



**Review Article**

**A Review Article on Ectodermal Dysplasia**

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Ectodermal dysplasia is a large group of inherited disorders characterized by a primary defect in hair, teeth, nails or sweat gland function, in addition to another abnormality in a tissue of ectodermal origin, e.g. ears, eyes, lips, mucous membranes of the mouth or nose, central nervous system. The different types of ectodermal dysplasia are caused by the mutation or deletion of certain genes located on different chromosomes. The signs and symptoms of ectodermal dysplasia differ markedly between the different types of the condition and depend on the structures that are affected. Currently there are about 150 different types of ectodermal dysplasias. The most common ectodermal dysplasias are **Hypohidrotic (anhidrotic) ED and Hidrotic ED**. Ectodermal dysplasia results from the abnormal morphogenesis of cutaneous or oral embryonic ectoderm (ie, hair, nails, teeth, eccrine glands). In some forms, mesodermal abnormalities are also present. The frequency of the different ectodermal dysplasias in a given population is highly variable. Collectively, the prevalence of ectodermal dysplasia is estimated at 7 cases per 10,000 births. There is no specific treatment for Ectodermal Dysplasia, only disease management are available.

**Key words:** Renal ultrasonography, voiding cystourethrography, Genetic testing, Clouston syndrome, palmo-plantar hyperkeratosis, Christ-Siemens-Touraine (CST) syndrome.

**INTRODUCTION**

Before a developing baby is large enough to be seen, a layer of cells covers the outside of the body. This surface layer of cells is called the ectoderm, and from it develops the skin, hair, nails, teeth, nerve cells, sweat glands, parts of the eye and ear, and parts of some other organs. Each of the listed parts of the body is then called an ectodermal structure. Dysplasia means Abnormal development or growth of tissues, organs, or cells.

The term “Ectodermal Dysplasia” was first introduced in 1929 to describe a number of

conditions that are present at or shortly after birth in which two or more of the body’s ectodermal structures (e.g hair, teeth, nails, sweat glands) fail to develop or grow properly (dysplasia).

Ectodermal dysplasia is a large group of inherited disorders characterized by a primary defect in hair, teeth, nails or sweat gland function, in addition to another abnormality in a tissue of ectodermal origin, e.g. ears, eyes, lips, mucous membranes of the mouth or nose, central nervous system. The ectoderm is the outermost layer of cells in embryonic

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**Fig.1: The child suffering from Ectodermal Dysplasia**

development and contributes to the formation of many parts of the body including all those described above. All ectodermal dysplasias are present from birth and are non-progressive.

#### **Alternative Names**

Anhidrotic ectodermal dysplasia; Christ-Siemens-Touraine syndrome

#### **Cause of Ectodermal Dysplasia**

The different types of ectodermal dysplasia are caused by the mutation or deletion of certain genes located on different chromosomes. Because ectodermal dysplasias are caused by a genetic defect they may be inherited or passed on down the family line. In some cases, they can occur in people without a family history of the condition, in which case a de novo mutation has occurred.

#### **Signs and Symptoms of Ectodermal**

#### **Dysplasia<sup>3</sup>**

The signs and symptoms of ectodermal dysplasia differ markedly between the different types of the condition and depend on the structures that are affected. Signs and symptoms are not usually apparent in newborns and may not be picked up till infancy or childhood.

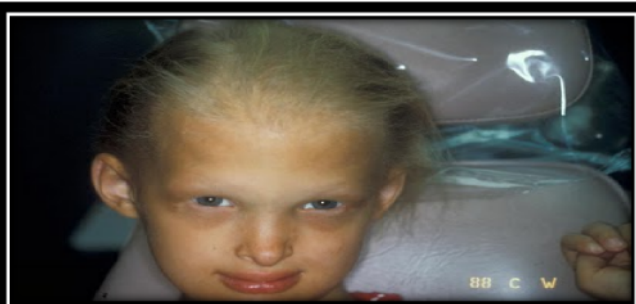



Ectodermal Dysplasia typically affects the four organs primarily involved, given in Table 1

#### **Classification of Ectodermal dysplasia<sup>4-6</sup>**

Currently there are about 150 different types of ectodermal dysplasias. In an attempt to classify these, different subgroups are created according to the presence or absence of the four primary ectodermal dysplasia(ED) defects:

- ED1: Trichodysplasia (hair dysplasia)
- ED2: Dental dysplasia

**Table 1:- Table showing symptoms of Ectodermal Dysplasia**

Affected organ	Features
<b>1.Hair</b> 	<ul style="list-style-type: none"> <li>• Scalp and body hair may be thin, sparse, and light in colour</li> <li>• Hair may be coarse, excessively brittle, curly or even twisted</li> </ul>
<b>2.Nails</b> 	<ul style="list-style-type: none"> <li>• Fingernails and toenails may be thick, abnormally shaped, discoloured, ridged, slow growing, or brittle</li> <li>• Sometimes nails may be absent</li> <li>• Cuticles may be prone to infection.</li> </ul>
<b>3.Teeth</b> 	<ul style="list-style-type: none"> <li>• Abnormal tooth development resulting in missing teeth or growth of teeth that are peg-shaped or pointed</li> <li>• Tooth enamel is also defective</li> <li>• Dental treatment is necessary .</li> </ul>
<b>4. Sweat gland</b> 	<ul style="list-style-type: none"> <li>• Eccrine sweat glands may be absent or sparse so that sweat glands function abnormally or not at all</li> <li>• Without normal sweat production, the body cannot regulate temperature properly</li> <li>• Children may experience recurrent high fever that may lead to seizures and neurological problems</li> <li>• Overheating is a common problem, particularly in warmer climates</li> </ul>

- ED3: Onychodysplasia (nail dysplasia)
- ED4: Dyshidrosis (sweat gland dysplasia)

Based on the above, the 150 different types of ectodermal dysplasias are categorised into one of the following subgroups made up from the primary ED defects:

- Subgroup 1-2-3-4
- Subgroup 1-2-3
- Subgroup 1-2-4
- Subgroup 1-2
- Subgroup 1-3
- Subgroup 1-4
- Subgroup 2-3-4
- Subgroup 2-3
- Subgroup 2-4
- Subgroup 3
- Subgroup 4

The most common ectodermal dysplasias are **hypohidrotic (anhidrotic) ED** which falls under subgroup 1-2-3-4 and **hydrotic ED** which comes under subgroup 1-2-3.

The three most recognised ectodermal dysplasia syndromes fall into the subgroup 1-2-3-4, as they show features from all four of the primary ED defects. They are:

- Ectrodactyly-ED-clefting syndrome
- Rapp-Hodgkin hypohidrotic ED
- Ankyloblepharon, ectodermal defects, cleft lip/palate (AEC) or Hay-Wells syndrome

### Diagnosis and test of Ectodermal Dysplasia

- Sweat pore counts, pilocarpine iontophoresis, and skin biopsy may document hypohidrosis and a reduction in the number of eccrine glands.
- Prenatal diagnosis using genetic mutation analysis may be performed for those Ectodermal dysplasias in which the genetic mutation is known.
- Biopsy of the mucus membranes

- Biopsy of the skin
- Genetic testing

### Commonly Occurring Syndromes<sup>6-9</sup>

#### 1. Hidrotic Ectodermal Dysplasia (Clouston Syndrome)

- Clouston syndrome (or hidrotic ectodermal dysplasia) is characterised by the clinical triad of **nail dystrophy, alopecia, and palmoplantar hyperkeratosis**.
- The disease was first described in the French-Canadian population (in which it is associated with a founder effect), but has since been identified in several other ethnic groups. The exact prevalence is unknown and the syndrome is likely to be underdiagnosed.



**Fig. 2: Showing symptoms of HED (palmoplantar hyperkeratosis)**

- Nail abnormalities like nails are thickened, slow growing, brittle, often hyperconvex and discoloured with striation. Additional reported features include micronychia, onycholysis and recurrent paronychia infections leading to nail loss.
- Palmoplantar hyperkeratosis, alopecia are other symptoms.

#### Causes

Clouston syndrome is transmitted as an autosomal dominant trait and is caused by mutations in the **GJB6 gene (13q12)**,

encoding the gap junction protein connexin 30 (Cx30).

## 2. Ankyloblepharon-ectodermal defects-cleft lip /palate (AEC or Hay-Wells) Syndrome

- Ankyloblepharon-ectodermal defects - cleft lip/palate (AEC) syndrome is an ectodermal dysplasia syndrome with defining features of ankyloblepharon filiforme adnatum (AFA), ectodermal abnormalities and a cleft lip and/or palate. The prevalence of AEC is unknown. A history of skin erosions, especially of the scalp neonatally is typical. Congenital erythroderma occurs in 78%.

- In childhood, other facial features become more apparent and include broad nasal root, hypoplastic alae nasi, short philtrum, thin vermilion border, maxillary hypoplasia and small mandible. Over time, cone-shaped teeth and hypodontia become evident. Other anomalies are limb changes with syndactyly of fingers and toes most common, hypospadias (males 78%) and trismus (less frequently described). Failure to thrive, growth delay and gastrointestinal issues are also common.



Fig. 3: Showing symptoms of AEC (cleft lip)

### Causes

AEC is caused by typically missense mutations in the **Tumor suppressor**

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**gene TP63.** Over 4/5th of the reported mutations occur in the sterile alpha motif domain, and about 1/5th occur in the transactivation inhibitory domain of TP63.

## 3. Ectrodactyly-ectodermal defects (EEC) syndrome

- EEC syndrome (also known as "Split hand-split foot-ectodermal dysplasia-cleft syndrome") is a genetic developmental disorder characterized by ectrodactyly, ectodermal dysplasia, and orofacial clefts (cleft lip/palate). The exact prevalence is not known. More than 300 cases have been described in the literature.



Fig.4: symptoms of EEC (ectrodactyly and syndactyly of the hands)

- The three cardinal signs of the syndrome are ectrodactyly and syndactyly of the hands and feet, cleft lip with or without cleft palate (that can result in speech defects), and abnormalities in several ectodermal structures including skin (i.e. hypopigmented and dry skin, hyperkeratosis, skin atrophy), hair (i.e. fine and sparse hair and eyebrows), teeth (small, absent or dysplastic teeth), nails (nail dystrophy) and exocrine glands (reduction/absence of sweat, sebaceous and salivary glands).

### Causes:

In more than 90% of cases, EEC is due to missense mutations in the sequence of

**the TP63 gene (3q27)** encoding the TP63 transcription factor that is essential for ectoderm and limb development.

#### 4. Rapp-Hodgkin Ectodermal Dysplasia

- Rapp-Hodgkin syndrome (RHS) is characterised by the association of anhidrotic ectodermal dysplasia with cleft lip/palate. The syndrome is usually evident at birth but the prevalence is unknown with less than 100 cases reported in the literature so far.

- Hypospadias in males, obstructed lacrimal puncta or epiphora, and a characteristic facies (maxillary hypoplasia, small mouth, thin upper lip and narrow nose) have also been reported.

##### Causes

- RHS is transmitted as an autosomal dominant trait as is caused by mutations in the gene encoding **the p63 transcription factor** (also known as the **tumor protein p73-like (TP73L) gene, localised to 3q27**).

#### 5. Hypohidrotic Ectodermal Dysplasia

- Hypohidrotic ectodermal dysplasia (HED) (also known as "**Anhidrotic ectodermal dysplasia**," and "**Christ-Siemens-Touraine syndrome**") is characterized by a triad of signs comprising sparse hair (atrachosis/hypotrichosis), abnormal (e.g. conical) or missing teeth (anodontia/hypodontia), and decreased or absent sudation due to a lack of sweat glands (anhidrosis/hypohidrosis) which leads to heat intolerance and may cause recurrent, potentially life-threatening hyperthermic episodes.

- Most of the patients suffer from "dry eye" problems (e.g. chronic conjunctivitis, blepharitis), nasopharyngeal dryness and asthma-like symptoms.

- HED is associated with typical facial features such as a protruding forehead, sparse and fine eyebrows and eyelashes, wrinkles under the eyes, characteristic periorbital hyperpigmentation, a saddle-bridged nose, and hypoplasia of the mandible.

##### Causes:-

- HED is due to mutations in genes of the ectodysplasin/NF- $\kappa$ B pathway, necessary for the correct development of several ectodermal structures.

- Mutations in the EDA, EDAR, and EDARADD genes cause hypohidrotic ectodermal dysplasia. 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.

##### Medical Care<sup>10</sup>

The care of affected patients depends on which ectodermal structures are involved. Note the following:

- For patients with anhidrosis/hypohidrosis, advise air conditioning for home, school, and work. Encourage frequent consumption of cool liquids to maintain adequate hydration and thermoregulation. Finally, advise patients to wear cool clothing.

- For patients with dental defects, advise early dental evaluation and intervention and encourage routine dental hygiene.

- Patients with xerosis or eczematous dermatitis may benefit from the use of topical emollients.

- Patients with severe alopecia can wear wigs to improve their appearance. Use of topical Minoxidil with or without a topical Tretinoin has been shown to



improve hair growth in a small number of patients.

- Patients with scalp erosions should be treated with topical and systemic antibiotics as needed.
- Use artificial tears to prevent damage to the cornea in patients with reduced lacrimation.
- Protect nasal mucosa with saline sprays followed by the application of petrolatum.
- Allogeneic stem cell transplantation has been performed in a small number of patients with autosomal dominant ectodermal dysplasia with immunodeficiency (EDA-ID); poor engraftment and post-transplant complications were common.

### **Surgical Care**

Early repair of cleft lip or palate may lessen facial deformities and improve speech. Other midfacial defects or hand/foot deformities may be surgically corrected in order to improve function and reduce physical disfigurement.

### **CONCLUSION**

In this review the diseases, its causes symptoms & types of Ectodermal Dysplasia has been given. It has been seen that, there is no specific treatment for Ectodermal Dysplasia, only disease management are available. So, we have concluded that further research work has been needed for the treatment of Ectodermal Dysplasia.

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