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The global distribution of permanent canine hypodontia: A systematic review

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Objective: To systematically review studies on canine agenesis prevalence in different populations and continents, based on the jaw, sex, location, and associated dental anomalies. **Methods:** Electronic and hand searches of English literature in PubMed, Web of Science, Scopus, OpenGrey, and Science Direct were conducted, and the authors were contacted when necessary. Observational studies (population-based, hospital/clinic-based, and cross-sectional) were included. For study appraisal and synthesis, duplicate selection was performed independently by two reviewers. Study quality was assessed using a modified Strengthening the Reporting of Observational Studies in Epidemiology checklist, with main outcome of prevalence of canine agenesis. **Results:** The global population prevalence of canine agenesis was 0.30% (0.0–4.7%), highest in Asia (0.54%), followed by Africa (0.33%), and the least in Europe and South America (0.19% in both continents). Canine agenesis was more common in the maxilla (88.57%), followed by both maxilla and mandible (8.57%), and the least common was mandible-only presentation (2.86%). The condition was more common in females (female:male ratio = 1.23), except in Asia (female:male ratio = 0.88) and Africa (female:male ratio = 1). In Asia, unilateral agenesis was almost twice as prevalent as bilateral, but in Europe, the bilateral form was more common. **Conclusions:** The overall prevalence of canine agenesis is 0.30%, with the highest prevalence in Asia, followed by Africa, Europe, and South America. The condition is more common in the maxilla than the mandible, and in females than males (except in Asia and Africa), with unilateral agenesis being more common in Asia and the bilateral form showing a greater prevalence in Europe.
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Key words: Canine agenesis, Prevalence, Continents

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INTRODUCTION

Congenital absence of teeth, hypodontia,[1] is the most prevalent craniofacial malformation and dental anomaly.[2] Its reported prevalence varies across studies, continents, racial groups, dentitions, sexes, and jaws. The prevalence ranges widely among Caucasians (3.9% to 11.3%)[3] and is higher among African populations (13.4%), followed by European (7%), Asian (6.3%), and Australian (6.3%) populations.[4] Female subjects are more likely to show hypodontia than male.[3-6] The occurrence of this condition can be classified as common, less common, and rare.[3] Canine agenesis refers to failure of canine formation, which are considered to be the most stable teeth; agenesis of maxillary canines is less common, while that of mandibular canines is rarely observed.[7] Nevertheless, the absence of canines complicates orthodontic treatment planning because of their esthetic and functional importance.[8]

Information regarding the global and regional distribution of canine agenesis is of paramount importance since it can elucidate the treatment need, complexity of treatment, and the resources required to manage these cases. Early detection may facilitate interventions to ameliorate the disease process, such as early primary tooth removal to enhance space closure or maintenance of the predecessor to ensure adequate alveolar bone for future replacement.[9] Some degree of multidisciplinary combined management may be required, especially in cases of unilateral agenesis. Furthermore, the assessment of agenesis prevalence by continents can reflect the comparative frequency of missing teeth in different regions of the world. There is a paucity of studies on the prevalence of canine agenesis, with very few studies reporting the prevalence of agenesis exclusively, and most only superficially referring to individual studies without analyzing the combined prevalence, and instead only focused on the prevalence of hypodontia in general.

The aim of the current review was to summarize the available worldwide data on canine agenesis. The primary objective was to systematically evaluate the available evidence related to its prevalence in different general populations and continents. The secondary objectives were to report the prevalence by jaw (maxilla and mandible), sex (male and female), and location (unilateral or bilateral), and to report the associated dental anomalies. Identifying the overall prevalence and pattern can enhance management and better treatment planning of this condition.

MATERIALS AND METHODS

Protocol and registration

This systematic review was conducted and reported in

Table 1. Search engines, keywords, dates of searches, and the data retrieved

Search engines	Keywords	Date	Results	Duplicates	Exclusion by title	Exclusion by abstract	Exclusion by full text	Final
PubMed	'Canine Or Cuspid' AND 'Agenesis OR missing OR hypodontia' AND 'Prevalence Or Incidence Or Association' AND 'Maxillary Or Mandibular' AND 'Population or Hospital' AND 'Dental anomalies'	2.5.19	32	2,490	20	6	0	1
Web of Science	'Canine Or Cuspid' AND 'Agenesis OR missing OR hypodontia' AND 'Prevalence Or Incidence Or Association' AND 'Maxillary Or Mandibular' AND 'Population or Hospital' AND {Dental anomalies}	2.5.19	36		20	4	1	2
Scopus	Same as above	2.5.19	496		413	54	1	9
OpenGrey	Same as above	2.5.19	6,115		2,695	1,001	1	1
Science Direct	'canine' AND 'agenesis' AND 'prevalence' AND 'maxillary or mandibular' AND 'population' AND 'dental anomalies'	2.5.19	23		9	6		3
Hand-searched articles			68		0	0		33
Total			6,770	2,490	4,280	1,123	52	49

The process of exclusion that led to the final list of included studies is presented.

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accordance with the Cochrane Handbook for Systematic Reviews of Interventions and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[10] The review protocol was registered in the National Institute of Health Research database (https://www.crd.york.ac.uk/prospero/; protocol no: CRD42019120204; registration Date: March 14, 2019). Ethical approval was unnecessary since we retrieved data from previously published studies in which informed consent had been obtained by the primary investigators.

Eligibility criteria

Inclusion criteria

1. Participants: Male and female subjects with no age restriction; sample size of 50 participants or more
2. Outcome measures
   a. Primary outcome: Overall prevalence of canine agenesis
   b. Secondary outcomes: Prevalence of canine agenesis in the maxilla and mandible, female:male ratio, ratio of unilateral to bilateral cases, dental

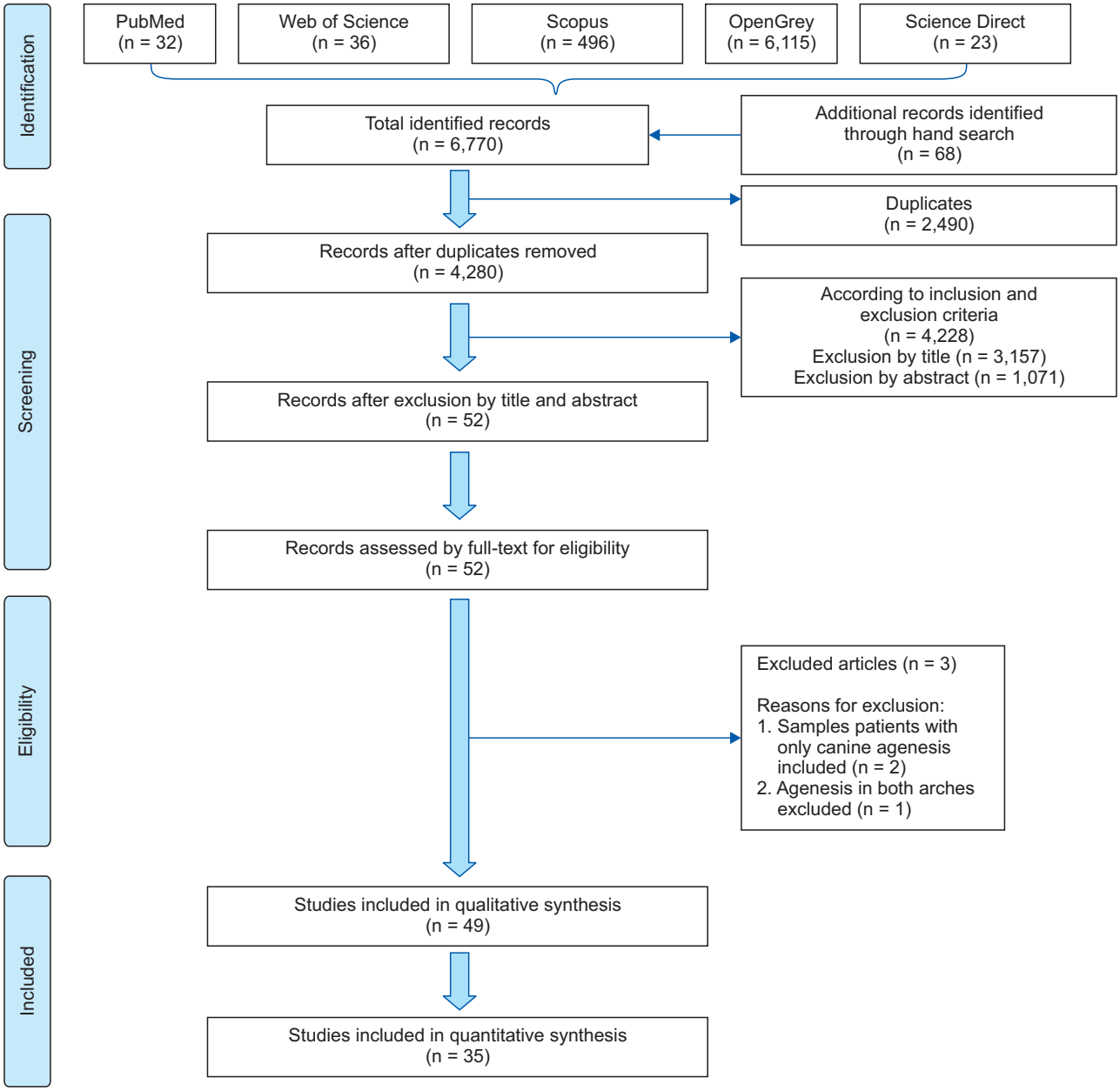

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart of the study selection process.

anomalies associated with canine agenesis
3. Study design: Observational studies (population-based studies, hospital/clinic-based studies, and cross-sectional studies), studies supported by radiographic imaging of the teeth or relevant history and records
4. Published English studies with no publication-year restriction

Exclusion criteria

1. Studies on syndromic patients (e.g., patients with a cleft involving the alveolus or those with Down's syndrome)
2. Case reports, case series, systematic reviews, or meta-analyses
3. Studies that reported canine agenesis in specific samples of patients with teeth agenesis that cannot be generalized to the general population, e.g., canine agenesis in hypodontia patients with no relevance to the general population.

Information sources, search strategy, and study selection

Comprehensive electronic database searches without publication-year restrictions were conducted for literature published until May 4, 2019 (Table 1 and Figure 1). Only articles in English were included from relevant databases such as PubMed, Web of Science, Scopus, OpenGrey, and Science Direct. In addition, hand searches of relevant journals, such as those listed in relevant systematic reviews, was performed. Articles and reference lists of the included studies were individually screened for additional relevant studies. The corresponding authors were contacted for obtaining clarifications or additional information when necessary.

The search strategy was implemented using a combination of Medical Subject Headings (MeSH) and free-text words for PubMed and optimized for each database (Table 1). Literature search, study inclusion, methodology quality assessment, and data extraction were carried out independently and in duplicate by two pairs of reviewers (S.S. & M.C.W. and S.A.M. & J.J.) who were not blinded to the authors, and the results were revised by the fifth author (M.M.S.F.).

Eligible articles were assessed in two phases. In the first phase, only titles and abstracts were screened. Full-text assessment was then conducted in the second phase to determine final eligibility. Articles were excluded when they did not meet one or more of the inclusion criteria. Any disagreements were resolved by discussion and consultation with the fifth author (M.M.S.F.) for consensus.

Data items

A standardized data extraction sheet was designed for data extraction by the two pairs of independent reviewers in duplicate (S.S. & M.C.W. and S.A.M. & J.J.). Data extraction included general information (the names of the authors, the year of publication, and the study setting), data pertaining to methods (study design), participant data (sample size, age, sex, country, region, race, and population) and outcome data (primary and secondary outcomes mentioned). Race referred to a group of people who shared similar physical characteristics.

Risk of bias across studies

Critical appraisal of the study was performed using a modified version of Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist[11]

Table 2. Population prevalence of canine agenesis among the assessed individuals

No.	Study	Number of individuals with canine agenesis	Study size (n)	Prevalence of agenesis by individual (%)
1	Mani et al.[17] (2014)	5	834	0.60
2	Alsoleihat and Khraisat[35] (2014)	4	85	4.71
3	Patil et al.[19] (2013)	18	4,133	0.44
4	Afify and Zawawi[47] (2012)	5	878	0.57
5	Rózsa et al.[16] (2009)	13	4,417	0.29
6	Kazanci et al.[20] (2011)	1	3,165	0.03
7	Bäckman and Wahlin[36] (2001)	0	739	0.00
8	Locht[41] (1980)	1	704	0.14
9	Bernadette et al.[34] (2013)	2	947	0.21
10	Gomes et al.[15] (2010)	2	1,049	0.19
11	Ng'ang'a and Ng'ang'a[25] (2001)	2	615	0.33
Total		53	17,566	0.30

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consisting of seven items related to (1) study design, (2) study setting, (3) participant criteria, (4) sample size, (5) variable description, (6) outcome measurements, and (7) statistical analysis. The quality of the studies was categorized as weak (3 and less), moderate (4 or 5), or high (6 or more) by two pairs of independent reviewers in duplicate (S.S. & M.C.W. and S.A.M. & J.J.). Any disagreements were resolved by discussion and consultation with the fifth author for consensus (M.M.S.F.).

Summary measures and synthesis of results

Relevant prevalences from every study were recalculated and summed to be reported as overall percentages across all studies (Tables 2 and 3) and in terms of agenesis in the maxilla and mandible, female:male ratio, and unilateral and bilateral agenesis.

Additional analyses

No subgroup analysis was performed.

Table 3. Prevalence of canine agenesis based on the total number of missing teeth

No.	Study	Number of cases of canine agenesis	Number of cases of tooth agenesis	Prevalence of agenesis by number of teeth (%)
1	Mani et al.[17] (2014)	8	508	1.57
2	Alsoleihat and Khraisat[35] (2014)	4	14	28.57
3	Endo et al.[5] (2006)	56	696	8.05
4	Abu-Hussein et al.[24] (2015)	3	167	1.80
5	Nik-Hussein[48] (1989)	2	81	2.47
6	Sisman et al.[26] (2007)	9	182	4.95
7	Sheikhi et al.[29] (2012)	27	454	5.95
8	Chung et al.[44] (2008)	25	329	7.60
9	Vahid-Dastjerdi et al.[32] (2010)	10	197	5.08
10	Zhang et al.[45] (2015)	106	941	11.26
11	Al-Abdallah[46] (2015)	21	584	3.60
12	Kazanci et al.[20] (2011)	2	153	1.31
13	Aktan et al.[21] (2010)	87	3,147	2.76
14	Bäckman and Wahlin[36] (2001)	0	89	0.00
15	Magnússon[38] (1977)	3	167	1.80
16	Nordgarden et al.[40] (2002)	14	834	1.68
17	Locht[41] (1980)	1	93	1.08
18	Rølling and Poulsen[43] (2009)	17	1,070	1.59
19	Behr et al.[30] (2011)	42	693	6.06
20	González-Allo et al.[31] (2012)	3	298	1.01
21	Topkara and Sari[33] (2011)	9	375	2.40
22	Bernadette et al.[34] (2013)	2	136	1.47
23	Gomes et al.[15] (2010)	2	108	1.85
24	Souza-Silva et al.[18] (2018)	9	114	7.90
25	Küchler et al.[22] (2008)	4	99	4.04
26	Calvano Küchler et al.[27] (2008)	3	78	3.85
27	Tavajohi-Kermani et al.[23] (2002)	2	226	0.88
28	Muller et al.[39] (1970)	18	940	1.91
29	Lai and Seow[28] (1989)	26	314	8.28
30	Lynham[37] (1990)	3	92	3.26
31	Ng'ang'a and Ng'ang'a[25] (2001)	3	79	3.80
Total		397	13,258	2.99

Table 4. Quality analysis of the 49 studies based on a modified STROBE checklist

No.	Author	Study design	Setting	Participant criteria	Sample size	Variable description	Outcome measurement	Statistical test	Total score
1	Gomes et al.[15] (2010)	√	√	√	√	√	√	√	7
2	Rózsa et al.[16] (2009)	√	√	√	√	√	√	√	7
3	Finkelstein et al.[6] (2018)	X	√	√	√	√	√	X	5
4	Mani et al.[17] (2014)	√	√	√	√	√	√	√	7
5	Alsoleihat and Khraisat[35] (2014)	X	√	√	√	√	√	√	6
6	Souza-Silva et al.[18] (2018)	√	√	√	√	√	√	√	7
7	Patil et al.[19] (2013)	√	√	√	√	√	√	X	6
8	Kazanci et al.[20] (2011)	√	√	√	√	√	√	√	7
9	Aktan et al.[21] (2010)	√	√	√	√	√	√	√	7
10	Edward et al. (2008)	X	√	√	√	√	√	X	5
11	Küchler et al.[22] (2008)	X	√	√	√	√	√	√	6
12	Tavajohi-Kermani et al.[23] (2002)	√	√	√	√	√	√	√	7
13	Shafi et al. (2008)	√	√	X	√	√	√	X	5
14	Endo et al.[5] (2006)	√	√	√	√	√	√	√	7
15	Aasheim and Ogaard (1993)	X	√	X	√	√	√	√	5
16	Abu-Hussein et al.[24] (2015)	√	√	√	√	√	√	√	7
17	Afify and Zawawi[47] (2012)	√	√	√	√	√	√	√	7
18	Altug-Atac and Erdem (2007)	X	√	X	√	√	√	X	4
19	Bäckman and Wahlin[36] (2001)	√	√	√	√	√	√	√	7
20	Bergstnou (1977)	X	√	√	√	√	√	X	5
21	Davis (1987)	X	√	√	√	√	X	X	4
22	Fekonja (2005)	X	√	√	√	√	√	X	5
23	Fukuta et al. (2004)	X	√	X	√	√	√	X	4
24	Nik-Hussein[48] (1989)	X	√	√	√	√	√	√	6
25	Ng'ang'a and Ng'ang'a[25] (2001)	√	√	√	√	√	√	√	7
26	Sisman et al.[26] (2007)	X	√	√	√	√	√	√	6
27	Calvano Küchler et al.[27] (2008)	X	√	√	√	√	√	√	6
28	Lai and Seow[28] (1989)	X	√	√	√	√	√	√	6
29	Lynham[37] (1990)	X	√	√	√	√	√	√	6
30	Magnússon[38] (1977)	X	√	√	√	√	√	√	6
31	Muller et al.[39] (1970)	X	√	√	√	√	√	√	6
32	Nordgarden et al.[40] (2002)	X	√	√	√	√	√	√	6
33	Locht[41] (1980)	X	√	√	√	√	√	√	6
34	da Cunha Coelho et al. (2012)	X	√	√	√	X	√	√	5
35	Gokkaya et al.[42] (2016)	√	√	√	√	√	X	√	6
36	Sheikhi et al.[29] (2012)	√	√	√	√	√	√	√	7
37	Rølling and Poulsen[43] (2009)	X	√	√	√	√	√	√	6
38	Rose (1966)	X	X	√	√	√	√	X	4
39	Behr et al.[30] (2011)	√	√	√	√	√	√	√	7
40	Chung et al.[44] (2008)	X	√	√	√	√	√	√	6

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Table 4. Continued

No.	Author	Study design	Setting	Participant criteria	Sample size	Variable description	Outcome measurement	Statistical test	Total score
41	González-Allo et al.[31] (2012)	√	√	√	√	√	√	√	7
42	Vahid-Dastjerdi et al.[32] (2010)	√	√	√	√	√	√	√	7
43	Zhang et al.[45] (2015)	X	√	√	√	√	√	√	6
44	Topkara and Sari[33] (2011)	√	√	√	√	√	√	√	7
45	Shetty et al. (2012)	√	√	X	√	X	√	√	5
46	Bernadette et al.[34] (2013)	√	√	√	√	√	√	√	7
47	Al-Abdallah[46] (2015)	√	√	√	√	√	√	√	7
48	Raju et al. (2011)	X	√	√	√	X	√	√	5
49	O'Dowling and McNamara (1990)	X	√	√	√	√	√	X	5

STROBE, Strengthening the Reporting of Observational Studies in Epidemiology.

RESULTS

Study selection

Initial database and hand searches yielded a total of 6,770 studies, of which 2,490 duplicates were excluded (Figure 1). Subsequent exclusion by title (3,157) and abstract (1,071) yielded 52 remaining articles, which were considered for this review. This included 18 articles identified from database searches and 34 articles identified with hand searches.

Study characteristics

Full texts of all 52 articles were assessed for eligibility. Two studies[12,13] were excluded since they did not report actual prevalence data or data that can be used to calculate the prevalence for their populations, and another study excluded samples with canine agenesis in both arches,[14] which affected the accuracy of the overall prevalence estimation.

Risk of bias within studies

Critical appraisal of the remaining 49 articles was performed using the modified STROBE checklist (Table 4). After excluding 14 studies (28.6%) that were of moderate quality (modified STROBE score of 4 or 5), 35 (71.4%) high-quality studies[5,15-48] (modified STROBE score of 6 or 7) were included in this systematic review.

Results of individual studies

Description of the studies

A total of 35 studies were included in this review. The demographic data are summarized in Table 5. Slightly less than two-thirds[15-34] (57.1%) of the selected studies were retrospective, about a third[35-46] (34.3%) were cross-sectional, while two studies[29,47] were both retrospective and cross-sectional. Almost half (48.6%)[17-21,24,29-35,42,45-47] of the studies were published after the year 2010. The sample size varied from 85 to 100,577, with a median of 1,622 participants. The study participants, aged 5–46 years, were recruited equally from orthodontic (36.1%) and dental clinics (36.1%), followed by the pediatric clinic (13.9%). One study[45] recruited patients from both orthodontic and pediatric clinics, another[44] recruited them from dental and orthodontic clinics, while another[37] recruited participants from the Australian defense force. Only two studies[39,43] were epidemiological surveys. Almost an equal number of studies were from Asia (n = 14, 40.0%) and Europe (n = 12, 34.3%), followed by South America (n = 4, 11.4%), North America (n = 2, 5.7%), Australia (n = 2, 5.7%), and Africa (n = 1, 2.9%). The global reported population prevalence of canine agenesis ranged from 0.0% to 4.7% (Table 6), with high variations among studies, and the median prevalence was 0.29%. The term population refers to the people living in a particular country. The prevalence of canine agenesis in the maxilla (between 0.03% and 4.7%) was higher than that in the mandible (between 0% and 1.12%).

Synthesis of results

Primary outcomes

Due to the high variation, the overall prevalence was calculated from studies that reported canine agenesis data either by individual (population prevalence based on the number of assessed individuals) or by the number of missing teeth (prevalence of canine agenesis based on the number of missing teeth). The overall prevalence of canine agenesis based on the total number of missing teeth (2.99%) (Table 3) was higher than the population prevalence based on the number of assessed individuals

Table 5. Demographic characteristics of the high-quality studies

No.	Author	Year of study	Study design	Study settings	Sample size	Age (yr)	Sex (M:F)	Country	Region	Race	Population
1	Endo et al.[5] (2006)	NA	Retrospective study	Pediatric and orthodontic clinics of Nippon Dental University	3,358	5–15	1:1.3	Japan	Niigata	Japanese	Orthodontic patients
2	Gomes et al.[15] (2010)	1998–2000	Retrospective study	Orthodontic patient at the Federal District Brazil (16 orthodontic clinics)	1,049	10–15	1:1.07	Brazil	Brasília	NA	Orthodontic patients
3	Rózsa et al.[16] (2009)	NA	Retrospective study	Department of Pediatric Dentistry and Orthodontics, University Budapest	4,417	6–18	1:1	Hungary	Budapest	Hungarian	Orthodontic and pediatric patients
4	Mani et al.[17] (2014)	2004–2010	Retrospective study	Radiology department of the dental clinic of the University Sains Malaysia	834	12–16	1:1.32	Malaysia	Kelantan	Malay	Dental patients
5	Souza-Silva et al.[18] (2018)	2014–2016	Retrospective study	Radiographic centre	3,400	8–30	1:1.17	Brazil	Northeast region	NA	Orthodontic patients
6	Patil et al.[19] (2013)	2008–2012	Retrospective study	Department of Oral Medicine and Radiology, Jodhpur Dental College General Hospital	4,133	13–38	1:0.93	India	Jodhpur	Indian	Dental patients
7	Kazanci et al.[20] (2011)	1996–2008	Retrospective study	Department of Orthodontics, Faculty of Dentistry, Ataturk University	3,165	9–25	1:1.58	Turkey	NA	Turkish	Orthodontic patients
8	Aktan et al.[21] (2010)	NA	Retrospective study	Eight clinics	100,577	5–37	1:2.37	Turkey	6 regions - Samsun, Gaziantep, Kayseri, Tokat, Konya, Bolu	Turkish	Dental patients

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Table 5. Continued

No.	Author	Year of study	Study design	Study settings	Sample size	Age (yr)	Sex (M:F)	Country	Region	Race	Population
9	Küchler et al.[22] (2008)	1999–2007	Retrospective study	Federal University of Rio de Janeiro's Continuing Education Clinical Program in Pediatric Dentistry	1,167	6–12	1:1.24	Brazil	Northern Rio de Janeiro	NA	Pediatric patients
10	Tavajohi-Kermani et al.[23] (2002)	NA	Retrospective study	Department of Orthodontics, University of Tennessee, and orthodontic practices in Memphis	1,016	8–18	1:2.3	USA	Pittsburgh	NA	Orthodontic patients
11	Abu-Hussein et al.[24] (2015)	2006–2013	Retrospective study	Hypodontia patients to Center for Dentistry, Research & Aesthetics	2,200	10.2–39.5	1:1.6	Israel	Jatt, Almothalat	Arab	Orthodontic patients
12	Ng'ang'a and Ng'ang'a[25] (2001)	2001	Retrospective case study	Private orthodontic practice	615	8–15	1:0.86	Kenya	Nairobi 30% from other parts of the country	Kenyans of African descent	Orthodontic patients
13	Sisman et al.[26] (2007)	2007	Retrospective study	Orthodontic patient files Department of Orthodontics of Erciyes University, Kayseri and Kırıkkale University	2,413	9–36	1:1.82	Turkey	Kirikkale	NA	Orthodontic patients
14	Calvano Küchler et al.[27] (2008)	2008	Retrospective study	Those attending the Federal University of Rio De Janeiro's continuing Education Clinical program in Pediatric Dentistry	975 patients	6–12	1:1.01	Brazil	Rio de Janeiro	NA	Pediatric patients

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Table 5. Continued

No.	Author	Year of study	Study design	Study settings	Sample size	Age (yr)	Sex (M:F)	Country	Region	Race	Population
15	Lai and Seow[28] (1989)	1989	Retrospective study	Current patient records kept at the Pediatric Dentistry Unit of the Dental School, University of Queensland	1,032 patients obtained after screening	6–19	1:0.95	Australia	Queensland, dental school	Caucasian	Pediatric patients
16	Sheikhi et al.[29] (2012)	2012	Retrospective and cross-sectional	Faculty of dentistry and dental clinics	2,422	7–35	1:1.74	Iran	8 provinces	Iranians	Dental patients
17	Behr et al.[30] (2011)	1994–2006	Retrospective study	Regensburg University Medical Centre	1,442 1,353 final	5–44	1:1.13	Germany	Eastern Bavaria	Caucasian	Orthodontic patients
18	González-Allo et al.[31] (2012)	2005–2009	Retrospective study	Clinical files from dental clinic	2,888 panoramic radiographs	7–21	1:1.06	Portugal	NA	Portuguese	Dental patients
19	Vahid-Dastjerdi et al.[32] (2010)	2010	Retrospective study	Records of Iranian orthodontic patients treated at two schools	1,751	9–27	1:0.99	Iran	Tehran	Iranians	Orthodontic patients
20	Topkara and Sari[33] (2011)	2011	Retrospective study	Department of Orthodontics of the Faculty of Dentistry of the Selcuk University	2,761 patients	9–46	1:1.55	Turkey	Konya	Caucasian patients	Orthodontic patients
21	Bernadette et al.[34] (2013)	2004–2012	Retrospective study	Patient's dental records from belonging to a Pediatric dental office	947	9–34	1:1.54	Romania	Tîrgu Mureş	NA	Pediatric patients
22	Alsoleihat and Khraisat[35] (2014)	2011	Cross-sectional	Un-admixed Druze school children (schoolchildren of two schools)	85	14–18	1:0.89	Jordan (East Jordan)	Al-Azraq	Druze practising consanguin eous marriages and endogamy	School children
23	Bäckman and Wahlin[36] (2001)	1976	Cross-sectional	Department of Odontology/ Pedodontics, UmeaÊ University	739	7	1:1	Sweden	Umeå, northern Sweden	Swedish	Dental patients
24	Lynham[37] (1990)	1990	Cross-sectional	Australian defense force recruits	662 obtained after screening	16–26	1:0.24	Australia	NA	NA	Australian defense force

Table 5. Continued

No.	Author	Year of study	Study design	Study settings	Sample size	Age (yr)	Sex (M:F)	Country	Region	Race	Population
25	Magnússon[38] (1977)	1977	Cross-sectional	School children	1,116 final sample	8–16	1:1.14	Iceland	Reykjavik	NA	School children
26	Muller et al.[39] (1970)	1970	Cross-sectional	Children part of a large survey	14,940 1. White – 13,459 2. African American – 1,481	11–15	Overall 1:1.01 White 1:1.01 African American 1:0.91	USA	Illinois	White and African American	Epidemiological study
27	Nordgarden et al.[40] (2002)	2002	Cross-sectional	97 public clinics	9,532	18	1:0.95	Norway	Oslo and Akershus counties	Norwegians	Dental patients
28	Locht[41] (1980)	1980	Cross-sectional	One school district	704	9–10	1:0.88	Denmark	Arhus municipality	Danish	Dental patients
29	Gokkaya and Kargul[42] (2016)	2016	Cross-sectional	Department of Pediatric Dentistry, Dental School of Marmara University	1,658	7–12	1:1.11	Turkey	Istanbul	Turkish	Dental patients
30	Rølling and Poulsen[43] (2009)	2009	Cross-sectional	One district, all children examined as part of a systematic oral health care	8,138	9–12	1:1	Denmark	Arhus municipality	Danish	All children, epidemiological
31	Chung et al.[44] (2008)	2008	Cross-sectional	Department of Orthodontics, Yongdong Severance Dental Hospital, Yonsei University	883		1:1.65	Korea	Seoul	Koreans	Orthodontic patients
32	Zhang et al.[45] (2015)	2008	Cross-sectional	General group enrolled in three university in Hebei province Orthodontic group visiting the Department of Orthodontics, Peking University	6,015 - general 3,481 - orthodontic	10–26	General 1:0.89 Orthodontic 1:1.5	China	Hebei province	Han origin	Dental and orthodontic patients

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Table 5. Continued

No.	Author	Year of study	Study design	Study settings	Sample size	Age (yr)	Sex (M:F)	Country	Region	Race	Population
33	Al-Abdallah[46] (2015)	2011	Cross-sectional	Department of Oral Medicine and Radiology, Institute of Dental Sciences	8,225	12–18	1:1.19	India	Bareilly, UP	North Indian	Dental patients
34	Afify and Zawawi[47] (2012)	2002–2011	Retrospective and cross-sectional study	Faculty of Dentistry, King Abdul Aziz University	878	12–30	1:1.04	Saudi Arabia	Western region	Saudi patients	Dental patients
35	Nik-Hussein[48] (1989)	1989	NA	Patients attending Faculty of Dentistry, University of Malaya	1,583	6–15	1:1.01	Malaysia	Kuala Lumpur	NA	Dental patients

M, male; F, female; NA, not available.

(0.30%) (Table 2). The prevalence in the general population excluding the orthodontic population was higher (0.38%) than that investigated among the orthodontic population (0.10%). The overall population prevalence was the highest in Asia (0.54%), followed by Africa (0.33%),[23] and was the least in Europe and South America (0.19% in both continents). Similarly, the prevalence of agenesis as a percentage of missing teeth was the highest in Asia (7.40%), followed by Oceania (Australia) (7.14%), South America (4.51%), Africa (3.80%), and Europe (2.55%), with the lowest prevalence in North America (1.85%) (Table 6).

Secondary outcomes

Pooled prevalence based on studies that reported the prevalence in the maxilla and mandible using data for individuals revealed the same findings, with the maxilla-only prevalence being the highest (88.57%), followed by the prevalence in both the maxilla and mandible (8.57%), and the mandible-only prevalence being the least (2.86%) (Table 7). Similarly, the overall prevalence by teeth was greater in the maxilla (73.73%) than the mandible (26.27%). By continent, the prevalence in the maxilla was the highest in Asia (0.78%), followed by Africa (0.33%) based on one study,[25] South America (0.19%) based on one study,[14] and the least in Europe (0.13%) based on five studies.[16,20,34,36,41] Meanwhile, the prevalence of agenesis in the mandible only and in both maxilla and mandible was only reported in Europe (0.01% and 0.03%, respectively; Table 7). Among all forms of canine agenesis, the overall prevalence of missing maxillary permanent canines was almost similar (35.60% and 39.63%, respectively). Likewise, in the mandible, the prevalence of missing mandibular permanent canines was almost similar (12.07% and 12.69%, respectively).

By sex, the overall ratio of canine agenesis was higher in females than in males, with a female:male ratio of 1.23. However, this was only true in Europe and South America, wherein females were twice as much affected than males. In Asia, the ratio was higher among males (ratio = 0.88), while the prevalence was the same for both sexes (ratio = 1) in Africa (Table 8). The overall bilateral:unilateral agenesis ratio was 1.13. The worldwide prevalence of unilateral agenesis was almost similar to that of the bilateral form (50.0% and 46.7%, respectively). However, in Asia, the prevalence of unilateral agenesis was almost double that of bilateral agenesis (66.7% and 33.3%, respectively). In Europe, the prevalence of bilateral (58.8%) agenesis was higher than that of unilateral agenesis (35.3%) (Table 9).

Common dental anomalies associated with canine agenesis were retained primary canines,[16,30] agenesis of other permanent teeth,[16,30] agenesis of the third molar,[31,32,45,46] supernumerary teeth,[16] ankylosis,[28] taur-

Table 6. Overall prevalence of canine agenesis in different geographic locations

Studies/continents	Prevalence of canine agenesis (%)	Prevalence of canine agenesis by individual (%)	Prevalence of canine agenesis by number of teeth (%)	Prevalence of canine agenesis in the general population, excluding the orthodontic group (%)	Prevalence of canine agenesis in the orthodontic group (%)
Overall					
Based on studies which reported the outcome of interest		0.30	2.99	0.38	0.10
Asia					
Endo et al.[5] (2006)	NA*	0.54	7.40	-	-
Mani et al.[17] (2014)	0.6				
Patil et al.[19] (2013)	0.44				
Abu-Hussein et al.[24] (2015)	NA*				
Sisman et al.[26] (2007)	NA*				
Sheikhi et al.[29] (2012)	NA*				
Vahid-Dastjerdi et al.[32] (2010)	NA*				
Alsoleihat and Khraisat[35] (2014)	4.7				
Gokkaya and Kargul[42] (2016)	NA				
Chung et al.[44] (2008)	NA*				
Zhang et al.[45] (2015)	NA*				
Al-Abdallah[46] (2015)	NA*				
Afify and Zawawi[47] (2012)	0.57				
Nik-Hussein[48] (1989)	NA*				
Europe					
Rózsa et al.[16] (2009)	0.29	0.19	2.55	-	-
Kazanci et al.[20] (2011)	0.03				
Aktan et al.[21] (2010)	NA*				
Behr et al.[30] (2011)	NA*				
González-Allo et al.[31] (2012)	NA*				
Topkara and Sari[33] (2011)	NA*				
Bernadette et al.[34] (2013)	0.21				
Bäckman and Wahlin[36] (2001)	0				
Magnússon[38] (1977)	0.27				
Nordgarden et al.[40] (2002)	0.10				
Locht[41] (1980)	0.14				
Rølling and Poulsen[43] (2009)	NA*				
South America					
Gomes et al.[15] (2010)	0.19	0.19	4.51	-	-
Souza-Silva et al.[18] (2018)	NA*				
Küchler et al.[22] (2008)	NA				
Calvano Küchler et al.[27] (2008)	NA*				
North America					
Tavajohi-Kermani et al.[23] (2002)	NA*	NA*	1.85	-	-
Muller et al.[39] (1970)	NA*				

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Table 6. Continued

Studies/continents	Prevalence of canine agenesis (%)	Prevalence of canine agenesis by individual (%)	Prevalence of canine agenesis by number of teeth (%)	Prevalence of canine agenesis in the general population, excluding the orthodontic group (%)	Prevalence of canine agenesis in the orthodontic group (%)
Australia					
Lai and Seow[28] (1989)	NA*	NA*	7.14	-	-
Lynham[37] (1990)	NA*				
Africa					
Ng'ang'a and Ng'ang'a[25] (2001)	0.33	0.33	3.80	-	-

NA, not available.
*Study reported the number of cases of canine agenesis, but did not report the number of individuals with canine agenesis.

odontism,[28] enamel hypoplasia and conical incisor,[28] and Class III malocclusion.[31,45]

DISCUSSION

This systematic review attempted to evaluate the global distribution of canine agenesis in isolation.[3,49] We presented the population prevalence of canine agenesis in terms of individuals, which better reflected the actual treatment need, unlike another review[4] that reported the prevalence in terms of the number of missing teeth. Reports based on individual prevalence without considering the population sample can be biased, since the bigger quantity of smaller-sized studies may overwhelm the smaller quantity of bigger-sized studies and distort the final summary. Therefore, we recalculated the prevalence in every included study to generate an overall prevalence.

In this review, an almost equal proportion of the included studies were conducted in Asia (37.1%) and Europe (37.1%); this was in contrast to the review on the overall prevalence of hypodontia, in which most studies were conducted in European countries (43.0%), followed by the Asian region (32.0%).[4] The global distribution in this review ranged from 0.0% to 4.7%, with a pooled overall prevalence of 0.30%, which is much lower than that of hypodontia (6.4%).[4] Polder et al.[3] reported that canines are one of the rarely missing teeth after the first and the second molars.

In this review, the prevalence of canine agenesis was higher in the Asian region than in the African, European, and South American regions. In contrast, the overall prevalence of hypodontia was the highest in Africa (13.4%, 95% confidence interval [CI]: 9.7, 18.0), followed by Europe (7% CI: 6.0, 8.0%) and Asia (6.3% CI: 4.4, 9.1).[4] This suggests that canine agenesis per se is more common in the Asian region than in the European region, possibly due to the racial differences between the two continents.

Our findings showing that canine agenesis was more common in the maxilla than the mandible are in agreement with the general pattern of hypodontia reported in two other systematic reviews addressing hypodontia, both of which reported marked differences between the jaws in relation to the frequency of agenesis of various tooth types.[3,4] Similarly, the greater prevalence in females is in agreement with the findings of these two systematic reviews.[3,4] However, in Asia, the higher prevalence in males may indicate a genetic inheritance of this trait among males. Bilateral agenesis was more prevalent than unilateral agenesis in Europe, similar to the general pattern of hypodontia except for the maxillary lateral incisors.[3] However, in Asia, the prevalence of unilateral agenesis was double that of the bilateral form, indicating a genetic inheritance pattern among Asians. The overall information presented in this review could provide valuable guidance to clinicians for treatment planning and managing patients with canine agenesis.

Since we aimed to report the prevalence based on the number of individuals with missing canines, we could not include studies reporting the number of missing canines instead of the number of individuals with missing canines; this limited our ability to present the data in terms of combined prevalence by number of teeth. Most studies assessed either orthodontic patients,[5,14,17,19,22-25,29,31,32,43] pediatric patients,[21,26,27,33] both orthodontic and pediatric patients,[15] both orthodontic and dental patients,[44] or dental patients.[16,18,20,28,30,35,39-41,45-47] Three studies were epidemiological surveys of school children,[34,37,42] one enrolled defense force recruits,[36] while only one study was a truly epidemiological study on a general population.[38]

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Table 7. Prevalence of canine agenesis by jaw in different geographic locations

Studies/continents	Prevalence in maxilla alone (%)	Prevalence in mandible alone (%)	Prevalence in both maxilla and mandible (%)	Continent prevalence in maxilla alone (%)	Continent prevalence in mandible alone (%)	Prevalence in both maxilla and mandible in the same individuals (%)
Overall						
Based on studies which reported the outcome of interest				88.57	2.86	8.57
Asia						
Endo et al.[5] (2006)	NA*	NA*	NA*	0.78	0.00	0.00
Mani et al.[17] (2014)	0.6	0	0			
Patil et al.[19] (2013)	NA	NA	NA			
Abu-Hussein et al.[24] (2015)	NA*	NA*	NA			
Sisman et al.[26] (2007)	NA	NA*	NA			
Sheikhi et al.[29] (2012)	0.58	0.25	NA			
Vahid-Dastjerdi et al.[32] (2010)	NA*	NA*	NA*			
Alsoleihat and Khraisat[35] (2014)	4.7	0	0			
Gokkaya and Kargul[42] (2016)	NA	0	0			
Chung et al.[44] (2008)	NA*	NA*	NA*			
Zhang et al.[45] (2015)	NA*	NA*	NA*			
Al-Abdallah[46] (2015)	NA*	NA*	NA			
Afify and Zawawi[47] (2012)	0.57	0	NA			
Nik-Hussein[48] (1989)	NA*	0	NA*			
Europe						
Rózsa et al.[16] (2009)	0.20	0.02	0.07	0.13	0.01	0.03
Kazanci et al.[20] (2011)	0.03	0	0			
Aktan et al.[21] (2010)	NA*	NA*	NA			
Behr et al.[30] (2011)	NA*	NA*	NA*			
González-Allo et al.[31] (2012)	NA*	NA*	NA*			
Topkara and Sari[33] (2011)	NA*	NA*	NA*			
Bernadette et al.[34] (2013)	0.21	0.00%	0.00%			
Bäckman and Wahlin[36] (2001)	0%	0	0			
Magnússon[38] (1977)	0.27	0	NA			
Nordgarden et al.[40] (2002)	0.09	0.01	NA			
Locht[41] (1980)	0.14	0	0.14			
Rølling and Poulsen[43] (2009)	NA*	NA*	NA*			
South America						
Gomes et al.[15] (2010)	0.19	0	0	0.19	0	0
Souza- Silva et al.[18] (2018)	NA*	NA*	NA			
Küchler et al.[22] (2008)	NA	NA	NA			
Calvano Küchler et al.[27] (2008)	NA	NA	NA			
North America						
Tavajohi-Kermani et al.[23] (2002)	NA	NA	NA	NA	NA	NA
Muller et al.[39] (1970)	0.06	0.01	NA			

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Table 7. Continued

Studies/continents	Prevalence in maxilla alone (%)	Prevalence in mandible alone (%)	Prevalence in both maxilla and mandible (%)	Continent prevalence in maxilla alone (%)	Continent prevalence in mandible alone (%)	Prevalence in both maxilla and mandible in the same individuals (%)
Australia						
Lai and Seow[28] (1989)	NA*	NA*	NA	NA*	NA*	NA*
Lynham[37] (1990)	NA	NA*	NA			
Africa						
Ng'ang'a and Ng'ang'a[25] (2001)	0.33	0	0	0.33	0	0

NA, not available.
*Study reported the number of cases of canine agenesis, but did not report the number of individuals with canine agenesis.

Table 8. Prevalence of canine agenesis by sex

Continents	Male: female	Overall male: female ratio
Overall		
Based on studies which reported the outcome of interest	1:1.23	
Asia		
Endo et al.[5] (2006)	NA	1:0.88
Mani et al.[17] (2014)	1:0.67	
Patil et al.[19] (2013)	1:0.8	
Abu-Hussein et al.[24] (2015)	NA	
Sisman et al.[26] (2007)	NA	
Sheikhi et al.[29] (2012)	NA	
Vahid-Dastjerdi et al.[32] (2010)	NA	
Alsoleihat and Khraisat[35] (2014)	1:3	
Gokkaya and Kargul[42] (2016)	NA	
Chung et al.[44] (2008)	NA	
Zhang et al.[45] (2015)	NA	
Al-Abdallah[46] (2015)	NA	
Afify and Zawawi[47] (2012)	1:0.67	
Nik-Hussein[48] (1989)	NA	
Europe		
Rózsa et al.[16] (2009)	1:2.25	1:2.25
Kazanci et al.[20] (2011)	NA	
Aktan et al.[21] (2010)	NA	
Behr et al.[30] (2011)	NA	
González-Allo et al.[31] (2012)	NA	
Topkara and Sari[33] (2011)	NA	
Bernadette et al.[34] (2013)	NA	
Bäckman and Wahlin[36] (2001)	0:0	

Table 8. Continued

Continents	Male: female	Overall male: female ratio
Europe		
Magnusson[38] (1977)	NA	
Nordgarden et al.[40] (2002)	NA	
Locht[41] (1980)	NA	
Rølling and Poulsen[43] (2009)	NA	
South America		
Gomes et al.[15] (2010)	0:2	0:2
Souza-Silva et al.[18] (2018)	NA	
Küchler et al.[22] (2008)	NA	
Calvano Küchler et al.[27] (2008)	NA	
North America		
Tavajohi-Kermani et al.[23] (2002)	NA	NA
Muller et al.[39] (1970)	NA	
Australia		
Lai and Seow[28] (1989)	NA	NA
Lynham[37] (1990)	NA	
Africa		
Ng'ang'a and Ng'ang'a[25] (2001)	1:1	1:1

NA, not available.

CONCLUSION

1. The global distribution of canine agenesis ranged from 0.0% to 4.7%, with a pooled overall population prevalence of 0.30%.
2. The population prevalence of canine agenesis was the highest in Asia (0.54%), followed by Africa (0.33%); the least prevalence was observed in Europe and South America (0.19% for both conti-

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Table 9. Prevalence of canine agenesis by location

Continents	Unilateral: bilateral	Prevalence of individuals with unilateral missing canine only (Individuals with unilateral missing canine only, excluding combined unilateral + bilateral in same individual/ all individuals with missing canines) (%)	Prevalence of individuals with bilateral missing canine only (Individual with bilateral missing canine only, excluding combined unilateral + bilateral in same individual/ all individuals with missing canines) (%)	Prevalence of individuals with combined unilateral and bilateral missing canines in the maxilla and mandible (%)
Overall				
Based on studies which reported the outcome of interest	1:1.13	50.0	46.7	3.3
Asia				
Endo et al.[5] (2006)	NA	66.7	33.3	0.0
Mani et al.[17] (2014)	1:1.5			
Patil et al.[19] (2013)	NA			
Abu-Hussein et al.[24] (2015)	NA			
Sisman et al.[26] (2007)	NA			
Sheikhi et al.[29] (2012)	NA			
Vahid-Dastjerdi et al.[32] (2010)	NA			
Alsoleihat and Khraisat[35] (2014)	4:0			
Gokkaya and Kargul[42] (2016)	NA			
Chung et al.[44] (2008)	NA			
Zhang et al.[45] (2015)	NA			
Al-Abdallah[46] (2015)	NA			
Afify and Zawawi[47] (2012)	NA			
Nik-Hussein[48] (1989)	NA			
Europe				
Rózsa et al.[16] (2009)	1:3	35.3	58.8	5.9
Kazanci et al.[20] (2011)	0:1			
Aktan et al.[21] (2010)	NA			
Behr et al.[30] (2011)	NA			
González-Allo et al.[31] (2012)	NA			
Topkara and Sari[33] (2011)	NA			
Bernadette et al.[34] (2013)	2:0			
Bäckman and Wahlin[36] (2001)	0:0			
Magnusson[38] (1977)	N			
Nordgarden et al.[40] (2002)	NA			
Locht[41] (1980)	1:0			
Rølling and Poulsen[43] (2009)	NA			
South America				
Gomes et al.[15] (2010)	2:0	100.0	0.0	0.0
Souza-Silva et al.[18] (2018)	NA			
Küchler et al.[22] (2008)	1:0.5			
Calvano Küchler et al.[27] (2008)	NA			

Table 9. Continued

Continents	Unilateral: bilateral	Prevalence of individuals with unilateral missing canine only (Individuals with unilateral missing canine only, excluding combined unilateral + bilateral in same individual/ all individuals with missing canines) (%)	Prevalence of individuals with bilateral missing canine only (Individual with bilateral missing canine only, excluding combined unilateral + bilateral in same individual/ all individuals with missing canines) (%)	Prevalence of individuals with combined unilateral and bilateral missing canines in the maxilla and mandible (%)
North America				
Tavajohi-Kermani et al.[23] (2002)	NA	NA	NA	NA
Muller et al.[39] (1970)	NA			
Australia				
Lai and Seow[28] (1989)	NA	NA	NA	NA
Lynham[37] (1990)	NA			
Africa				
Ng'ang'a and Ng'ang'a[25] (2001)	1:1	50.0	50.0	0

NA, not available.

nents).

3. The highest prevalence was of the maxilla-only form (88.57%), followed by the presentation in both maxilla and mandible (8.57%), while the mandible-only form showed the lowest prevalence (2.86%).
4. Canine agenesis was more common in females, with an overall female:male ratio of 1.23, except in Asia (0.88) and Africa (1).
5. In Asia, the prevalence of unilateral agenesis was almost double that of bilateral agenesis, but in Europe, bilateral agenesis was more common.

With a clearer picture of the occurrence of canine agenesis and its accompanying predilection, management of the condition can be better predicted and planned. Future research on prevalence is suggested to report both in terms of missing teeth and individuals, also moving forward, research linked to its aetiology and genetic-based treatment can be considered.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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