RESEARCH PAPER | Medical Science | Volume : 3 | Issue : 12 | Dec 2013 | ISSN - 2249-555X

Heredity as Etiopathogenic Factor in Hypodontia. Clinical Aspects in Twins

KEYWORDS: heredity, hypodontia, clinical forms

Viorica Tarmure	Elina Teodorescu	Aranka Ilea
Lecturer, University of Medicine and Pharmacy "Iuliu Haţieganu" Cluj-Napoca, Department of Orthodontics	Lecturer, University of Medicine and Pharmacy "Carol Davila" Bucharest, Department of Orthodontics	Assistant teacher, University of Medicine and Pharmacy "Iuliu Haţieganu" Cluj-Napoca, Department of Oral Rehabilitation

Paula Jiman	Andreea Simona Pop
University of Medicine and Pharmacy "Iuliu Haţieganu" Cluj-Napoca, Department of Orthodontics	PhD student, University of Medicine and Pharmacy "Iuliu Haţieganu" Cluj-Napoca, Department of Orthodontics

ABSTRACT *Hypodontia, congenitally missing teeth, has a plurifactorial etiology. Among the factors causing it, an important role is played by heredity. It was determined that hypodontia is caused by gene defect and that the clinical forms depend on the variation in expressivity of the gene mutations and on the reduced penetration. This study's aim is to observe the role of heredity in the occurrence of hypodontia in families in witch at least two of the members present this anomaly.*

The study covers a total of 69 individuals, 30 males and 39 females. Hypodontia was present in 30 individuals (43.48%) of which 7 were males (23.33%) and 23 females (58.97%). The transmission was predominantly maternal for the girls and paternal for the boys. As clinical forms we've observed symmetric and asymmetric agenesis of upper lateral incisors or second premolars, unilateral or diagonal (1.5 and 3.5) agenesis, extensive and atypical hypodontia involving even the stable teeth such as the canine and first permanent molar (in a single patient).

What was interesting was the different clinical manifestations of the genetic transmission in bivitelline twins, for example, a brother having hypodontia of 3.1, 4.1, and the other a labio-palatal cleft and agenesis of 2.2, or univitelline, seeing twin brothers, having the same teeth missing (1.2, 2.2).

1. Introduction

Hypodontia is a numeric tooth anomaly manifesting itself through the presence of fewer than normal teeth and even their complete absence. It has a plurifactorial etiology and its clinical manifestations vary extremely, thus requiring a multidisciplinary approach to most of the patients. The different types of clinical aspects require a team treatment: orthodontic, prosthodontic, surgical [1-6].

The published specialized literature underlines the interest toward this anomaly. This involves the frequency of occurrence (data from the literature shows a variable frequency between 1.6-9.65%)[7], the associated pathology (crowdings, labio-palatal clefts, prognathism), as well as finding what causes it [7-12].

The etio-pathogenetic factors of hypodontia constitute a controversial and much discussed problem, even though the anomaly has been described thousands of years ago in the iron age with a case of bilateral hypodontia of a permanent upper lateral incisor [13,14].

Among the factors causing it, an important role is given to heredity, the study of twins having been used to show the importance of the genetic component during odontogenesis in controlling the number, size and shape of teeth. There are described cases of monozigous twins who had even the same type of hypodontia, as well as cases with variations [15].

Hypodontia can occur as an isolated case or as part of a syndrome. The isolated forms can occur sporadically or familialy. The latter can be the result of a defected single dominant gene, recessive or X-linked. Recent studies have shown that an abnormal situation exists in the chromosome 4p, the location of the gene responsible for hypodontia. Further more, the „guilty gene" has been found by detecting a mutation in the MSX1 gene. Other involved gene is PAX 9. MSX1 is associated with premolar and occasionally molar agenesia, PAX9 is associated with molar and occasionally premolar agenesia[16]. Hypodontia of M3, in most of the cases cannot be explained with one simple dominant autosomal transmission model and has been connected with the filogenetic reduction of the dental formula. Speculations regarding a polygenic type of heredity have also been described in the literature [15].

The progresses made by the Human Genome Project (HGP) in the last years have increased considerably the possibility of planning the inherited traits in familial hypodontia as well.

The first step in approaching the familial transmission of hypodontia involves the identification and characterization, from a clinical point of view, of the families with hypodontia. The important traits in selecting the families are the structure and size of the pedigree. The family must be large in size, with a minimum number of deceased members. Knowing the genetic model (meaning the model of inheritance of a condition) and the certitude of the diagnosis are primordial in detecting the genes responsible for the genetic transmission of hipodontia [17,18].

Significant clinical variations can be observed even among familial hypodontia that is trasmitted as a dominant autosomal trait. This suggests that multiple defects of genes can cause familial hypodontia and that's why large families instead of heterogeneous groups from different families are preferred [19].

Volume : 3 | Issue : 12 | Dec 2013 | ISSN - 2249-555X

We've proposed in this study to observe the role heredity plays in the occurence of hypodontia by investigating some families having at least two members with this anomaly.

2. Methods and materials

From an unselected lot of 2017 children between 7 and 15 years of age, 162 have been clinically diagnosed as having hypodontia. Of these cases, based on history taking, we were able to establish the presence of the anomaly in 10 families. Among them, between 5 and 11 members of each family have been examined clinically.

Having diagnosed an extensive bilateral hypodontia (EBH), we must establish the risk of the proband in developing the anomalies in future generations. The familial investigation shows the family history, with information from relatives of Ist, IInd, and IIIrd degree. For this we have constructed the family tree of each familiy according to the example in Figure 1 (Family B.V.).

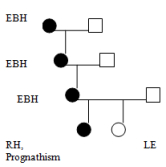


Fig. 1 (Fam. B.V.) Pedigree showing 4 generations affected
White circles – unaffected females; black circles – affected females; white squares – unaffected males
(EBH – extensive bilateral hypodontia; RH – reduced hypodontia; LE (late eruption)

3. Results

The examined group had 69 members, 30 males (43.48%) and 39 females (56.52%).

Of the total examined members, 30 (43.48%) had hypodontia.

The synthesis of the examination data of each of the 10 families is presented in Table I.

Seven males of the 30 examined had hypodontia, representing a percentage of 23.33%, and 23 females of the 39 examined were affected, representing 59.97%.

Taken as a whole group, the boys affected by hypodontia represented 10.14% and the girls 33.33%, the ratio being 1:3.

The clinical forms of hypodontia encountered are presented in Table II. They vary, from reduced hypodontia uni- or bilateral, to extensive hypodontia.

Table I – The number of affected persons in each family according to gender

Family	Number of examined members	Males	Unaffected males	Affected males	Females	Unaffected females	Affected females
I (B.V.)	11	5	5	-	6	2	4
II (M.I.)	11	5	3	2	6	6	-
III (N.A.)	5	2	2	-	3	-	3
IV (B.L.)	5	2	2	-	3	1	2
V (G.S.)	5	3	3	-	2	-	2
VI (B.I.)	6	3	-	3	3	3	-
VII (A.V.)	7	2	2	-	5	-	5
VIII (L.V.)	6	2	2	-	4	-	4
IX (C.S.)	5	2	2	-	3	1	2
X (P.M.)	8	4	2	2	4	3	1
Total	69	30	23	7	39	16	23

Table II – Clinical forms

Family	Number of affected persons and their gender	Clinical forms
I B.V.	4(♀)	Great-grandmother - Bilateral extensive hypodontia Grandmother - Extensive hypodontia 1.2, 1.4, 1.5, 2.2, 2.4, 2.5, 3.5, 4.5 Mother - Extensive hypodontia 1.2, 1.5, 2.2, 2.5, 3.5, 4.5 Older daughter (11yrs. old) - Hypodontia 1.2, 2.2, 3.5, 4.5; Associated prognathism
II M.I.	2(♂, bivitelline twins)	M.G. - Complete unilateral cleft; Hypodontia 2.2 M.I. – Hypodontia 3.1, 4.1; Persistence of 7.1, 8.1
III N.A.	1(♀)2(♂, univitelline twins)	Mother - Hypodontia 1.2, 2.2; Prognathism N.S.- Hypodontia 1.2, 2.2 N.A.- Hypodontia 1.2, 2.2
IV B.L.	2(♀)	Mother – Extensive hypodontia Daughter – Extensive hypodontia with persistence of temporary teeth and the presence of upper central incisors only from the permanent series
V G.S.	2(♀)	Mother – Extensive hypodontia Daughter – Extensive hypodontia with presence of stable but atypically shaped permanent teeth; Ectodermal polydysplasia
VI B.I.	3(♂)	Grandfather – Reduced hypodontia Father - Hypodontia 1.3, 2.3 Son (12 yrs. old) - Hypodontia 1.2, 1.3, 2.2, 2.3
VII A.V.	5(♀)	Grandmother - Hypodontia 1.2; 2.2-peg-shaped Mother - Hypodontia 1.2; 2.2-peg-shaped Mother's sister - Hypodontia 1.2; 2.2-peg-shaped Older daughter - Hypodontia 1.2; 2.2-peg-shaped Younger daughter- Hypodontia 1.2, 2.2 with space closed
VIII L.V.	4(♀)	Grandmother – Bilateral hypodontia 1.2, 2.2 Mother – Bilateral hypodontia 1.2, 2.2 Older daughter – Hypodontia 1.2, 2.2 with biological closing of the space Younger daughter - Hypodontia 1.2, 2.2, eruption of 1.3, 2.3 near the central incisors and persistence of 5.3, 6.3 until adult age
IX C.S.	2(♀)	Mother - Hypodontia 1.2, 2.2, 3.5 Daughter - Hypodontia 1.5, 3.5
X P.M.	2(♂), 1(♀)	Father's sister - Hypodontia 1.2 Father - Hypodontia 1.2, 2.2 Son – Atypical extensive hypodontia

To illustrate, we'll present some cases belonging to two families.

Volume : 3 | Issue : 12 | Dec 2013 | ISSN - 2249-555X

CASE 1 – Family II, M.I.,M.G., twin brothers, bivitelline

The hereditary factor manifested itself clinically in different forms. Among the two twin brothers, one had hypodontia of 3.1, 4.1 with persistence of 7.1, 8.1 (Fig. 2), the other had a left unilateral labio-palatal cleft and agenesis of 2.2 (Fig. 3).

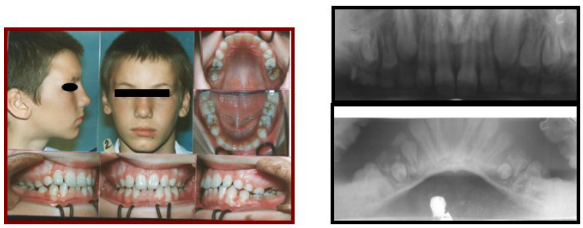
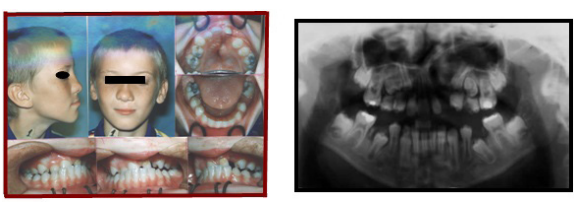


Fig. 2 M.I. (10 yrs. old); Hypodontia 3.1; 4.1; Persistence of 7.1, 8.1

(a) Clinical aspect; (b) Radiological aspect



(a) (b)

Fig 3 M.G. (10 yrs. old); Unilateral cleft; Hypodontia 2.2

(a) Clinical aspect; (b) Radiological aspect

CASE 2- Family III, N.A, N.S.
The hereditary factor manifested itself clinically in the same manner. Both of the twin brothers, had hypodontia of 1.2, 2.2. Fixed-appliance orthodontic treatment was carried out, in order to open the spaces of the missing teeth, followed by implant supported prosthodontics.

Fig 4. N.A., N.S.; Hypodontia of 1.2, 2.2

Extraoral aspect

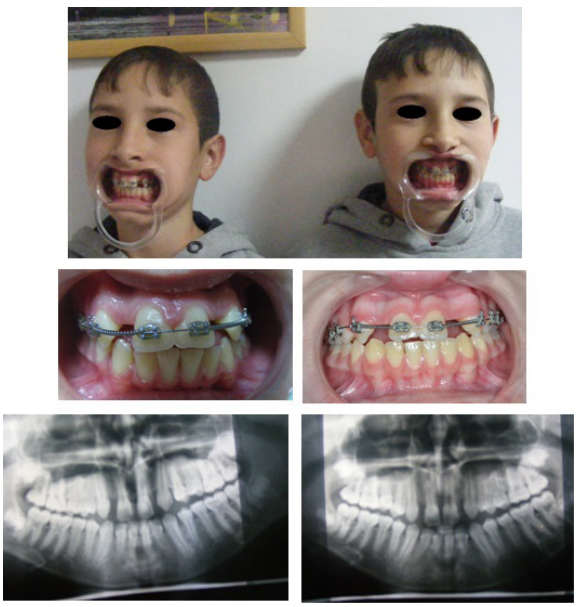


Fig 5. N.A., N.S.; Hypodontia of 1.2, 2.2

Intraoral aspect and X-ray

4. Discussion

In the study on the 10 families with 5 to 11 members, the anomaly was observed in 43.48% of the examined persons, with at least two members of each family being affected, predominantly the female gender (58.97%) compared to the male gender (23.33%). The types have varied, from symmetrical agenesis of upper lateral incisors or second premolars, to unilateral or diagonal hypodontia, and even extensive and atypical hypodontia involving stable teeth as well, such as the canine. The heredity in the studied families has been predominantly maternal in girls and predominantly paternal in boys.

Regarding the presented cases, in the first family we observed that the genetic transmission was clinically different, with the presence of a labio-palatal cleft in one of the twins and hypodontia of 3.1, 4.1 in the other.

In the second family, the genetic factor caused the same type of anomaly involving the same teeth. Thus, the mother has extensive hypodontia without any associated anomalies, and without having needed orthodontic treatment. The hypodontia manifested by the sons is among the anomalies asociated with prognathism due to lack of maxillary development as a consequence of the missing upper lateral incisors and adequate orthodontic treatment has been initiated for each anomaly. The missing teeth' spaces was reopened in order to avoid the aparition of an anterior crossbite.

Suinhufvud, quoted by Ulm M.R.[20], has explained the selectivity of hypodontia with the help of a model more anatomic than evolutionary. This scientist suggested that certain areas (for example the areas where embryos fuse), during the time of tooth development, have a greater affinity to epigenetic influences, and, as a result, to hypodontia. For example, the maxillary tooth having most often variations in shape or that is missing most frequently, specifically the upper lateral incisor, develops through embryologic fusion between the maxilla medial nasal buds. In the case of the mandible, hypodontia of the permanent teeth occurs in the area of the second premolar. This corresponds to the distal end of the primary dental lamina and becasue of the increased affinity to hypodontia, this area is called „fragile area"[20]. What is interesting is that this mandibular hypodontia occurs specifically in the

Volume : 3 | Issue : 12 | Dec 2013 | ISSN - 2249-555X

permanent dentition; the loss of a temporary second molar is rare. The third area in which hypodontia occurs frequently is that of where the two lower central incisors develop. Here, the fusion of 2 mandibular processes forms the so called medial suture of the future mandible. This is very possible to be another „fragile area"[20,21].

Kjaer I., Kocsis G., Nocal M. have explained the location of hypodontia through the development of some neuronal fields in the maxilla/mandible (fields of incisors, canines-premolars, molars). The area with a single field/region in which innervation occurs last is the most possible to have hypodontia.

Normal development of the teeth is especially influenced by the defects manifested during the canio-facial development. Disturbances in the embryonal mesenchyme of the maxilla are often seen (discovered) through their effects on the teeth. Early cranio-facial disturbances that can transform ulteriorly in anomalies of the maxilla, are often masked through the remodelling of the bones, therefore, hypodontia can serve as a very good indicator of the evolution of maxilla defects[22].

5. Conclusions

1. From this study emerges the role of heredity of an etiopathogenetic factor of hypodontia in all 10 families.
2. The females were more frequently affected (33.33%) compared to the males (10.14%), respectively yielding a ratio girls:boys of 3:1.
3. The clinical forms of manifestation have been similar in more members of the studied families in one third of the cases; in two thirds of the cases, the clinical manifestations have been different.

REFERENCE [1]. AKEREDOLU, Prosthetic treatment of oligodontia with a tooth-supported overdenture-a case report. Niger J Med 2002; 11(3):134-137. | [2]. ASHEIM B, OGAARDS B., Hypodontia in 9 year old Norwegians related to need of orthodontic treatment. Scandinavian Journal of Dental Research 1993; 101(5):25-60. | [3]. BIGGERSTAFF R H., The orthodontic management of congenitally absent maxillary lateral incisors and second premolars: a case report. American Journal of Orthodontics & Dentofacial Orthopedics 1992 Dec; 3(23):537-545 | [4]. COCÂRLĂ E, SCHAPIRA M., Aspects of prosthodontic therapy in children. Rev Stom 1974; 2. | [5]. GYULA TAKACS, BACIUT B, POPA M., Problems of oral implantology. Tipografia Universitatii de Medicina si Farmacie "Iuliu Hatieaganu" Cluj-Napoca, 1997. | [6]. SYMONS A L, STRITZEL F, STAMATION J., Anomalies associated with hypodontia of the permanent lateral incisor and second premolar. Journal of Clinical Pediatric Dentistry 1993 Winter; 17(2):109-111. | [7]. TARMURE V, Aspecte clinice si terapeutice in hipodontie, Editura Medicala Universitara Iuliu Hatieganu, Cluj Napoca, 2006 | [8]. COCÂRLÂ E., Orthodontics. p 100-101, 172-175, Cluj-Napoca, 1995. | [9]. DIAGNE F, DIOP-BA K, YAM A A, DIOP F., Prevalence of dental agenesis: a radiologic and clinical study in Dakar. Orthod Fr 2001 Dec; 72(4):313-315. | [10]. NG'ANG'A RN, NG'ANG'A PM., Hypodontia of permanent teeth in a Kenyan population. East Afr Med J 2001 Apr; 78(4):200-203. | [11]. PRIPING P, ZERRES K., ADULT-syndrome: an autosomal-dominant disorder with pigment anomalies, ectrodactyly, nail dysplasia, and hypodontia. American Journal of Medical Genetics 1993 Mar; 45(5)642-648. | [12]. TSAI T P, HUANG C S., Distribution paterns of primary and permanent dentition in children with unilateral cleft lip and palate. Cleft Palate – Craniofacial Journal 1998 Mar; 39(6):154-160. | [13]. CAPASSO L, CARAMIELLO S, DI MUZIO M., Assenza congenita degli incisivi laterali superiori permanenti con persistenza dei canini decidui in un Soggeto del eta del Ferro della necropoli di Sulmona. Minerva Stomatologica 1991 May; 40(5):365-471. | [14]. STERIZK G, STEINBICKER V., The etiology of hypodontia. Forts chritte der Kiefenorthopadie 1994 Apr; 67(4):61-66. | [15]. GOLDENBERG H, DAS P., Clinical, radiographic and genetic evaluation of a novel form of autosomal-dominant oligodontia. Journal of Dental Research 2000 Iul; 79(7):1469-1475. | [16]. Regina C.R. Peres, Raquel M. Scarel-Caminaga, Alexandre R. De Espírito Santo, Sérgio R.P.Line. Association between PAX-9 promoter polymorphisms and hypodontia in humans. Archives of Oral Biology, 50, 861-871, 2005. | [17]. COLLINS M A., Dental anomalies associated with amelogenezis imperfecta. Oral surgery, oral medicine, oral pathology, oral radiology and endodontics 1999 Sep; 88(3):358-364. | [18]. LYNGSTADAAS S P, NORDBO H, THRANE P S., On the genetics of hypodontia and microdontia: synergism or allelism of major genes. Journal of Medical Genetics 1996 Sep; 33(2):137-142. | [19]. NOMURA S. HASEGAWA S. NODA T, ISHIOKA K., Longitudinal study of jaw growth and prosthetic management in a patient with ectodermal dysplasia and anodontia. International Journal af Paediatric Dentistry 1993 Mar; 3(1):29-38. | [20]. ULM M R, ULM C, PLOCKINGER B., Sonographic depiction of fetal tooth germs. Prenatal Diagnosis 1995 Apr; 15(4):368-372. | [21]. IONESCU E, Anomaliile Dentare, ed. Cartea Universitara, Bucharest, 2005 | [22]. KJAER I, KOCSIS G, NODAL M., Aetiological aspect of mandibular tooth agenesis-focusing on the role of nerve, oral mucoasa and supporting tissues. European Journal of Orthodontics 1994 Oct; 23(2):238-239.