TOOTH AGENESIS - A REVIEW

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Abstract

Tooth agenesis or congenital tooth absence is the absence of development of at least one permanent tooth and a common dental anomaly in man. Hypodontia may occur either as part of a syndrome or as a non-syndrome developed by MSX 1 and PAX 9 are causative genes co-expressed in dental mesenchymal resulting in early developmental arrest of the developing tooth. As compared with permanent dentition, the prevalence of hypodontia in primary dentition is found to be very small. Most commonly missing tooth is a third molar. Most commonly missing tooth is a third molar. It is evident from the literature that the etiology of hypodontia is varied, and genetic, epigenetic, and environmental factors that contribute. Research has suggested that clinical hypodontia management requires careful planning across multidisciplinaires.

INTRODUCTION

Tooth agenesis is the failure of the development of the tooth which causes a definite absence of the tooth. This is the most common dental disorder, affecting one quarter of the general population. The main cause is the abnormal function of particular genes like MSX 1 and PAX 9 play key roles during odontogenesis (Junior and Echeverrigaray, 2012). From our previous studies we found that the teeth serve as an integral factor for identification and tooth agenesis might significantly contribute in this area (Harrita and Santhanam, 2019; Palati et al., 2019; Abitha and Santhanam, 2019). The most common type of dental disorder in which the incidence ranges from 2.3% to 10.1% is hyperdontia, an agenesis of one or more permanent teeth excluding third molars(Tan et al., 2011). The definition of oligodontia is congenital absence of six or more teeth, excluding third molars. Anodontia is the most severe form of hypodontia and involves absence of the entire permanent or primary dentition and it is very rare without an accompanying genetic syndrome(Gorlin et al., 1980). Additionally, tooth agenesis can be identified as a non - syndromic (isolated) or syndromic condition based on the absence or existence of other clinical manifestations(Weide et al., 1993). In tooth agenesis, genetic factors play a role as indicated by family incidence, varying prevalence data between groups, strong association with hereditary syndromes and molecular studies find defects in many genes(Watted et al., 2014; Manohar and Abilasha, 2019; Sarbeen et al., 2016)

Previous meta-analyzes found that hypodontia prevalence in populations differs greatly between males and females. Matthews et al 2004 reveals that females were more frequently affected by hypodontia than males and the highest prevalence in the chinese population(Mattheeuws, 2004). In contrast to this trend, Polder et al 2004 reported the lowest prevalence rate of 2.2% was found in females among Saudi Arabia (Polder et al., 2004). Tooth agenesis is sometimes associated with Molar Incisor Hypomineralization(MIH)(Padavala and Sukumaran, 2018)

The present aim of this review is to present documented knowledge on tooth agenesis obtained from reliable sources of information. Specifically, this review was to discuss the prevalence and factors associated with tooth agenesis and also to evaluate the etiology, diagnosis, occurrence patterns and management of tooth agenesis.

METHODOLOGY

The literature search on tooth agenesis was carried out for scientific articles published from 2000-2020 using two databases-google scholar and pubmed intending to recover all original reports related to the purposes and objectives of this review. The keywords used for the search were 'hypodontia', 'agenesis' - 'prevalence', 'etiology', 'teeth', 'factors', 'occurrence pattern'. Searches of the reference list from relevant review articles were also employed to identify further relevant study. Hand searching of reference lists in selected articles also carried out. For all the selected studies data were extracted using specially designed extraction forms quality assessment of selected studies were conducted for 30 collected full

text articles. The level of evidence of the reviewed articles were categorized as per the criteria of Centre for Evidence-Based Medicine, Oxford, UK

Etiology

It is evident from the literature that hypodontia etiology is varied, and that genetic, epigenetic and environmental factors may be key factors(Brook et al., 2009). Then etiology of tooth agenesis can be categorized as general and local factors. (Table 1)

Pathogenesis

Two encoding transcription factors expressed throughout the embryogenesis in mesenchymal cells PAX9 and MSX1, both members of highly conserved multigene families required. Another is BmP4 (bone morphogenetic protein4) encodes a pleiotropic growth and differentiation factor secreted by mesenchymal to induce morphogenesis in(Kapadia et al., 2007) . In marked contrast, all tooth agenesis causing human PAX9 mutations are heterozygous with most affecting only permanent teeth(Al-Ani et al., 2017). In a previous study, Hobkirk JA et al 2011 revealed that During odontogenesis the wingless, hedgehog, fibroblast growth factors and bone morphogenic protein are regulated by the epithelial-mesenchymal signal at molecular level. Defects seen in any of these pathways may cause problems such as tooth agenesis(Hobkirk et al., 2010). The genes commonly involved in tooth agenesis are listed in table 2.

Prevalence of Tooth Agenesis

Prevalence in Primary dentition & permanent dentition

The prevalence of hypodontia in primary dentition showed less than 1% prevalence in caucasians, whereas Japanese population registered a much higher prevalence. Deciduous lateral maxillary and central mandibular incisors make up 90% of the affected deciduous teeth.The frequency of permanent detention rises over time and ranges from 1.6 to 36.5 % depending on the population of the inquiry(Al-Ani et al., 2017)

Prevalence across continents

A metaanalysis showed that hypodontia prevalence in europe was 5.5% higher and australia was 6.3% higher compared to north america which was 1% (Polder et al., 2004). Two different studies reported that hypodontia prevalence was 4.6% in Saudi Arabia and 2.8% in United America respectively(Celikoglu et al., 2010; Polder et al., 2004). Another review has shown that prevalence of hypodontia apart from third molar varied between 2.6% in saudi arabia and 11.3% in ireland, 4% and 4.5% were seen in united kingdom(Vastardis, 2006)

Prevalence by type of malocclusion

Al moheral et al 2009 examined the distribution of hypodontia cases with one to three missing teeth between the malocclusion classes 1-3 (Kim, 2011; Moher et al., 2009) but Kim 2011 showed a higher prevalence in class III. The combined OR for class III compared to class I (or) II was 2.19 (95% CI) (Kim, 2011)

Tooth agenesis and cleft anomalies

Comporesi et al 2010 compared the prevalence of dental anomalies in children with unilateral (uclp) and bilateral cleft lip and palate (BCLP) with control group. Results showed that absence of lateral incisors was significantly greater in UCLP and BCLP group when

compared with group without cleft lip and palate(Camporesi et al., 2010) Most recently melissa lancia et al(2020) results showed lack of association with rs 12532 in MSX1 in risk of unilateral non-syndromic cleft Lip & Palate in tooth agenesis(Lancia et al., 2020)

Teeth commonly affected

Most commonly affected teeth were found to be mandibular second premolar and maxillary lateral incisors and also most predominantly females are more affected than male(Ceyhan et al., 2014). Polder et al 2004 resulted in the lesser affected teeth as central maxillary incisors, mandibular canines and first molar maxillary and mandibular(Polder et al., 2004). A greater percentage of missing teeth was seen in maxilla (combined prevalence of 53.2% (CI: 49.3-57%) compared with 46.8% (CI:43-50.7%) in the mandible and also concluded that mild hypodontia was most common followed by moderate (congenital missing teeth 3 to 5) and next severe hypodontia (missing teeth 6 or more) (Khalaf et al., 2014)

Diagnosis of Tooth agenesis

Tooth agenesis may be diagnosed during infancy and should be considered a marker for adult neoplasms(Ritwik and Patterson, 2018). Only the diagnosis can be performed only whenever agenesis has been already established especially in children about 9-12 years old, when panoramic x-ray is obtained. In most cases patients notices missing teeth with DNA specificity based on polymorphic variant also be available and accessible by clinicals resulting in most accurate diagnosis and allowing for a better approach to this anomaly.(Junior and Echeverrigaray, 2012) General dentists must be able to perform simple oral biopsies for the diagnosis of oral lesions. The capacity to differentiate between benign and premalignant or malignant oral lesions is essential for establishing a correct diagnosis(Sheriff et al., 2018). Prevalence of oral lesions is said to be increased in older individuals compared to younger counterparts(Palati et al., 2020). Role of saliva used as a diagnostic tool for detecting oral squamous cell carcinoma using high sensitive salivary biomarkers known as MMP-9, chemerin, choline+betaine+pipecolic acid L-Carnitine(Shree et al., 2019)

Clinical implications and managements of hypodontia

Hypodontia has significant clinical implications as it can seriously affect a person's physical and emotional status. The primary motive factor for individuals seeking treatment for tooth agenesis is esthetics(Shahrani and Al Shahrani, 2014). Unfortunately, there is no established procedure for managing hypodontia therapy night patients ranging from single and multiple restorations to surgery(Valle et al., 2011). A recent book by Hobrick et al provides comprehensive reviews for clinicals about the available options for the management of hypodontia adopting a multidisciplinary approach. Currently, Tooth sensitivity has become not quite prevalent and with less awareness on its treatment so awareness among people to maintain good oral health for preventing such type of illness(Gunasekaran and Abilasha, 2016). Majority of dental practitioner had heard about evidence based dentistry and their knowledge about terms used Evidence Based Dentistry Practitioner is significant for the dentist for a good plan in treatment (Ahad and Gheena, 2016;Uma et al., 2020;Prasanna and Gheena, 2016;Krishnan et al., 2018). In dentistry, photography plays major role in registering clinical information in the oral cavity and it also used to improve learning process, communication and dental marketing (Hannah et al., 2018)

DISCUSSION

When comparing the sexes across various sources, Polder et al 2004 found that female had a prevalence value of 1.37 times higher than male similar to this results Khaled khalif et al 2015 also supports this finding where it was found that female had prevalence of 1.22 times. Similarly Z.S.Albashariach 2006 found females were 0.1 times to 1.64 times higher than male. As previously discussed mild hypodontia (congenitally missing 1 or 2 teeth) is a fairly common dental anomaly. The most commonly missing teeth are due to other dental anomalies which are commonly associated with microdontia, abnormal tooth shape, palatally impacted upper canines, abnormal tooth eruption and irregularities in tooth position (Arte et al., 2001). With velocardiofacial syndrome in children needing thorough clinical and radiological dental examination and observed high prevalence, missing permanent teeth were mandibular incisors (Heliövaara et al., 2011). This condition causes aesthetic concerns by patients as well as psychological issues (González-Allo et al., 2012).

In a study, Weronika Gawron et al 2019 found that women with ovarian cancer are 3.3 to 8.1 times more likely than healthy females to have hypodontia. Nevertheless, no specific genes were found which could be responsible for the coexistence of ovarian cancer and tooth agenesis(Gawron-Jakubek et al., 2019). H.Vastardis et al 2000 estimated prevalence 0.25% in the normal population and later w.zhang et al 2014 found it almost affects 20% of the current population in Asians(Song et al., 2014). Most commonly missing teeth after the third molar was found to be mandibular lateral incisors and second premolar whereas in Malaysia most commonly missing tooth was upper lateral incisors (1.7%) followed by lower and upper second premolars (1.8%) (Ceyhan et al., 2014)

The management of such patients will require multidisciplinary care which is very close for health care providers especially in those with severe hypodontia and this study revealed the essential role of resin bonded bridges (RBB) in managing patients with hypodontia. The conservative design of resin-bonded bridges enables young adults to step into fixed prostheses rather than waiting for a cessation of development before the eventual procurement of crowns covered by dental implants(King, 2006). It is therefore important to have an up to date knowledge of the prevalence of this condition in order to plan and prioritize funding of healthcare provision, including with those hypodontia for further progress, identifying pathways of human genome and compare with different population with early interventions which would be great support and for rehabilitation

CONCLUSION

The review life helps to provide deeper understanding about cause, prevalence, etiology and factors associated with tooth agenesis which benefits patients clinicians and geneticists to provide alternative treatment plans in future. The early diagnosis prevents or reduces complications which may cause ethestic and functional disorder which decrease quality of life.

Conflict of interest

None declared

AUTHOR CONTRIBUTIONS

Naz Fathima Raj Mohamed : literature search, data collection, analysis, manuscript writing
Gifrina Jayaraj: data verification, manuscript drafting
Yuvaraj babu K : data verification, manuscript drafting

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Table 1: Etiology of tooth agenesis

Local Factors	Conditions such as trauma in the early stages of development, hormonal conditions , radiation , infectious diseases and unintentional removal of tooth germ.(AlQarni et al., 2013)
Systemic Factors	Cleft lip and palate, down syndrome,syphilis, Rieger syndrome, scarlet fever, rickets during pregnancy(Bilgin and Kaya, 2018)

Table 2: Genes commonly involved in tooth agenesis

GENE	EFFECT
AXIN2	Increased colorectal cancer risk (Dreesen et al., 2014)
MSX1, PAX9, EDA1,WNT10A and EDUARDO	hypodontia(Azzaldeen et al., 2017)
EDA1, EDARAD, EDAR and WNT10A	Ectodermal dysplasia(Inserm and INSERM, 2020)
GREM2	Tooth agenesis, Microdontia, Taurodontism and short tooth roots(Machida et al., 2015)
Dlx-1 and Dlx-2	Tooth agenesis- Upper molars(Swinnen et al., 2008)

Table 3: Description Of Included Articles

AUTHOR	YEAR	TYPE OF STUDY	QUALITY ASSESSMENT	KEY FINDINGS
Khalaf et al., 2014	2014	Systematic review	Level2	Among african population females was found to be higher risk of agenesis than males
Bilgin and Kaya, 2018	2018	Systematic review	Level 2	Highest prevalence in africa followed by europe,asia, australia and lowest prevalence in north america and carribean
Kim, 2011	2011	Systematic review	Level2	Highest prevalence in class III malocclusion than class I and class II

| Camporesi et al., 2010 | 2010 | Clinical statistical study | Level3 | Compared to control group without cleft anomalies absence of lateral incisor was greater in unilateral and bilateral cleft lip and palate |
| Polder et al., 2004 | 2004 | Randomised controlled study | Level 2 | Least affected teeth maxillar of central incisors mandibular canines, maxillary and mandibular first molar |

AlQarni et al., 2013	2013	Systematic review	Level2	Most common is mild hypodontia followed by moderate and severe hypodontia
Junior and Echeverrigaray, 2012	2012	Expert opinion	Level 5	Early diagnosis marker for risk of neoplasms in adulthood include colorectal neoplasms epithelial ovarian cancer
Vastardis, 2006	2006	Expert opinion	Level 5	Latest advance- better knowledge in the genetic network used for early diagnosis was DNA examination in polymorphic variants was the most accurate method to diagnose this anomaly.

Mattheeuws, 2004	2004	Systematic review	Level 2	Most commonly affected teeth is mandibular second premolar (44.2%)and maxillary lateral incisors(36.6%) And maxillary second premolars(34%)
Celikoglu et al., 2010	2010	Case controlled study	Level 3	Prevalence of hypodontia apart from third molar was found to be 2.6% saudi arabia and 4.5% in united kingdom