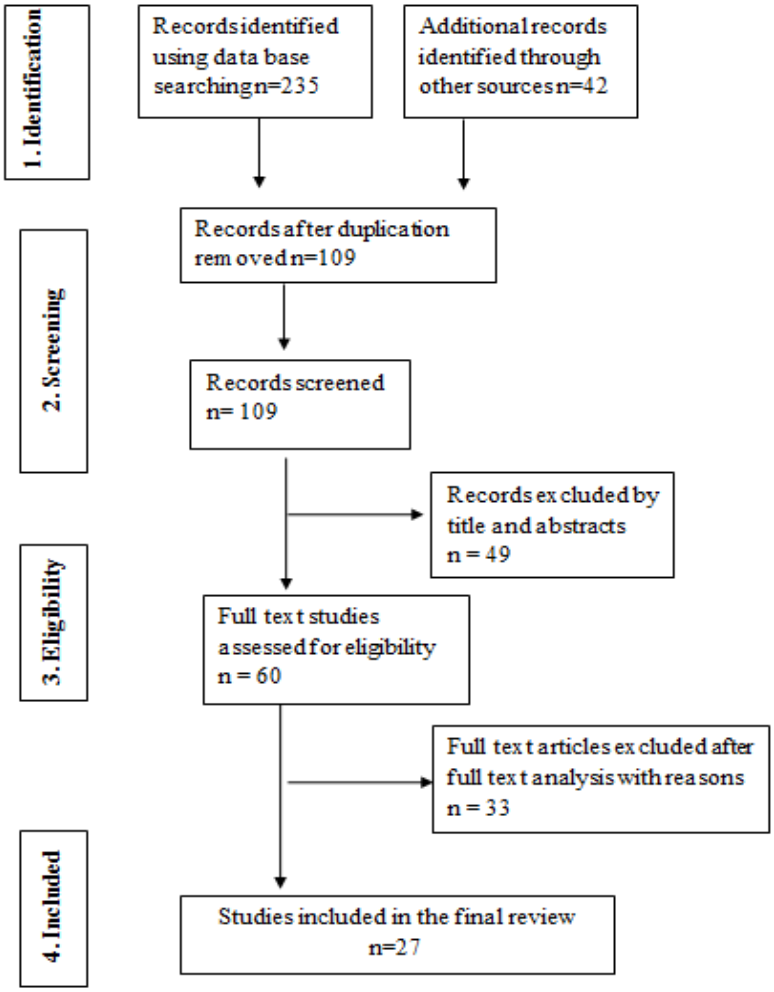

Figure 1. PRISMA Flow Chart of the Included Studies (Adapted from Preferred Reporting Items for Systematic Reviews and Meta-analyses 2009 Flow Diagram)

Table 2. Summary of Included Studies in the Systematic Review

Author (Year)	State	Biopsy (n)	Total OT		Total ameloblastoma		Age		M:F	Man:Max
			N	(%)	N	(%)	Mean	Range		
ɣChawla et al., 2013	Nagpur, Maharashtra	7,700	199	2.5	91	45.7	32.5	10-60	1.2:1	01:01.3
*Gupta and Ponniah, 2010	Chennai, Tamil Nadu	11,843	489	4.13	331	67.69	34.53	5-75	1.41:1	10.5:1
□□ Singh et al., 2020	Lucknow Uttar Pradesh	893	56	6.2	29	51.79	NS	19-40	1.07:1	Mandibular predilection
□Singhal et al., 2013	Puducherry	1,883	61	3	16	26	33	10-80	01:01.3 M-7, F-9	Mandibular predilection Ant-3, post 13
□Mullapudi et al., 2011	Hyderabad Andra Pradesh	77	70	91	50	71.4	25	21-30	1.1:1	4.5:1
□Pandiar et al., 2015	Kozhikode, Kerala	6,946	395	6.08	102	25.9	32.69	5-88	1.4:1	2.43:1
□Selvamani et al., 2014	Davangere, Karnataka	3,026	103	3.4	58	56.3	39.5	21-73	2.1:1	96.8% in mandible
**Kaur et al., 2021	Nagpur, Maharashtra	8,787	345	3.92	203	58.84	35.16	11-75	1.07:1	24.1:1
□Gotur et al., 2017	Meerut Uttar Pradesh	3,182	255	8.01	88	34.5	26.08	7-79	1.2:1	6.09:1
□Gill et al., 2011	Ahmedabad Gujarat	-	209	-	99	47.4	29.55	5-69	1.1:1	6.1:1
□□Syed et al., 2019	Goa	-	114	2.61	66	57.9	NS	NS	NS	6.33:1
□Nalabolu et al., 2017	Bhimavaram Andra Pradesh	7,400	161	2.17	79	49.06	NS	11-70	2.2:1	3.9:1
□Varkhede et al., 2011	Mumbai, Maharashtra	2075	120	5.78	49	40.83	NS	10-80	1.3:1	8.8:1
□Parashar et al., 2018	Indore, Madhya Pradesh	-	80	-	42	52.5	NS	0-69	1.5:1	Mandibular predilection
□Deepthi et al., 2016	South Kerala	7,117	305	4.29	153	50.2	37.79	4-74	01:01.1	3.2::1
□Krishnapillai et al., 2010	Dharwad, Karnataka	5,650	121	2.14	73	60.3	30.2	10-78	1.3:1	11.2:1
□Kadashetti et al., 2014	Wardha, Maharashtra	NS	102	5.78	37	36.27	NS	5-75	4:01	4.67:1
□Bhagwat et al., 2017	Marathwada Maharashtra	2,652	127	4.79	45	35.43	3rd decade	NS	1.14:1 m-24 f-21	4.63:1 Man-37,max-8
□Mehngi et al., 2018	Karnataka & Madhya Pradesh	-	104	-	45	43.26	NS	21-30	1.25:1	8:01
□Nazir et al., 2019	Bangalore, Karnataka	-	400	-	23	17.3	25.3	10-49	1.4:1	92.7% in mandible
□Saxeena et al., 2012	Meerut, Uttra Pradesh	61	35	57.38	11	31.43	NS	0-18	1:01	2.2:1
□Bansal et al., 2015	Mumbai, Maharashtra	-	256	-	39	15.2	13.6	4.5-18	2:01 m-26 f-13	97.4%-man 2.6%-max
□Ebenezer et al., 2011	Chennai Tamil Nadu	-	107	-	15	14.02	31.1	5-74	1.5:1	6.5:1 [71% in mandible]
□□Ahire et al., 2018	Mumbai, Maharashtra	6,797	250	7.14	77	30.8	35.72	1-10th Peak-3-5	2.66:1 M-56 F-21	11:1 [89% in mandible] Man-59,max-7
ɣKiruthika et al., 2021	Salem, Tamil Nadu	101	12	11.9	4	33.3	31	-	01:01.4	3:01
□Deepa et al., 2016	Belgaum, Karnataka	4,080	108	2.64	36	33.3	29.8	4-80	01:01.4	-
□Sharma et al., 2017	Madikeri, Karnataka	-	92	-	20	21.74	-	0-70	1.5:1	Mandibular predilection

*, 1992 WHO classification of OT; □, 2005 WHO classification of OT; □□, 2017 WHO classification of OT; **, 1992, 2005, and 2017 WHO classification of OT; ɣ, Not specified

and Nazir and Usman (2019) concluded that mandibular predisposition was present in 96.8% and 92.7% of their samples respectively. The mandible to maxilla ratio has been reported to be as high as 24.1:1 by Kaur et al., (2021) (Table 2).

Tumor types

In 23 studies, the histological characteristics of ameloblastoma were classified using the 2005 WHO classification of OT (Table 2). 2017 WHO criteria were used in four of the studies (Gotur SP et al., 2017; Kadashetti et al., 2014; Nalabolu et al., 2017; Singhal et al., 2013), and one study utilized 1992 WHO classification (Page et al., 2021). Further, two of the included studies had no mention about the edition of WHO nomenclature (Anila et al., 2021; Deepa et al., 2016). The prevalence and histological features of ameloblastoma were examined in one study by Kaur et al. with the WHO classification

Table 3. Histopathological and Radiographic Features of Included Studies in the Systematic Review

Author (Year)	Clinical &Histopathologic types						Radiographic image			
	S/M		U	D	P/E	Others	UR	MR	Mixed	Others
	F	Px								
Chawla et al., 2013	18 (19.8)	20 (22)	31 (34.1)	2 (2.2)	-	20 (22)	29 (34.1)	56 (65.9)	-	-
Gupta and Ponniah, 2010	207 (42.33)		117 (23.93)	-	7 (1.43)	-	NS	NS	NS	NS
Singh et al., 2020	ND		6 (1%0.7)	ND	ND	ND	NS	NS	NS	NS
Singhal et al., 2013	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Mullapudi et al., 2011	22 (48.9)	18 (40.1)	NR	2 (4)	3 (6)	5 (11)	ND	36 (72)	ND	ND
Pandiar et al., 2015	47 (64.4)	15 (20.54)	24 (23.5)	5 (4.9)	-	11 (15.06)	179 (45.2)	155 (39.2)	22 (5.5)	39 (10.1)
Selvamani et al., 2014	17 (54.8)	2 (3.4)	27 (46.5)	1 (1.7)	-	11 (19)	1	ND	0	ND
Kaur et al., 2021	33 (16.2)	46 (22.6)	68 (33.49)	8 (3.94)	-	46 (22.7)	NS	NS	NS	NS
Gotur et al., 2017	25 (28.4)	13 (14.8)	27 (30.7)	3 (3.4)	-	20 (22.7)	NS	NS	NS	NS
Gill et al., 2011	29 (29.3)		70 (70.7)	-	-	-	NS	NS	NS	NS
Syed et al., 2019	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Nalabolu et al., 2017	7 (4.3)	16 (9.9)	38 (23.6)	10 (6.2)	5 (3.1)	3 (1.8)	NS	NS	NS	NS
Varkhede et al., 2011	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Parashar et al., 2018	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Deepthi et al., 2016	124 (80.4)		28 (17.6)	-	1 (2)	-	NS	NS	NS	NS
Krishnapillai et al., 2010	23 (31.5)	8 (10.9)	27 (37)	4 (5.5)	0	12 (16.4)	20 (27.3)	37 (50.6)	4	ND
Kadashetti et al., 2014	ND	ND	ND	ND	ND	ND	NS	NS	NS	NS
Bhagwat et al., 2017	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Mehngi et al., 2018	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Nazir et al., 2019	16 (68)	5 (23)	2 (9)	-	-	-	6 (28)	17 (72)	-	-
Saxeena et al., 2012	5 (8.2)	3 (4.9)	1 (1.6)	NS	NS	2 (3.2)	NS	NS	NS	NS
Bansal et al., 2015	4 (10.3)	16 (41.0)	19 (48.7)	-	-	-	23 (59)	12 (30.7)	1 (2.6)	3 (7.7)
Ebenezer et al., 2011	8 (53.3)		7 (46.7)	-	-	-	NS	NS	NS	NS
Ahire et al., 2018	NS	NS	46 (59.7)	NS	1 (1.29)	NS	NS	NS	NS	NS
Kiruthika et al., 2021	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Deepa et al., 2016	21 (39)		14 (26.1)	-	1 (1.9)	-	NS	NS	NS	NS
Sharma et al., 2017	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS

S/M, Solid/multicystic; F, Follicular; Px, Plexiform; U, Unicystic; D, Desmoplastic; P/E, Peripheral/Extraosseous; UR, Unilocular; MR, Multilocular; ND, Not defined; NS, Not specified

systems of 1992, 2005, and 2017 (Gotur et al., 2017). Similarly, Deepa et al., (2016). employed 2005 WHO classification and compared the epidemiological traits of ameloblastoma with that of 1992 classification systems from the existing literature.

Histopathological appearance

Nine of the included studies had not reported the histopathological data of ameloblastoma (Bhagwat et al., 2017; Deepa et al., 2016; Deepthi et al., 2016; Kadashetti et al., 2014; Mehngi et al., 2018; Mullapudi et al., 2011; Nalabolu et al., 2017; Nazir et al., 2019; Parashar et al., 2018). Kadashetti et al., (2014) found few cases of unicystic form, although the frequency of each variant was not precisely defined. The solid/multicystic pattern is the most common ameloblastoma found in majority of the included study (Table 3). According to Mullapudi et al., (2011) solid pattern accounts for almost 90% of all occurrences of ameloblastoma (Pandiar et al., 2015). It is a benign OT that grows slowly and has two distinct histological patterns: follicular and plexiform. Proliferating odontogenic epithelial cells are organized in islands in the follicular type, whereas epithelial cells are structured in continuous anastomosing strands in the plexiform type. Other histologic variants include granular, acanthomatous, desmoplastic and basal cell (Anila et al., 2021; Bansal et al., 2015; Effiom et al., 2018; Gill et al., 2011; Gotur et al., 2017; Kadashetti et al., 2014; Kaur et al., 2021; Pandiar et al., 2015; Selvamani et al., 2014; Varkhede et al., 2011). The unicystic ameloblastoma was the most prevalent histopathologic pattern reported by Gill et al. with a mean age of 25.9 years, which was lower than the patients with solid/multicystic ameloblastoma, who had a mean age of 33.2 years (Gill et al., 2011). Similarly, unicystic pattern was more frequently reported in the study sample of Chawla et al., (2013) Regardless of the fact that desmoplastic and peripheral ameloblastoma was generally considered to be rare (Chae et al., 2015; Hendra et al., 2020; Intapa, 2017), eleven of the included studies found desmoplastic variants (Anila K et al., 2021; Effiom et al., 2018; Gill S et al., 2011; Kadashetti V et al., 2014; Kaur et al., 2021; Mullapudi et al., 2011; Pandiar et al., 2015; Selvamani et al., 2014; Varkhede et al., 2011) and peripheral ameloblastoma in six studies (Kiruthika et al., 2021; Krishnapillai et al., 2010; Page et al., 2021; Pandiar et al., 2015; Varkhede et al., 2011).

Table 4. Frequency of Malignant Lesions Reported and Recurrence in the Included Studies

Author (Year)	Clinical &Histopathologic types						Radiographic image			
	S/M		U	D	P/E	Others	UR	MR	Mixed	Others
	F	Px								
Chawla et al., 2013	18 (19.8)	20 (22)	31 (34.1)	2 (2.2)	-	20 (22)	29 (34.1)	56 (65.9)	-	-
Gupta and Ponniah, 2010	207 (42.33)		117 (23.93)	-	7 (1.43)	-	NS	NS	NS	NS
Singh et al., 2020	ND		6 (1%0.7)	ND	ND	ND	NS	NS	NS	NS
Singhal et al., 2013	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Mullapudi et al., 2011	22 (48.9)	18 (40.1)	NR	2 (4)	3 (6)	5 (11)	ND	36 (72)	ND	ND
Pandiar et al., 2015	47 (64.4)	15 (20.54)	24 (23.5)	5 (4.9)	-	11 (15.06)	179 (45.2)	155 (39.2)	22 (5.5)	39 (10.1)
Selvamani et al., 2014	17 (54.8)	2 (3.4)	27 (46.5)	1 (1.7)	-	11 (19)	1	ND	0	ND
Kaur et al., 2021	33 (16.2)	46 (22.6)	68 (33.49)	8 (3.94)	-	46 (22.7)	NS	NS	NS	NS
Gotur et al., 2017	25 (28.4)	13 (14.8)	27 (30.7)	3 (3.4)	-	20 (22.7)	NS	NS	NS	NS
Gill et al., 2011	29 (29.3)		70 (70.7)	-	-	-	NS	NS	NS	NS
Syed et al., 2019	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Nalabolu et al., 2017	7 (4.3)	16 (9.9)	38 (23.6)	10 (6.2)	5 (3.1)	3 (1.8)	NS	NS	NS	NS
Varkhede et al., 2011	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Parashar et al., 2018	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Deepthi et al., 2016	124 (80.4)		28 (17.6)	-	1 (2)	-	NS	NS	NS	NS
Krishnapillai et al., 2010	23 (31.5)	8 (10.9)	27 (37)	4 (5.5)	0	12 (16.4)	20 (27.3)	37 (50.6)	4	ND
Kadashetti et al., 2014	ND	ND	ND	ND	ND	ND	NS	NS	NS	NS
Bhagwat et al., 2017	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Mehngi et al., 2018	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Nazir et al., 2019	16 (68)	5 (23)	2 (9)	-	-	-	6 (28)	17 (72)	-	-
Saxeena et al., 2012	5 (8.2)	3 (4.9)	1 (1.6)	NS	NS	2 (3.2)	NS	NS	NS	NS
Bansal et al., 2015	4 (10.3)	16 (41.0)	19 (48.7)	-	-	-	23 (59)	12 (30.7)	1 (2.6)	3 (7.7)
Ebenezer et al., 2011	8 (53.3)		7 (46.7)	-	-	-	NS	NS	NS	NS
Ahire et al., 2018	NS	NS	46 (59.7)	NS	1 (1.29)	NS	NS	NS	NS	NS
Kiruthika et al., 2021	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Deepa et al., 2016	21 (39)		14 (26.1)	-	1 (1.9)	-	NS	NS	NS	NS
Sharma et al., 2017	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS

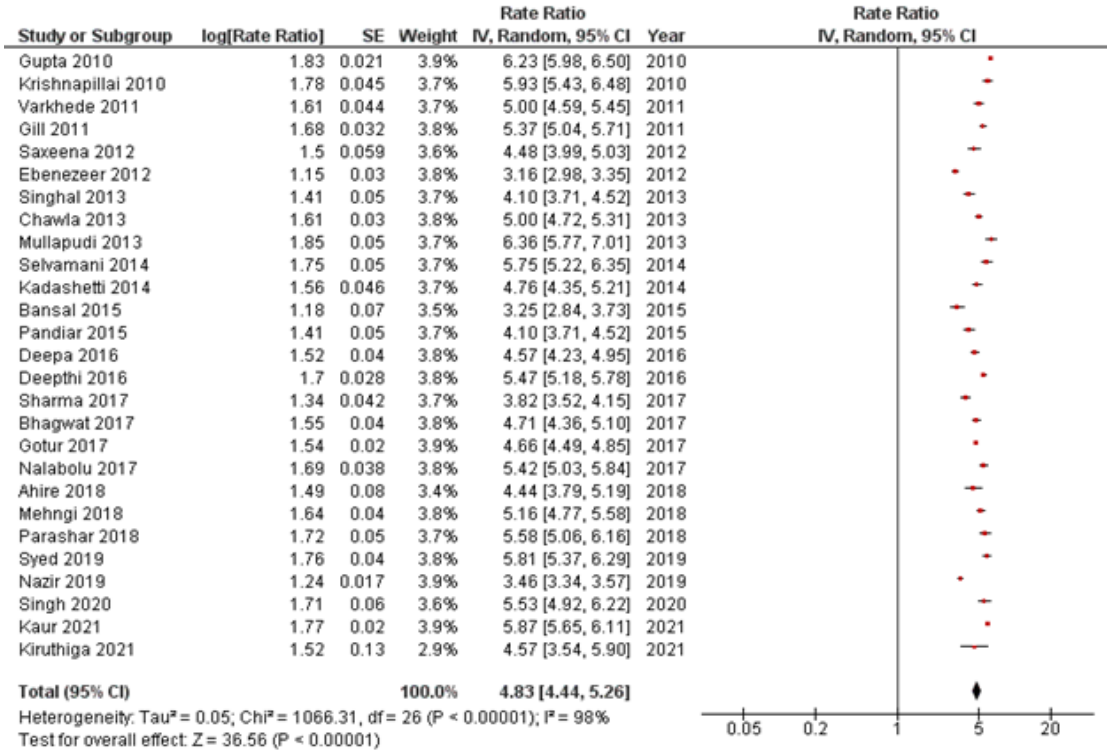

Figure 2. Forest Plot Showing Pooled Prevalence Rate of Ameloblastoma

Radiological appearance

Multilocular ameloblastoma was shown to be more predominant than unilocular pattern in the literature (Ebenezer et al., 2010). In a study by Pandiar et al., (2015) about 96.9% of samples had well-defined borders with unilocular radiolucency (Selvamani et al., 2014). Further, a higher frequency of unilocular radiolucencies was also reported by Tatapudi et al. and Bansal et al. In the studies included, around 2.6-5.5% of a mixed radio-opaque/radiolucent lesion was also noticed (Selvamani et al., 2014). The radiological features of ameloblastoma are shown in Table 3.

Malignant transformation

All of the documented malignant tumors were mostly detected in the mandible and mostly appeared after the sixth decade (Kaur et al., 2021). The most consistently cited malignant lesions in the included studies were ameloblastic carcinoma and ameloblastic fibrosarcoma/ odontogenic sarcoma (Gill et al., 2011; Gotur et al., 2017; Kiruthika et al., 2021; Selvamani et al., 2014). Table 4 shows other malignant lesions that have been identified in the review.

Management and recurrence

As ameloblastoma is a benign, locally invasive tumor with a high recurrence, its management remains a controversial issue. Deepthi et al., (2016) established that 18% of ameloblastoma recur, with the statistically insignificant association between recurrence and age, gender, or anatomical site (Bhagwat et al., 2017). According to the findings by Krishnapillai and Angadi, (2010) and almost 60% of follicular ameloblastoma recurred more often than the other forms (Table 4). The study by Chawla et al., (2013) reported recurrence in unicystic variant. It is vital to examine whether the tumor is primary or recurring, the age, size, anatomical location, and persistence of the lesion, the occurrence of cortical bone damage, and soft tissue infiltration before contemplating surgical intervention.

The treatment may be conservative or radical depending on these aspects. Major surgical intervention poses a challenge in the younger age group because it influences the growth of the craniofacial bones. The plexiform ameloblastoma recurred as granular cell ameloblastoma in a study by Bansal et al., (2015) after a follow-up of 11 years. Five solid and 13 unicystic cases were reported to have had conservative surgical intervention, which included enucleation with peripheral ostectomy. Twelve solid and three unicystic patients were managed with segmental resection or hemi-mandibulectomy, as well as bone grafts and surgical plates (Ebenezer et al., 2010). However, there is a dearth of clinical trials in India that analyse the treatment algorithms for ameloblastoma in a proficient manner, resulting in reliable data that could supplement the restricted literature.

Discussion

The current systematic review included studies conducted over a 12-year period that demonstrated a diverse prevalence rate of ameloblastoma in India. Diverse methodologies, suboptimal reporting of cases to healthcare institutions, a lack of reliable case confirmation methods, and varying diagnostic expertise may contribute to differences in the estimation of prevalence rate. Furthermore, prevalence rates reported over short intervals in certain studies may be less credible (Rocha et al., 2021).

Ameloblastoma, the second most common OT (Avelar et al., 2011), occurs primarily in the posterior mandible. The majority of cases occurred in the second to fourth decades of life (Mehngi et al., 2018). In Africa and South America, the highest prevalence was in the third decade, while in Europe and North America, it appeared in the fifth and sixth decades. Ameloblastoma seems to be more prevalent in developing countries like India, where it strikes at a younger age. This disparity in the demographic distribution of ameloblastoma could be attributed to hastened aging process caused by poor nutrition and limited access to healthcare facilities (Bhagwat et al., 2017; Intapa, 2017).

In the context of gender distribution, males were more afflicted than females, which correlate with other studies from all over the world. However, the upsurge of females was recorded in the literature, which corresponded to the findings of this study (Filizzola et al., 2014). The review reinforces that the mandible is often the favoured site, which is consistent with prior findings around the globe. Gingiva, alveolar process, buccal and mandibular vestibule, retromolar pad, and edentulous areas were the most commonly involved anatomical site reported (Intapa, 2017).

The distribution of histological subtypes in the review is concurrent with that being documented in the literature, and multiple investigations have found that plexiform and follicular patterns are the most common (Bianco et al., 2020; Rocha et al., 2021). The follicular pattern is the most frequently identified histological appearance among the Indian population. Acanthomatous, granular, and basal cell patterns were uncommon, whereas the mixed type was fairly common. Ameloblastoma is radiographically identified as unilocular or multilocular radiolucencies that typically induce cortical disturbances, tooth dislocation, or root resorption. Younger people are more likely to be diagnosed with unicystic ameloblastoma with a higher incidence of unilocular radiolucency (Avelar et al., 2011).

There is a high likelihood of histological and radiographic ambiguity between ameloblastoma, odontogenic cysts, and other OT, which can lead to misinterpretation. A comprehensive evaluation of several characteristics such as clinical, radiographic, and histopathological manifestations is mandatory to establish an accurate diagnosis (Hresko et al., 2021). Computed tomography, magnetic resonance imaging, and cone-beam computed tomography is currently regarded as routine diagnostic tool (Intapa, 2017).

Conservative treatment modalities include enucleation/ enucleation coupled with curettage and the use of adjuvant treatment such as Carnoy's solution and cryotherapy. The medical condition of the patient, age, anatomic site of the tumor, and its borders should be addressed prior to undertaking surgical excision with a safety margin. Prior

studies disclose that all patients who have undergone surgical resection did not experience recurrence. When employing the radical treatment, however, the aesthetic, phonetic, and functional issues induced by a probable facial distortion must be evaluated. The radical treatment comprises of a 1–2 cm marginal excision with rapid bone repair. Following the recent innovation in the understanding of the molecular signalling pathways aligned with ameloblastoma, targeted therapies are also available. Patients who have endured radical surgery should be recommended reconstructive and rehabilitative approaches (Filizzola et al., 2014).

The treatment of choice of the unicystic ameloblastoma is the conservative therapy, especially in young adults, due to the perceived influence on the growth of the craniofacial skeleton, masticatory functions, and psychosocial issues that a radical intervention would cause. However, patients who had conservative treatment, on the other hand, experienced local recurrence. Therefore, radiographic monitoring of patients should be continued for at least 10 years, since recurrence following conservative therapy is around 7 to 25% (Effiom et al., 2018; Hendra et al., 2020; Wright et al., 2017; Rocha et al., 2021; Hresko et al., 2021).

The prevalence of ameloblastoma was influenced by several registries, and the validity of these registries were determined by its integrity, whether it was population-based or hospital-based. In this regard, it is significant to mention that the reported prevalence rate is solely based on the number of ameloblastoma patients who sought treatment in a healthcare system. As a result, the exact prevalence rate would most probably be underestimated. Despite these limitations, the existing evidence enables some key conclusions and recommendations to be established.

In conclusion, The systematic review reveals a significant male predilection to ameloblastoma, with a peak incidence in the third decade of life and the mandible as the preferred anatomical site. The solid/multicystic ameloblastoma is the most prevalent histopathologic pattern. Post-operative clinical and radiological follow-up is critical for the early diagnosis of recurrence. The WHO classification of OT should be used as a baseline for histopathological evaluation of ameloblastoma. More epidemiological investigations on the prevalence rate of ameloblastoma are essential, particularly in India, in an effort to precisely determine the national profile of ameloblastoma.

Author Contribution Statement

The authors confirm contribution to the paper as follows: Study conception and design: Thuckanaickenpalayam Ragunathan Yoithapprabhunath, Kenniyan Kumar Srichinthu, Data collection: Thuckanaickenpalayam Ragunathan Yoithapprabhunath, Janardhanam Dineshshankar, Ravi Aravindhan, Santhanam Vidyalakshmi. Interpretation of results: Kenniyan Kumar Srichinthu, Ramdas Madhavan Nirmal. Draft manuscript preparation: Thuckanaickenpalayam Ragunathan Yoithapprabhunath, Kenniyan Kumar Srichinthu, Ramdas Madhavan Nirmal. All authors reviewed the results and approved the final version of the manuscript.

Acknowledgements

We thank Prof. Dr. Anzil KS Ali, Royal Dental College, Kerela and Dr. G.K. Divya Priya, MDS, Cuddalore Government Dental College and Hospital, for their valuable suggestions in study design, conducting statistical analysis and tables articulation.

Funding statement

None.

Registering dataset

The study included secondary data analysis, therefore doesn't require approval from scientific body, although the protocol of this study was registered on the International Platform of Registered Systematic Review and Meta-analysis Protocols (INPLASY registration number: INPLASY202260048; INPLASY DOI number: 10.37766/inplasy2022.6.0048 Available at: https://inplasy.com). The present study was not a part of the approved student thesis.

Ethics approval

Ethical approval was not required for present study because in this study data was retrieved and synthesized from the already published studies (secondary data analysis).

Conflict of Interest

None.

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