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# Prosthodontic Management of Children with Ectodermal Dysplasia: Review of Literature

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# Abstract

Hypohidrotic ectodermal dysplasia is a hereditary disorder of two or more ectodermal structures. It may include hypodontia, hypotrichosis and hypohidrosis. Patient with this disease often needs complex prosthetic treatment. The option for a definitive treatment plan may include removable, fixed or implant supported prosthesis, single or in combination. The present review focuses on the classification, genetic aspects, and clinical manifestation along with various treatment modalities.

**Keywords:** Ectodermal dysplasia; Hypodontia; Hypohidrosis; Hypotrichosis; Prosthetic treatment

# Introduction

Ectodermal dysplasia (ED) is a large group of heterogeneous heritable conditions characterized by congenital defects of two or more ectodermal structures and their appendages: hair (hypotrichosis, partial or total alopecia), nails (dystrophic, hypertrophic, abnormally keratinized), teeth (enamel defect or absent) and sweat glands (hypoplastic or aplastic) [1,2]. Thurnam published the first report of a patient with ectodermal dysplasia in 1848 [3]. The term ectodermal dysplasia was not coined until 1929 [4]. In 1971 only eight forms of ED were known [1,5]. Now approximately 200 different ED have been delineated; about 30 have been identified at the molecular level with identification of the causative gene [6].

#### Classification

There are several classifications given by different authors. Some are based on clinical features and others on genetic component of the disorder [7,8]. Clinically there are two major types of ED namely hidrotic and anhidrotic (hypohidrotic form). The hidrotic form, inherited as an autosomal trait, affects teeth, hair and nails but usually spares the sweat glands and was first described by Clouston in 1929 [9]. Whereas the hypohidrotic form (Christ-Siemens-Touraine Syndrome) is most common type seems to be an X-linked recessive trait, with an incidence of this syndrome estimated to be 1 to 7 per 10,000 live births [10,11]. Hypodontia, hypotrichosis and hypohidrosis which form a triad are the characteristic feature of the hypohidrotic form [12,13].

Other attempts at classifying EDs were proposed later [2,4,7,14,15]. Lamartine reclassified the ED according to the function of their mutated genes into 4 functional groups: cell-cell communication and signaling; adhesion; transcription regulation; and development [16]. Recently, a new classification for ED has been proposed, based on the molecular genetic data by Priolo [17] who divided the ED into two groups. The first group includes disorder in which a defect in the epithelial-mesenchymal interaction and the second group involved defect in cell-cell adhesion and communication.

# **Genetic Aspects**

Hypohidrotic (or anhidrotic) ectodermal dysplasia (HED) is the most frequent form of ED that can be inherited in an X-linked (XL), autosomal recessive or autosomal dominant manner [18]. X-linked HED was the first in which the defective gene was cloned thereby leading to the identification of a novel signaling molecule of the tumor necrosis factor (TNF) superfamily named ectodysplasin (EDA) [19]. This EDA gene was located to Xq 12-13 by Zonana et al. [20]. Autosomal forms of HED are due to mutation in the EDA receptor (EDAR). EDAR binds specifically the A1 isoform of EDA (EDA-A1) but not the EDA-A2 isoform that utilizes a distinct receptor. Autosomal HED may also be caused by mutation in a cytosolic, EDAR-specific adapter molecule named EDAR-associated death domain (EDARADD) [17,18,21,22].

The EDA, EDAR and EDARADD genes provide instructions for making proteins that work together during embryonic development. These proteins form part of a signaling pathway that is critical for the interaction between two cell layers, the ectoderm and the mesoderm. It is essential for the formation of several structures that arises from ectoderm, including the skin, hair, nails teeth and sweat glands. Mutation in these genes prevents normal interaction between the ectoderm and mesoderm and impairs the normal development of hair, sweat glands and the teeth [7,8]. The improper formation of these ectodermal structures leads to the characteristic features of HED. In rare cases, HED is associated with immune deficiency caused by mutations in further downstream components of the EDA pathway that are necessary for the activation of the transcription factor NFkappa b [18-20,23,24].

# **Clinical Manifestations**

Hypohidrosis is possibly the most remarkable characteristic of ED because it may not be the apparent in the first year of life but present later as a fever of unknown origin. The inability to sweat results in intolerance to heat, occasionally causing hyperpyrexia after mild exertion or even after a simple meal [25]. Resultant high fevers may lead to seizures and other neurological sequelae. This is one of the most common causes of mortality with a 30% rate in infancy and early childhood [26]. Other problems associated are pharyngitis, rhinitis, cheilitis and dysphagia may result from decreased number of mucous glands in the respiratory and gastrointestinal tracts [27]. In

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some cases, decreased function of certain components of the immune system (depressed lymphocyte function, cellular immune function), potentially causing an increased susceptibility to certain infections. Many affected infants and children experience attacks of wheezing and breathlessness and respiratory infections [28].

The skin covering majority of the body may be abnormally thin, dry and soft. Fine linear wrinkles and increased pigmentation are often present around the eyes, appearing prematurely aged. Scalp hair, eyebrows, eyelashes, and other body hair may be sparse, poorly developed, or absent. There may be hyperkeratosis of the palms of the hands and soles of the feet. Fingernails and toenails also may show faulty development. Other reported clinical manifestations are frontal bossing; sunken cheeks, prominent supraorbital ridges, a saddle nasal bridge, large low set ears and hypoplastic-appearing alaeque nasi. In addition, the midface is depressed and hypoplastic; the cheek bones are high and broad (malar hypoplasia) and appear flat and depressed, thick everted lips and or a large chin [26,29,30]. The facial appearance of affected individuals is so characteristic of the condition that unrelated patient may even be mistaken for a sibling [25].

# **Dental Abnormalities**

The most striking oral feature of ED may range from hypodontia to anodontia of the primary or permanent teeth (with or without cleft lip and cleft palate), associated with hypoplasia of the alveolar bone structure. Consequently, the vertical dimension of the lower face is reduced; the vermilion border disappears resulting in protuberance of lips [31,32]. A cephalometric study by Vierucci and co-workers have shown children with hypohidrotic type ectodermal dysplasia showed maxillary retrusion due to sagitally under developed maxilla, forward and upward displacement of the mandible and collapsed lower anterior facial height [33]. It is not uncommon for the face of an affected child taking appearance characteristics of old age [34]. The average number of missing permanent tooth is reported as 23.7. The maxillary central incisors, maxillary first molars, and maxillary canines are teeth most often present [35]. If teeth are present they are often conical in shape, malformed and widely spaced. The cases of true anodontia were extremely limited to rare conditions. Tanner states in the case of ED such abnormal appearance may affect normal social and psychological development in young patients [36]. Therefore, dental care for a patient with anodontia is extremely important. In such cases, multidisciplinary team is generally advocated to be the most appropriate approach [30,37]. Treatment decisions of the dental team depend on the patients' needs, wishes, their willingness to undergo minor or major treatment with different impact, and also on the economic possibilities.

# **Treatment Considerations**

# **Removable prosthodontics**

Prosthetic treatment modes using removable prosthetic dentures (RPD), overdentures or complete dentures are the primary treatment alternatives for the clinical management of young ED patients with severe hypodontia or anodontia. In complete anodontia, the treatment would comprise of complete dentures either conventional or implant supported. In patients with partial anodontia removable/fixed partial dentures and over dentures may be considered [38,39]. It is often characterized by underdeveloped residual ridges and loss of vertical dimension of occlusion [40]. These approaches may be used either individually or in combination to provide optimal results. Complete denture prosthesis given to patient alters the alveolar height, provides a better musculocutaneous profile and brings about a significant

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improvement in mastication, esthetics, phonetic function and psychological support. The usual treatment for ED focuses on a series of complete or partial dentures during the years when the dento-facial growth is happening and definite rehabilitation following completion of jaw growth [25,41].

Treatment should be commenced as early as possible in order to avoid possible resorption and atrophy of the alveolar ridges, and to control the vertical dimension, which can be severely affected by the total or partial lack of teeth. There is no definitive time to begin treatment, but Till and Marques and Pigno et al. recommend that an initial prosthesis could be delivered when the child starts school, so that the child could have a better appearance and have time to adapt to the prosthesis [11,42]. According to Kupietzky and Houpt, it is feasible to fabricate a denture for a patient as young as 3 years of age [43]. This early restoration of facial appearance is essential for normal psychological development [44]. In each situation, the parents should be aware of the possibility that the young patient may refuse the treatment procedure initially and may not wear the dentures. To facilitate this problem in young children, some clinicians have reported the delivery of one denture at a time [11,40]. Till and Marques advocate this method and recommend that denture made for the arch with the best prognosis delivered first, followed by the delivery of the second denture 2-4 months later [42].

The problems associated with early placement of complete denture are mainly associated with periodic adjustment due to growth changes and difficulties in achieving good retention and stability [44]. They require regular adjustment and should be replaced when a decreased vertical dimension of occlusion and an abnormal mandibular posture are detected due to growth. Replacement will be needed at least 3 times between the period of early and late mixed dentition and permanent dentition [37]. Without dentures, the antero-rotation of the mandible causes an upward and forward displacement of the chin, with a reduction in the height of the lower third of the face and a tendency to class III malocclusion. The presence of dentures allows a backwarddownward rotation of the mandible, with consequent normal positioning of the chin in space (13,14). In HED patients, dryness of the oral mucosa and the underdeveloped maxillary tuberosities and alveolar ridges are problematic factors for resistance and stability of dentures. When planning dentures in these patients, care should been taken to obtain a wide distribution of occlusal load fully extending the denture base [44,45]. Rockman et al. demonstrated a technique using magnets to enhance the retention of maxillary and mandibular prosthesis in a 9 year old boy [27]. If an overdenture is fabricated, retention can be augmented by various attachments anchored to the available teeth [11,46].

# **Fixed prosthodontics**

Fixed prosthodontic treatment is generally not used in the treatment of ED, because many patients are often quite young when they are first treated. Also fixed partial denture with rigid connectors should be avoided in young, actively growing patients because they could interfere with jaw growth, especially if the prosthesis crosses the midline. Individual crown restorations are often used, but large pulp sizes and shorter crown heights may cause concern. Direct composite restoration is generally used for restoring the normal morphology to hypoplastic teeth commonly found in ED patients [47]. They are often used in combination with RPD [11]. Also orthodontic treatment may be needed to align the teeth into acceptable position before RPD fabrication [29,48]. Suri et al. describes the simultaneous use of functional and fixed appliances to modify the pattern of dentofacial

development and align teeth in preparation for prosthodontic habilitation of a growing 10 year old child with HED [35]. Sagittal and vertical dentofacial relationships and facial esthetics were significantly improved.

### Implant prosthodontics

The placement of implants in growing children is not recommended as a routine practice. Experiments designed to study the effect of dental implants on dentoalveolar growth and development in pigs demonstrated that implants, owing to an absence of a periodontal ligament, behave like ankylosed teeth i.e., they remain stationary and do not erupt together with adjacent teeth leading to inhibition of growth and development of the alveolar process. Submergence of an implant is disadvantageous for a number of reasons. First, an infraocclusion occurs, which disrupts carefully constructed occlusal relationships and leads to compensatory eruption of opposing teeth and tipping of adjacent teeth. Second, a vertical discrepancy develops between the mucosal margin of the implant and the gingival margins of adjacent teeth [49].

Most studies of mandibular growth suggest that transverse growth of the mandible between the canine regions is minimal, and that which occurs, ceases early. Consequently, implants in the anterior mandible and united by a restoration spanning the symphysis may not constrain transverse growth [49,50]. Kearns et al. suggested that transfer growth at the mandibular symphyseal suture usually ceases in the first six months of life [51]. For this reason, there should be no difficulties with the placement of implants in the anterior mandible. Problems with implant placement in the mandible may be minimal if implants are not intermixed with natural teeth [26,52]. Cronin et al. stated that transverse growth of the maxilla occurs at the mid palatal suture [53]. Sutural growth ceases at about 17 years of age in boys (i.e., about 2 years earlier than the condylar growth and growth in body height). Thus, fixed implant construction crossing the mid palatal suture will result in a transversal growth restriction of the maxilla. The insertion of implants in the growing maxilla should be avoided until adult early adulthood.

Guckes et al. evaluated the survival of implants placed in individuals with a form of ED with mean age of 20.5 years (8-68 years) and showed survival rates of 91% in the mandible after 24 months, whereas the success in the maxilla was 71% [54]. Statistically, they found that implants placed in the anterior maxilla were 2.8 fold more likely to fail than those placed in the anterior mandible. In a study by Sweeney et al. on dental implant in ectodermal dysplasia patients suggested that prior to cessation of growth; implant placement in the symphyseal region of the anterior mandible may be performed with caution [12]. He stated that the mean age of patients receiving maxillary implant was 18 years and mandibular implant was 17 years.

Determining the ideal time for implant treatment in children seems quite difficult. Treatment guidelines issued by the National Foundation for Ectodermal Dysplasias indicate that implants are only recommended for the mandible anterior portion in children older than school age (Table 1).

#### Conclusion

The nature of ED has been described with special emphasis on prosthodontic management. These patients often need a multidisciplinary approach to treatment planning and dental

| Authors                 | Year Reported | Gender | Age   | Dentition   | Treatment  |
|-------------------------|---------------|--------|-------|-------------|--|
| Nandini Y [55]          | 2013          | М      | 14    | Oligodontia | Removable partial denture with metal crown on existing teeth   |
| Aydinbelge et al. [56]  | 2013          | F      | 7     | Oligodontia | Maxillary overdenture and implant supported mandibular overdenture   |
| Kalaskar et al. [57]    | 2013          | F      | 7     | Oligodontia | Flexible denture overdenture   |
| Sadashiva et al. [58]   | 2013          | F      | 14    | Oligodontia | Overdenture  |
| Ladda et al. [59]       | 2013          | М      | 8     | Anodontia   | Complete denture   |
| Paulus et al. [60]      | 2013          | М      | 6     | Oligodontia | Maxillary and mandibular implant borne prosthetic  |
| Jain et al. [61]        | 2012          | М      | 11    | Oligodontia | Maxillary flexible overdenture and mandibular conventional complete denture  |
| Singer SL [62]          | 2012          | М      | 11    | Oligodontia | RPD in maxilla and implant supported prosthesis in maxilla   |
| Shigli et al. [46]      | 2012          | М      | 10    | Oligodontia | Removable partial denture  |
| Bildik et al. [63]      | 2012          | М      | 14    | Oligodontia | upper teeth with copings and fabrication of upper and lower complete dentures  |
| El Osta et al. [64]     | 2011          | F      | 9     | Oligodontia | Preformed pediatric crown with Removable partial denture followed by orthodontic<br>treatment and fixed prosthesis after 8 years |
| Manuja et al. [65]      | 2011          | М      | 9     | Oligodontia | Complete denture   |
| Li et al. [66]          | 2011          | М      | 19    | Oligodontia | Bone augmentation and distraction osteogenesis followed by implant   |
| Gupta et al. [67]       | 2011          | М      | 4     | Oligodontia | Removable Partial Denture in maxillary and complete denture  |
| Pae et al. [68]         | 2011          | М      | 12    | Oligodontia | Overdenture for maxilla and crown retained denture for the mandible  |
| Bhargava et al. [41]    | 2010          | F      | 5     | Oligodontia | Upper and lower removable denture  |
| Bulut et al. [48]       | 2010          | М      | 12    | Oligidontia | Maxillary Overdenture and implant supported mandibular overdenture   |
| Derbanne et al. [69]    | 2010          | М      | 2     | Oligodontia | Complete denture   |
| loannidou et al. [70]   | 2010          | М      | 10-18 | Oligodontia | Removable partial denture along with midline jackscrews  |
| Van Sickels et al. [71] | 2010          | F      | 15    | Oligodontia | Orthodontic intervention along with removable prosthesis   |
| Raducanu et al. [72]    | 2010          | М      | 7     | Oligodontia | Partial and complete removable dentures with acrylic crown   |
| Ramesh et al. [47]      | 2010          | М      | 9     | Anodontia   | Complete denture   |
|                         |               | M      | 12    | Oligodontia | Complete denture   |
|                         |               | M      | 7     | Anodontia   | Complete denture   |
| Khazaie et al. [73]     | 2010          | M      | 12    | Oligodontia | Maxillary anterior bonded composite restoration and a mandibular complete denture  |
| Bani et al. [31]        | 2010          | М      | 8     | Anodontia   | Complete dentures  |
|                         |               | М      | 3     | Anodontia   |  |
| Vieira et al. [28]      | 2007          | М      | 6     | Anodontia   | Complete denture   |

Table 1: List of recent reported cases of oligodontia and anodontia in children with different treatment modalities.

treatment to regain esthetics and function of the stomatognathic system. Considering the age, different rehabilitation options can be considered, from classic conventional solutions such as complete denture, removable partial denture, overdentures and to the most up to date implant supported prosthetics. These early dental interventions can improve the patient's appearance and psychological problems as long as close follow up and prosthetic modification are maintained due to possible continuing growth.

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