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A comprehensive review of the literature and data analysis on hypo-hyperdontia

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Abstract: The objectives of this study were i) to conduct a comprehensive review of the literature on hypo-hyperdontia, and ii) to categorize the reported cases based on occurrence. An extensive search of the literature covering the period from January 1966 to January 2014 was conducted using the Embase, Google Scholar, Medline, and PubMed databases. The key words used in the search strategy were "concomitant", "agenesis", "hypodontia", "hyperdontia", "supernumerary teeth", "syndromes", and "hypohyperdontia" in various combinations. The retrieved data were analyzed based on gender, occurrence, and occurrence of both hypodontia and hyperdontia. Descriptive statistics were carried out using the chi-squared test. For hypo-hyperdontia overall, seven case studies and 40 cases involving 103 patients were reported. Our comprehensive review revealed that hypo-hyperdontia occurs most commonly in males ($P < 0.05$), and the bimaxillary type (65%) was reported most commonly in comparison with the maxillary, pre-maxillary and mandibular types ($P < 0.001$). Twenty syndromic cases and two case studies on familial occurrence of hypohyperdontia were reported. Almost 57% of cases affected the anterior region, whereas 43% of cases affected the anteroposterior region. The anterior region was most commonly affected by hyperdontia whereas the posterior region was most commonly affected by hypodontia. Hypo-hyperdontia is commonly seen in males, and the most common type is bimaxillary occurrence. G/BBB syndrome is commonly associated with hypo-hyperdontia, being relatively frequent in the anterior region, where mesiodens is frequently seen, and second premolars are the most commonly missing teeth. (J Oral Sci 56, 295-302, 2014)

Keywords: agenesis; hypodontia; hyperdontia; hypohyperdontia; supernumerary teeth; syndromes.

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Introduction

Hypodontia is a condition in which an individual has less than the normal complement of teeth, whereas hyperdontia is characterized by the presence of supernumerary teeth. These two conditions are reported to be opposite extremes in the development of the dentition. The occurrence of hypodontia and hyperdontia in the same individual is a rare mixed numeric variation. However, not many surveys have reported the occurrence of these opposite numeric anomalies of the teeth. If both condi-

tions occur in the same individual, it has been described as "concomitant hypo-hyperdontia" (1). Subsequently, Nathanail (2) coined the term "oligopleiodontia" for this condition. Later, Gibson (3) adopted the term "hypohyperdontia", suggesting that the word "concomitant" could be discarded with the increased familiarity of this term, and since then, the condition has frequently been referred to as "hypo-hyperdontia". There has been no definitive classification for this rare condition. However, Gibson (3) classified hypo-hyperdontia into premaxillary, maxillary, mandibular, and bimaxillary subdivisions. This condition may affect the primary and/or permanent dentition and may involve the maxilla and/or the mandible.

Both environmental and genetic factors have been proposed to explain these anomalies in isolation. Differentiation of neural crest cells and interactions between epithelial and mesenchymal cells during the initiation of odontogenesis, disturbances in migration, and proliferation have been suggested to give rise to this condition (4,5). It is inconclusive whether a specific gene or an enzyme defect plays a significant role. Most recently, Mallineni et al. (6) reported syndromic occurrence of hypo-hyperdontia, although the precise etiology is not clearly understood.

The reported prevalence of hyperdontia in the permanent dentition of Caucasians is between 0.15% and 3.9%, being more common among the mongoloid racial groups, with a frequency higher than 3% (7). In contrast, hypodontia excluding the third molars has a reported prevalence of 1.6% to 9.6% in the general population (8). Only a few surveys have reported both hypodontia and hyperdontia occurring in the same individual. In a comprehensive literature review of hypo-hyperdontia, Anthonappa et al. (5) reported a prevalence of between 0.002% and 3.1%. Recently this condition has been investigated by a few researchers, in the form of case reports and case studies. However, its characteristics have not been reported in detail. The purpose of the present study was i) to conduct a comprehensive review of the literature on hypo-hyperdontia, and ii) to categorize the reported cases based on occurrence.

Materials and Methods

This was a traditional narrative review that aimed to describe the prevalence, etiology, and previously reported cases of hypo-hyperdontia. An extensive search of the literature from January 1966 to January 2014 was conducted using the Embase, Google Scholar, Medline, and PubMed databases. The key words used in the search strategy were "concomitant", "agenesis", "hypodontia", "hyperdontia", "supernumerary teeth", "syndromes", and "hypohyperdontia" in various combinations. The citation lists from the included references were subsequently examined, and a hand search was also performed in an attempt to identify additional reports, letters to the editor, and opinion letters in the relevant journals. The retrieved data were divided into maxillary (only the maxillary arch), mandibular (only the mandibular arch), and bimaxillary (both the maxillary and mandibular arches) subdivisions based on the occurrence of this condition, and also categorized according to age, gender, and associated anomalies. Furthermore, concomitant hypo-hyperdontia was divided into syndromic and non-syndromic conditions and anterior, posterior, and antero-posterior types based on occurrence. Anomalies associated with hypo-hyperdontia were evaluated using the retrieved data. Detailed analysis of the occurrence of hyperdontia and tooth type of hypodontia was conducted to determine the common occurrence of hypodontia and hyperdontia. Descriptive statistics involving the chi-squared test were used to determine the occurrence of this condition and differences between the genders. The level of significance was set at $P < 0.05$.

Results

Overall, seven case studies and 40 case reports of hypo-hyperdontia involving 103 patients had been published in the English literature (Tables 1 and 2) (9-49). Our comprehensive review revealed that hypo-hyperdontia occurs more commonly in males (58%) than in females, with 1.3:1 ratio ($P < 0.05$). The average age of the reported patients was 11.29 years. Based on occurrence, the bimaxillary type (65%) was the most commonly reported (2-6,13,16,17,28-49) followed by the maxillary (21%) type (1,3,9-18) and mandibular (14%) type (3,16,19-27), the results being statistically significant ($P < 0.001$) (Fig. 1). For the maxillary arch type, 42% of cases affected the pre-maxillary region (1,3,10,12,13,16). Our literature search retrieved 20 (19.4%) cases of hypo-hyperdontia that occurred in association with different syndromes, and the rest was non-syndromic (Fig. 2). The syndromes that were reported in association with hypo-hyperdontia included bilateral cleft lip and palate, cleft palate and abnormalities of the cervical vertebrae, Down syndrome, Dubowitz syndrome, Ellis-van Creveld syndrome, fucosidosis, G/BBB syndrome and Marfan syndrome (Table 3). Two case studies on familial occurrence of hypo-hyperdontia included one instance of two siblings with Ellis-van Creveld syndrome (39), while the other case was in two identical twins (44). Almost 57% of cases affected the anterior region and 43% affected the anteroposterior region; posterior hypo-hyperdontia

Table 1 Published cases of maxillary and mandibular hypo-hyperdontia

Authors	Age	Gender	Hypodontia	Hyperodontia
Maxillary hypo-hyperdontia				
Munns (9)	17	F	12, 22	Supplemental 15
Cammilleri (1)	17	F	12, 22	Mesiodens
Brook and Winter (10)		F	12	Mesiodens
Gibson (3)	8	M	12	Mesiodens
	9	M	22	Mesiodens
	11	M	15, 22	Mesiodens
	13	F	15, 25	Mesiodens
	11	F	15	Supplemental 22
	9	M	25	Two supplemental molars in 17 and 26 regions
Moore (11)	11	M	13, 23	Supernumerary tooth between 11 and 12
Segura and Jimenez-Rubero (12)	13	M	22	Mesiodens
Oliveria et al. (13)	8	M	Gemination	2 Mesiodens
El-Bahannasawy and Fung (14)	5	F	53	Supplemental 54, 15
da Silva et al. (15)	9.8	-	15, 22	Three supernumerary teeth 24 region
Varela et al. (16)	-	M	22	Mesiodens
	-	F	22	62
	-	F	22	52,12
Zadurska et al. (17)	8	M	15, 25	2 Mesiodens
	10	M	15	22
	11	F	15, 25	12
Nirmala et al. (18)	9	F	13, 23	Mesiodens
Mandibular hypo-hyperdontia				
Low (19)	7	M	31, 41	Mesiodens
Gibson (3)	8	F	31, 41	Mesiodens
	14	F	42	Four denticles in 45, 46 region
Das et al. (20)	8	F	31, 41	Mesiodens
Varela et al. (16)	-	F	35	Supernumerary tooth 42
	-	M	35, 45	32
Raghavan (21)	9	F	31, 41	Mesiodens
Nayak et al. (22)	8	M	31, 41	Mesiodens
Nuvvula et al. (23)	15	F	31, 41	Mesiodens
Venkataaraghavan et al. (24)	9	F	31, 41	Mesiodens
Verma et al. (25)	15.5	M	31, 41	Mesiodens
Marya et al. (26)	20	M	31, 41	Mesiodens
Nirmala et al. (27)	8	M	31	Mesiodens
	9	M	31	Mesiodens
	10	M	31	Mesiodens

Table 2 Reported cases of bimaxillary occurrence of hypo-hyperdontia

Authors	Age	Gender	Hypodontia	Hyperodontia
Glenn (28)	9.6	-	15	Supplemental 43
Nathanail (2)	11	F	35, 45	Maxillary mesiodens
Mercer (29)	20	M	15, 35, 45	Maxillary mesiodens
Spyropoulos et al. (30)	16	F	15, 14, 12, 22, 24, 25, 35, 37, 44, 45	Mandibular incisor
	15	M	13, 45	Maxillary mesiodens
	13	M	31	Supplemental 22
Gibson (3)	8	F	45	Supplemental 22
	13	F	15, 25, 35	Maxillary mesiodens
	10	F	45	Maxillary mesiodens
	13	M	35, 45	Maxillary mesiodens
	9	F	15, 25, 35, 45	Supplemental 22
	10	M	22, 23, 25, 35, 31, 41, 45	Maxillary mesiodens
	14	M	48	Maxillary mesiodens
	17	M	38, 48	Maxillary mesiodens

Table 2, continuation

Authors	Age	Gender	Hypodontia	Hyperodontia
	14	M	18, 38, 48	Maxillary mesiodens
	15	M	18, 28, 38, 48	Maxillary mesiodens
	16	F	18, 28, 38, 48	Maxillary mesiodens
	15	F	18, 28, 38, 48	Maxillary mesiodens
Ranta (4)	5	M	53, 63, 74, 34	Supplemental 72, 32
Ranta (31)	6.1	F	16, 15, 25, 26, 35	Supplemental 52, 12
Macpherson (32)	6	F	52, 62	83, 82, and 72 regions
Symons (33)	8	M	31, 41	11 and 13 regions
Trotman and McNamara (34)	9	F	15	Supplemental 11, 21, 31
Hewson et al. (35)	9	M	45	Supplemental maxillary central incisor
Zhu et al. (36)	15	M	12, 22	Apical to 46
Chow and O'Donnell (37)	13	F	15, 45	32 and 42 regions
Scheiner and Sampson (38)	8	F	35, 45	Two maxillary mesiodenes
Hattab et al. (39)	9	M	12, 22, 31, 32, 33, 41, 42, 43	Maxillary mesiodens
	8	F	12, 22, 31, 32, 41, 42	Supernumeray in 11 region
Sharma (40)	12	F	23	15, 14, 12, 21, 22, 24, 25, 32, 34, 35, 42 region
Matsumuto et al. (41)	8	F	25, 32	22 region
Acerbi et al. (42)	12	M	15, 25, 34, 35, 45	Maxillary mesiodens
Oliveira et al. (13)	9	F	35, 45	Maxillary mesiodens
Patchett et al. (43)	9	M	35, 45	Supplemental 11, palatal supernumerary teeth
Anthonappa et al. (5)	12	F	31, 41	Supplemental 23
	9	M	15, 35	Supplemental 21
	11	M	32	Supplemantal 15
	5	M	71, 81, 42	Maxillary mesiodens
	7	M	31, 41	Two supernumerary teeth 11 and 21 region
	5	F	72, 32	Maxillary mesiodens
	6	M	35, 45	Maxillary mesiodens
Sharma (44)	7	M	25	Two maxillary mesiodens
	7	M	35	Maxillary mesiodens
da Silva et al. (15)	34.9	-	12, 22	Mandibular anterior region
	28.7	-	12, 22	Mandibular anterior region
	19.9	-	12, 22, 37, 47	Mandibular anterior region
	17.8	-	12, 11, 21, 22	Mandibular anterior region
	16.4	-	12	Mandibular anterior region
	12.9	-	12, 25	Mandibular anterior region
	19	-	12, 22	Mandibular anterior region
	11.1	-	12	Mandibular anterior region
	13.6	-	12, 22	Mandibular anterior region
Lertsirivorakul (45)	9	F	15, 14, 25, 35, 36, 45, 46, 47	Supplemental 22
Varela et al. (16)	-	M	35, 45	Maxillary mesiodens
	-	M	35	12
Aminabadi et al. (46)	5	F	53, 51, 61, 71, 82, 12, 35, 33, 32, 31, 41, 42, 43, 45	24 region
Manjunatha et al. (47)	26	M	31, 41	Supplemental 22
Mallineni et al. (6)	5	M	82, 42	51, 61 region
Sharma (48)	9	F	35, 45	Supplemental 12
	8	M	32, 42	Maxillary mesiodens
Zadurska et al. (17)	9	M	15, 13, 12, 35, 41, 45	Odontoma
	10	F	35	12
	12	M	35, 45	Maxillary mesiodens
	13	M	12, 22, 36, 46	35, 45
	17	F	15, 14, 24, 25, 35, 45	22
	29	M	13	41
Gupta and Popat (49)	11	M	31, 41	Maxillary mesiodens

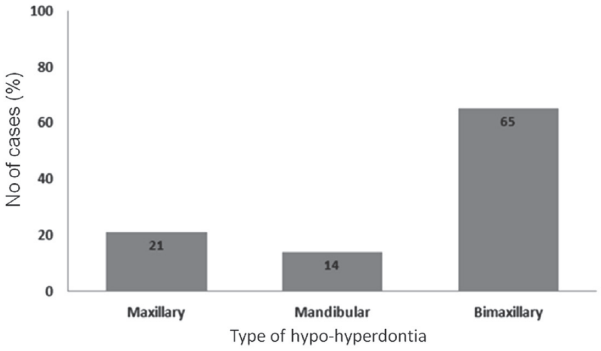

Fig. 1 Comparison of reported cases of different types of hypo-hyperdontia.

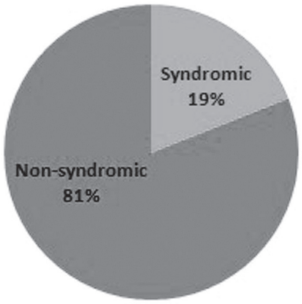

Fig. 2 Occurrence of hypo-hyperdontia based on accompanying syndromes.

Table 3 Syndromes associated with hypo-hyperdontia

Condition	Author	Year
Bilateral cleft lip and palate	Ranta (4)	1983
Dubowitz syndrome	Ranta (31)	1987
Fucosidosis	Macpherson (32)	1991
Cleft palate and abnormalities of cervical vertebra	Trotman and McNamara (34)	1994
Down syndrome	Chow and O'Donnell (37)	1997
Ellis-van Crevald syndrome	Hattab et al. (39)	1998
Down syndrome	Acerbi et al. (42)	2001
G/BBB syndrome	da Silva et al. (15)	2008
Ellis-van Crevald syndrome	Aminabadi et al. (46)	2010
Marfan syndrome	Mallineni et al. (6)	2012

has not been reported. The anterior region is commonly affected by hyperdontia in patients with hypo-hyperdontia, and mesiodens (48%) is frequently associated. Hypodontia sometimes affected the posterior region in patients with hypo-hyperdontia, the second premolar (38%) being commonly missing. Taurodontism (16,27), dens evaginatus (48), and double tooth (12) have been frequently reported anomalies associated with hypo-hyperdontia.

Discussion

Hypo-hyperdontia is an "extremely rare numerical mixed condition in which teeth may be supernumerary or absent, relative to the normal compliment". Although ample literature has exclusively described hypodontia or hyperdontia, only a few surveys have reported the occurrence of hypo-hyperdontia (5,6,23,49). It has been suggested that hypodontia and hyperdontia represent opposite ends of the developmental scale for dentition (31). Hypodontia is commonly seen in female individuals, whereas hyperdontia is frequently reported in males (50). It has been reported that when these two numeric variants occur in the same individual, no differences are evident between the genders (5). Nevertheless, the present comprehensive review revealed that hypo-hyperdontia occurs more commonly in males (58%) than in females, with a 1.3:1 ratio ($P < 0.05$). Gibson classified this condition as bimaxillary, maxillary, premaxillary (right lateral incisor to left lateral incisor) and mandibular. Furthermore, Nirmala and colleagues reported a case in which both maxillary canines were missing, whereas mesiodens was present in the premaxillary region, and considered this presentation to be the pre-maxillary type. However, as it is very difficult to differentiate the maxillary and pre-maxillary types, the hypo-hyperdontia has been divided into three categories: the maxillary type (the maxillary arch alone), mandibular type (the mandibular arch alone) and bimaxillary type (both the maxillary and mandibular arches). Based on occurrence, our comprehensive review revealed that the bimaxillary hypo-hyperdontia type (65%) was reported most commonly, followed by the maxillary (21%) and mandibular (14%) types, and the results were statistically significant ($P < 0.001$). It was also shown that hypo-hyperdontia commonly affects both the maxil-

lary and mandibular arches, rather than either arch alone. Among the maxillary arch type, the pre-maxillary region was affected in 42% of the subjects. Based occurrence in arches hypo-hyperdontia is divided into two types anterior (hypo-hyperdontia involving only anterior region), posterior (hypo-hyperdontia involving only posterior region) and anteroposterior (hypo-hyperdontia invoving both anterior an dposterior region). Our search revealed almost 57% of cases reported in anterior region where 43% of cases reported on anteroposterior occurrence. Thus, it is evident that posterior hypo-hyperdontia alone is extremely rare, and has not been reported.

Our literature search retrieved 20 (19.4%) cases of hypo-hyperdontia occurring with different syndromes (4,6,15,31,32,34,37,39,42,46), and the remaining cases were non-syndromic. Among these 20 reported cases, both the maxillary and mandibular arches were affected in 19 subjects. Syndromes associated with hypo-hyperdontia have included Down syndrome (37,42), Dubowitz syndrome (31), Ellis-van Creveld syndrome (39,46), fucosidosis (32), G/BBB syndrome (15) Marfan syndrome (6), bilateral cleft lip and palate (4), and cleft palate and abnormalities of the cervical vertebrae (34). Fifty percent of cases have been reported in G/BBB syndrome (15), and it is evident that syndromic hypo-hyperdontia is reported very rarely. A rare example of syndromic hypo-hyperdontia in the same arch (maxilla) was reported in a patient with G/BBB syndrome (15). Further case studies and research will be needed to clarify the association of hypo-hyperdontia with various syndromes.

Although, several hypotheses to explain tooth agenesis have been suggested, the concept of a polygenic multi-factorial model for hypodontia has been accepted by several authors. Likewise, several theories, including atavism, dichotomy, hyperactivity of the dental lamina, and the concept of multi-factorial inheritance, have been reported for hyperdontia. However, the precise etiologies of both forms of numerical anomaly have not been documented in detail. Two case studies of familial occurrence of hypo-hyperdontia included one involving two siblings with Ellis-van Creveld syndrome (39) and another involving two identical twins in India (44). This association appears to suggest a genetic influence on this condition.

Supernumerary teeth have been reported in both the primary and permanent dentition, and in the entire tooth-bearing areas of the dental arches (50,51). There appears to be a greater predilection for certain areas, over 90% of such cases affecting the pre-maxillary region, followed by the mandibular premolar region. Similarly, the present review revealed that maxillary mesiodens is a frequent type of hyperdontia associated with hypo-hyperdontia. The anterior region is commonly affected by hyperdontia in subjects with hypo-hyperdontia, and mesiodens (48%) is the frequently associated with supernumerary teeth (37%) in the anterior and posterior regions (15%). Maxillary mesiodens (65%) is more commonly associated with hypo-hyperdontia than mandibular mesiodens (35%). Second premolars (38%) are commonly missing in cases of hypo-hyperdontia, followed by lack of lateral incisors (24%). This indicates that hypodontia is very common in the posterior region in cases of hypo-hyperdontia. Nevertheless, hyperdontia frequently affects the anterior region, whereas hypodontia commonly affects the posterior region.

The average age of reported patients was 11.29 years, and most cases were observed during the mixed dentition period. A high proportion of such cases may go undiagnosed if there are no associated symptoms. Visits of patients to a dentist for reasons such as delayed eruption, an erupted supernumerary tooth, missing teeth, unerupted teeth and referrals for the management of extra teeth would provide an opportunity for further clinical and radiographic investigations to establish whether hypo-hyperdontia is present (5,6,23). Panoramic radiographs are essential for indentifying hypodontia and/or hyperdontia, as they visualize the entire dentition.

The present comprehensive review revealed that taurodontism (16,27), deninvaginatus (48) and double teeth (12) are anomalies frequently associated with hypo-hyperdontia. The management of this condition is challenging and warrants a multidisciplinary approach, because no standard treatment protocols have been documented in the literature. Most erupted supernumerary teeth of abnormal size and shape are removed for esthetic reasons. Supplementary teeth may be extracted and also preserved if necessary if hypodontia is evident at the same site or in the adjacent region. Early diagnosis is essential for proper management, allowing the clinician to implement the most appropriative treatment to minimize future complications. Supernumerary or missing teeth/tooth can be identified by counting, and assessment of the complete dentition with panoramic radiographs is essential for recognizing both of these numerical anomalies.

Hypo-hyperdontia is an extremely rare numerical mixed condition that exhibits both extra teeth and missing teeth relative to the normal compliment. Both clinical and radiographic examinations play a vital role in indentifying hypo-hyperdontia. Hypo-hyperdontia is most frequently reported in males, and the most common type is bimaxillary hypo-hyperdontia. G/BBB syndrome

is commonly associated with this condition. In patients with hypo-hyperdontia, hyperdontia is common in the anterior region whereas hypodontia is frequently evident in the posterior region. Posterior hypo-hyperdontia and primary hypo-hyperdontia are very rare.

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