A Review of Hypodontia: Classification, Prevalence, Etiology, Associated Anomalies, Clinical Implications and Treatment Options

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ABSTRACT
A retrospective review of literature was carried out to determine the classification, prevalence, etiology, associated anomalies, clinical implications and treatment options for hypodontia. Many methods of classification have been reported in the literature. Some researchers have classified hypodontia as isolated family form or as an inherited form; others have defined the congenital absence of teeth according to the number of missing teeth and yet classified hypodontia according to the severity of the condition. The prevalence of hypodontia in the primary dentition is found to be very low whereas the occurrence of tooth agenesis varies in the permanent dentition based on ethnic and sex differences. The tooth most commonly found to be missing is the third molar. With regard to the remaining 28 teeth, meta-analysis has revealed that the teeth most commonly affected are the mandibular second premolars, maxillary lateral incisors, maxillary second premolars and the mandibular incisors. From the literature it is evident that the etiology of hypodontia is varied and that genetic, epigenetic and environmental factors may be contributory factors. Tooth anomalies reported in the literature to be associated with hypodontia, include microdontia, canine impaction, taurodontism, transposition and rotation of teeth, and hypoplastic alveolar bone. Researchers have suggested that clinical management of hypodontia requires careful multidisciplinary planning and has financial implications. The suggested members of the team should include general dental practitioners, dental nurses, orthodontists, pediatric dentists, prosthodontists, oral and maxillofacial surgeons, specialist laboratory technicians, clinical psychologists, clinical geneticists, dermatologists, speech and language therapists.

Keywords: Hypodontia, Classification, Etiology, Associated anomalies, Management.

INTRODUCTION
Hypodontia is generally defined as the developmental absence of one or more teeth, excluding the third molars, either in primary or permanent dentition. Researchers have used a variety of terminology to describe the condition, such as a reduction in teeth number, teeth aplasia, congenitally missing teeth, absence of teeth, agenesis of teeth and lack of teeth.1-11 The missing teeth are those which have failed to erupt clinically in the oral cavity and even in radiographs there is no sign of the teeth starting to appear; the cause is usually disturbance during the early stages of tooth development.3,12 Hypodontia is one of the most common human dental developmental anomalies.2,3,7,8,12-15

CLASSIFICATION
Many methods of classification have been reported in the literature.2,5,7,8,12-14,16-23 Some researchers have found the congenital absence of teeth to occur either as an isolated family form or as an inherited form. The inherited form could be either autosomal-dominant, autosomal-recessive or an X-linked trait.20 Others have defined the congenital absence of teeth according to the number of missing teeth.8,14,17,21,23-25 Hypodontia refers to the condition where there is an absence of fewer than six teeth. The term oligodontia is usually used to describe a larger number of missing teeth (six or more). Anodontia is the complete absence of teeth.

Dhanrajani5 classified hypodontia according to the severity of the condition following the method of previous researchers.13,26 He used ‘mild to moderate hypodontia’ to denote agenesis of two to five teeth, and referred to the absence of six or more teeth, excluding the third molars, as ‘severe hypodontia’. ‘Oligodontia’ is the absence of multiple teeth, usually associated with systemic disorders.5 Many other researchers have used similar methods of classifying the congenital absence of teeth.19,27 In general, they identify three categories of hypodontia, excluding third molars, as follows:

• Mild with 1 or 2 missing teeth
• Moderate with 3-5 missing teeth
• Severe with 6 or more missing teeth

Hypodontia is also classified as either isolated hypodontia or syndromic hypodontia. Isolated hypodontia refers to those cases without syndrome.28,29 Thus, hypodontia can occur either as part of a syndrome or as a nonsyndromic, familial form; in the latter it occurs as an isolated trait, affects variable numbers of teeth and appears either sporadically or as an inherited condition within a family pedigree.23,29
PREVALENCE

Primary Dentition

The prevalence of hypodontia in the primary dentition is found to be very low. The range has generally been between 0.1 and 0.9% of the population. The chance of having the permanent successors missing is, by contrast, very high. In a study involving a sample of Saudi children, the teeth found to be missing most frequently in the primary dentition were the upper and lower lateral incisor. Larmour et al reviewed many previous studies and found that the prevalence of hypodontia in deciduous dentition was between 0.5% in the Icelandic population and 2.4% in the Japanese population.

Permanent Dentition

The occurrence of tooth agenesis varies in the permanent dentition. Polder et al used meta-analysis and found that the prevalence of missing permanent teeth varies from 2.2 to 10.1%, excluding third molars, which are absent in around 20% of individuals in the recorded population. The highest prevalence was found in Australian Caucasians, with 6.3%, followed by European Caucasians (5.5%) and then North American Caucasians (3.9%). Polder et al also showed the prevalence in African Americans (3.8%), Saudi Arabs (2.5%) and Chinese (6.9%) but they did not include these in their meta-analysis, since according to them the samples used in studies of these populations were too small. Another review has shown that the prevalence of hypodontia apart from the third molars varied between 2.6% in Saudi Arabia and 11.3% in Ireland, while in the United Kingdom it was found to be between 4 and 4.5%. The authors suggest that these variations in prevalence may result from (a) the different age groups in the samples, since in younger groups there might be some teeth which are still to erupt, whereas in older patients teeth might have been extracted, (b) differences in sampling methodology, (c) racial differences and (d) differences in the diagnostic criteria employed. The authors also concluded that higher incidences of tooth agenesis in females were found in women, with a ratio of 1:1.5. Recently, Mattheeuws reviewed 19 papers from a total of 42 studies on the subject and reported that girls tended to have a slightly higher occurrence of missing teeth than boys of the same age. Another review showed that occurrence was higher in females than in males, with a ratio of 3:2. In American white children, it was found that more girls (63%) had hypodontia than boys (37%), while among the Irish population the ratio of girls to boys with hypodontia was 1.3:1.

DISTRIBUTION OF HYPODONTIA TEETH

The tooth most commonly found to be missing is the third molar. Lynham found the third molar to be missing in one-fifth of the Australian population. With regard to the remaining 28 teeth, meta-analysis has revealed that the teeth most commonly affected are the mandibular second premolars (41%), maxillary lateral incisors (23%), maxillary second premolars (21%), and the mandibular incisors (6%). In the Australian population, apart from the third molars, the most commonly affected teeth have been found to be the second premolars and upper lateral incisors. In African Americans, it is the mandibular second premolars which have been found to be missing most frequently, while among the Japanese the most frequently missing tooth was the mandibular second premolar (23.7%), followed by the maxillary second premolar (21.5%), maxillary lateral incisor (17.2%) and mandibular first incisor (14.0%). The same pattern has recently been reported in the Irish population whereas in American white children the most commonly
missing teeth apart from the third molars were the second premolars (50%), lateral incisors (23%) and maxillary second premolars (15%). Davis[46] found that in Asian populations the mandibular lateral incisors were the most affected. By contrast, in all United Kingdom studies the most frequently affected teeth are the mandibular second premolars, while in all Caucasian studies the mandibular second premolars and the maxillary lateral incisors are the teeth most commonly found to be missing. Some researchers have found the maxillary permanent canine to be missing but the instances of this are very rare.32 Hypodontia of the maxillary central incisors, canines or first permanent molars is rare, occurring principally in cases of severe hypodontia.13

The most common congenitally absent teeth in the European population are the third molars, followed by the mandibular second premolars, the maxillary lateral incisors and lastly the maxillary second premolars.47,48 It has been found that 9 to 37% of different populations have the third molars missing.49 It has been proposed that if the third molars were congenitally absent then the probability of having other missing teeth is 13 times greater.36,50 The prevalence of missing mandibular second premolars is around 2.8%, while maxillary lateral incisor agenesis is in the range of 1 to 1.6%.49 There appears to be a degree of symmetry in the absence of all teeth except the maxillary lateral incisors, where the absence of the left lateral was more common than the right.50 In a review article it has been suggested that symmetrical hypodontia is predominant.33 Unilateral missing teeth are more common than bilateral teeth, although not in the upper lateral incisors.22 However, Hashem et al42 found no evidence of symmetry of missing teeth between the right and left sides among the Irish population. Another group of researchers have revealed that congenital absence commonly affects just one tooth of a pair, not both, which means that hypodontia occurs unilaterally. They have also found no suggestion in these data of directional asymmetry.42 However, among the Chinese population a different pattern has been found, the most commonly affected teeth being the lower incisors, followed by the upper second premolars and then the upper lateral incisors.42 All the review studies have shown that mild hypodontia is the most common, affecting 80% of those who have the condition.7,22,32,36

Recently, a study presented a pattern for the missing teeth in nonsyndromic severe hypodontia, using a published method called the ‘tooth agenesis code’ (TAC) procedure.51 The TAC procedure is based on the formula 2ⁿ⁻¹, in which n = tooth number. For example, the tooth value for the first premolar (tooth 4) is 2⁴⁻¹ = 8. The TAC is the sum of the tooth values. If two teeth were missing in the upper right quadrant (e.g. two premolars), the TAC value for that quadrant would be 2³ + 2⁴ = 24. Van Wijk and Tan52 reported that the common patterns in the upper arch are agenesis of the lateral incisors and of both premolars, with a percentage of 13%, and in the lower arch the pattern is agenesis of all mandibular molars, with a percentage of 11.5%.29

**ETIOLOGY**

From the literature it is evident that the etiology of hypodontia is varied and that genetic, epigenetic and environmental factors may be contributory factors.10,11,14,20,26,33,52-55 As with other conditions, the causes of missing teeth can be classified into general and local. The general category includes cases where there is a genetic cause, particularly syndromes such as Down syndrome, cleft lip and palate and ectodermal dysplasia. Local factors that result in hypodontia include early irradiation of tooth germs, hormonal and metabolic influences, trauma, osteomyelitis and unintended removal of a tooth germ during the extraction of a primary tooth.21 Many researchers have suggested models and concepts of tooth agenesis.26,56-61 These models and concepts have been reviewed recently and incorporated into a single model from a clinical perspective.55 This model will be discussed briefly at the end of the following section.

**GENETIC FACTORS**

All previous studies on monzygotic or bzygotic twins claim that dental development, including both the size and the shape of teeth, is governed principally by genetic processes, in which hundreds of genes take part.10,55,62,63 The evidence for genetic control is more significant in the etiology of hypodontia and the occurrence among individuals related to hypodontia patients is higher than in the general population.14,20,28,29,33,47,53,64,65 Many other studies have been done on genetic diseases. These studies have been classified in various ways according to the affected tooth structure (enamel vs dentin), by their specificity (syndromic vs nonsyndromic) and also by their pattern of inheritance: Autosomal dominant, autosomal recessive or X-linked recessive.65 There are numerous reports in the literature on the clinical genetics of tooth agenesis. Shimizu and Maeda have recently reviewed genetic studies which deal with hypodontia in human and mouse models. They report that nonsyndromic or familial hypodontia is more common than the syndromic type and that it might follow autosomal dominant, autosomal recessive or X-linked patterns of inheritance.33
Grahnen, in his family study in Sweden, reported that hypodontia is determined by genetic factors. However, among the subjects of Grahnen’s study, the type of inheritance in the majority of cases of familial hypodontia seems to have been autosomal dominant. Furthermore, some types of hypodontia, such as peg-shaped upper lateral incisors, are claimed to be the result of modifying genes.

Advances in the fields of molecular biology and human genetics have enlarged our understanding of tooth development, by exploring the important role played by homeobox genes in tooth formation and craniofacial development. Many researchers have found a direct relation between tooth formation and some of the regulatory homeobox genes: MAX1, PAX9 and AXIN2. MSX1 (muscle segment homeobox 1) is essential in mediating epithelial-mesenchymal interaction during tooth development and has been found to be associated with familial hypodontia and certain forms of syndromic hypodontia. MSX1 mutations predominantly affect second premolars and third molars. However, some other genetics studies have not found any correlation between MSX1 and premolar hypodontia. PAX9 (paired box gene 9) is also expressed in the prospective mesenchymal compartment of developing teeth. This gene has been identified in association with variable forms of hypodontia that affect the posterior region, particularly molar teeth. The PAX9 gene has also been found to be associated with different forms of oligodontia. AXIN2 (axis inhibition protein-2) mutations are associated with hypodontia and involve a wider range of tooth types.

Although previous studies have provided evidence for the role played by genetic factors in causing hypodontia, there is as yet no clear understanding of the genetics underlying this condition.

ENVIRONMENTAL FACTORS

Although, as discussed above, it appears that tooth agenesis is frequently caused by genetic factors, occasionally hypodontia can be associated with environmental factors. Major environmental factors such as infection of the tooth bud or trauma, or extraction of the preceding primary tooth, have been found to be associated with hypodontia owing to their effect on dental and organ development. Somatic diseases such as syphilis, scarlet fever, rickets or nutritional disturbances during pregnancy or infancy which might affect tooth and other organ development. Also, glandular dysfunction could occur as a result of cranial irradiation in the very early stage of development and this can then lead to dental anomalies.

SYNDROMIC HYPODONTIA

More than 120 syndromes listed in the Online Mendelian Inheritance in Man (OMIM) database are associated with tooth anomalies. The London dysmorphology database reported 150 syndromes as being associated with hypodontia. The absence of many teeth is commonly associated with specific syndromes or systematic abnormalities and is particularly related to ectodermal dysplasia. Nevertheless, hypodontia is a very common dental anomaly in patients with oral and facial clefts, Rieger syndrome, Down syndrome (trisomy 21), Witkop syndrome, van der Woude syndrome, Book syndrome, hemifacial microsomia and many others.

In addition to inherited defects, tooth agenesis could occur as a result of somatic diseases such as syphilis, scarlet fever, rickets or nutritional disturbances during pregnancy or infancy which might affect tooth and other organ development. Also, glandular dysfunction could occur as a result of cranial irradiation in the very early stage of development and this can then lead to dental anomalies.

DENTAL ANOMALIES ASSOCIATED WITH HYPODONTIA

Many dental characteristics have been reported to be associated with hypodontia, including microdontia, canine impaction, taurodontism, transposition and rotation of teeth and hypoplastic alveolar bone. Microdontia (reduction in tooth size) is considered one of the most common dental anomalies. It is common to see hypodontia of a maxillary lateral incisor on one side and a peg-shaped lateral incisor on the other side. It has been noted that even relatives of hypodontia patients usually have relatively reduced tooth size even if they do not have hypodontia. It has also been reported that hypodontia is
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associated with palatally impacted canines, and there was a 26% increase in the transposition of the maxillary canine and first premolar in cases of maxillary lateral incisors agenesis. There is also a relationship between tooth rotation and hypodontia. Pirinen and Baccetti suggested that if there is a unilateral maxillary lateral incisor or premolar agenesis, it is more likely that the corresponding teeth on the other side will be rotated. Other researchers have found an increase of 10.8% in taurodontism of mandibular first molars associated with severe hypodontia. Baccetti and Statt cortex found an increase of 10.8% in taurodontism of mandibular first molars associated with severe hypodontia. There are not usually any noticeable changes to or effects on the skeletal pattern in the mild types of hypodontia, but it may be possible to see changes in cases of severe hypodontia. It has been reported that individuals with severe hypodontia or oligodontia associated with hypohidrotic ectodermal dysplasia had a flat or concave facial profile, obtuse nasolabial angle, retrognathic maxilla, reduced anterior face height and mandibular plane angle and reduced facial vertical height.54

SKELETAL PATTERN IN HYPODONTIA CASES

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TOOTH SIZE AND SHAPE VARIATIONS IN HYPODONTIA

Many studies in the dental literature have reported an association between hypodontia and microdontia of the remaining teeth. A reduction in tooth size was found in many members of the Hailuoto population in Finland, and this was found to be associated with hypodontia. Another group of researchers studied the tooth size discrepancy in the anterior region in 17,000 schoolchildren in Hawaii. They reported that when the maxillary lateral incisor was congenitally absent on one side, the adjacent central incisor was larger in size than its counterpart, suggesting a possible compensatory local interaction affecting the size of the adjacent tooth. A reduction in the tooth dimensions of relatives of patients with severe hypodontia has also been revealed. McKown et al also found reduced tooth dimensions of some teeth in relatives of hypodontia patients. Furthermore, they compared the crown dimensions of hypodontia patients and their relatives on the one hand and those of a group of control subjects on the other. They found that both the hypodontia patients and their relatives had a smaller tooth size when compared to the control subjects. The degree of reduction in size was also found to be associated with the degree of severity of hypodontia. The closest group to the control group was the relatives of the hypodontia patients, while the group most affected by reduction in tooth size was the group of patients with severe hypodontia. Conversely, patients with supernumerary teeth have been shown to have increased tooth dimensions. Recent studies have also measured crown dimensions in hypodontia patients and have come to similar conclusions: That tooth size reduction is associated with hypodontia. Mirabella et al investigated the size differences (mesiodistal length only) between patients with congenitally missing lateral incisors; both types unilateral and bilateral agenesis. They found narrower teeth on their sample compared to those with no missing teeth, with the exception of the maxillary first molars. No differences were found in tooth size reduction between patients with unilateral or bilateral congenitally missing teeth. Yaqoob et al claim that the relationship between moderate or severe hypodontia and generalized microdontia is well established, but that there has been little research into the association between mild hypodontia and microdontia.

Shape alteration of the remaining teeth has been reported to be associated with hypodontia. Davies reported the frequency of subjects with hypodontia and/or peg-shaping of one or more teeth as 22.2%. A relationship between a peg-shaped upper lateral incisor on one side and the absence of the contralateral tooth was subsequently found. This finding suggested that hereditary genetics may play a weak role in the etiology of a missing tooth in hypodontia patients who have peg-shaped upper lateral incisors. Sofae et al found that there is a higher prevalence of peg-shaped lateral incisors on the left than on the right side. This is also accompanied by smaller central incisors. It is more common to see the remaining teeth tending to be smaller when a peg-shaped lateral incisor tooth is present. Conical teeth or alterations in the shape of the remaining teeth were usually associated with the degree of severity of hypodontia.

A direct relationship between alteration in tooth shape and the malformation that occurs within hypodontia has been reported in the dental literature. The deficiency of cusps in human teeth is also documented as being associated with hypodontia. It has been noticed that the palatal cusps of the posterior teeth—mainly the upper first premolar and upper first permanent molars—were usually affected and malformed.
of the hypodontia groups were more tapered in shape. The teeth between hypodontia and control subjects in the position of the incisal corners of the upper central incisors. The teeth of the same population, as mentioned above, it is still unequal torque between teeth. As mentioned previously, hypodontia not an easy condition to manage and treat. Many studies have shown the importance of the role of interdisciplinary teams in the management of hypodontia. A recent book by Hobkirk et al provides a comprehensive review for clinicians about the available options for the management of hypodontia adopting a multidisciplinary approach.

The prime motivating factor for individuals seeking orthodontic treatment is esthetics. Some hypodontia patients seek treatment to manage depression caused by the deterioration in their appearance and/or functions. Hypodontia requires great care with extensive and complex treatments.

Unfortunately, there is no established formal procedure to manage patients with hypodontia. Their management may necessitate the help of many specialties. Treatment might range from single restorations to surgery and multiple restorations. Management will depend upon the pattern and severity of tooth absence, the amount of spaces present and, of course, the patient’s attitude. The general principle in management is to deal with the space within the dental arches: i.e., redistribution of space is usually the case in extensive conditions. Different options and methods of treatment have been suggested, including orthodontic movement and/or restorative replacements in the form of dentures, crowns, bridges, autotransplantation and dental implants, etc. Many factors should be evaluated before the commencement of management. These include the age of the candidate, the dental occlusion, soft tissue and skeletal patterns and the facial morphology of hypodontia, the number, color and morphology of the remaining teeth, the location of the absence, amount of alveolar ridge, oral hygiene, interest of the candidate, expectation of treatment, team/patient interaction and time as well as the cost of treatment. Furthermore, from an orthodontic perspective, variations in the size and shape of teeth with abnormal morphology are leading to incorrect bracket placement, since the standard prescription is still being used for hypodontia patients. The standard prescription will lead to different root angulation, inappropriate crown rotation and unequal torque between teeth. As mentioned previously, hypodontia not an easy condition to manage and treat. Many studies have shown the importance of the role of interdisciplinary teams in the management of hypodontia.

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The clinical management of hypodontia requires careful multidisciplinary planning and has financial implications. A number of procedures can be carried out to cope with patients’ wishes and which take into account their age. The cooperation between the different specialties in the team provides a wide variety of expertise which is not easy to find in one individual and the delivery of the treatment requires great care to meet the objectives of the treatment. At one of the international conferences on hypodontia an international agreement was announced about who should be on the team. The conclusion was that the members of the team should include the following: General dental practitioners, dental nurses, orthodontists, pediatric dentists, prosthodontists, oral and maxillofacial surgeons, specialist
laboratory technicians, clinical psychologists, clinical geneticists, dermatologists, speech and language therapists.27 This is the ideal team, but in many situations it is possible to assemble such a team. Several papers have been published focusing on the importance and the role of the interdisciplinary team in the care of hypodontia patients both functionally and esthetically.104,107-109 This multidisciplinary approach is often costly but the benefits outweigh the cost. This approach maximizes the clinical outcomes for patients.

CONCLUSION

Hypodontia presents a complex problem to the dentists worldwide. It is evident that a significant amount of research has been done in this field and the classification, prevalence, etiology, associated anomalies, clinical implications and treatment options for hypodontia are well documented.

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