Makara Journal of Health Research

Volume 25
Issue 3 *December*

Article 9

12-30-2021

Ectodermal Dysplasia: A Review

Yasemin Yavuz
Department of Restorative Dentistry, Faculty of Dentistry, Harran University, Sanlıurfa 63100, Turkey, yyavuz-21@hotmail.com

Mehmet Sinan Doğan
Department of Pediatric Dentistry, Faculty of Dentistry, Harran University, Sanlıurfa 63100, Turkey

Myroslav Goncharuk-Khomyn
Department of Public Health and Humanitarian Disciplines, Medical Faculty, Uzhhorod National University, Uzhhorod 88000, Ukraine, myroslav.goncharuk-khomyn@uzhnu.edu.ua

Recommended Citation
Yavuz Y, Doğan MS, Goncharuk-Khomyn M. Ectodermal Dysplasia: A Review. Makara J Health Res. 2021;25.

Makara J Health Res. 2021;25(3):200–204
doi: 10.7454/msk.v25i3.1305

Makara Journal of Health Research

Ectodermal Dysplasia: A Review

Yasemin Yavuz[1*], Mehmet Sinan Doğan[2], Myroslav Goncharuk-Khomyn[3,4]

[1]Department of Restorative Dentistry, Faculty of Dentistry, Harran University, Sanlıurfa 63100, Turkey
[2]Department of Pediatric Dentistry, Faculty of Dentistry, Harran University, Sanlıurfa 63100, Turkey
[3]Department of Public Health and Humanitarian Disciplines, Medical Faculty, Uzhhorod National University, Uzhhorod 88000, Ukraine
[4]Faculty of Dentistry, Uzhhorod National University, Uzhhorod 88000, Ukraine

Abstract

Background: Ectodermal dysplasia is a complex group of genetic disorders identified through the abnormal development of ectodermal structures. It is a genetic disorder that affects the development or functions of tissues such as the teeth, hair, nails, and sweat glands.

Methods: This review aimed to introduce the outcomes and increase awareness of ectodermal dysplasia reviewing by the literature.

Results: The characteristic features of this disease, including hypodontia, hypohidrosis, and hypotrichosis, have been discussed.

Conclusions: Ectodermal dysplasia is a heterogeneous group of hereditary disorders with similar clinical findings. It leads to the development of tissue malformations and affects the quality of life of the patient. This review demonstrates that dentists can provide viable and safe alternative conventional treatment modalities for oral rehabilitation in patients with ectodermal dysplasia.

Keywords: clinical aspects, dentistry, ectodermal dysplasia

INTRODUCTION

Ectodermal dysplasia (ED) is a congenital, diffuse, nonprogressive, hereditary disorder that was first described by Thurman. It is defined by the abnormal development of two or more structures derived from the embryonic ectodermal layer and is considered as a large, genetically transmitted, rare complex of multisystem disorders. An accurate diagnosis of this condition can help families cope with the situation and seek proper medical care.

This review aimed to describe the possible craniofacial deformities and characteristics of X-linked hypohidrotic ED (XLHED), i.e., hypodontia, hypohidrosis, and hypotrichosis, and to demonstrate the consequences associated with this disease. Additionally, we aimed to increase awareness regarding this condition using clinical images of some of the patients at our hospital.

ED is generally termed as anhidrotic dysplasia, hidrotic ED, and hypohidrotic ED and is categorized into various subgroups.[1–3] The ectoderm, one of the three germ layers present in the developing embryo, gives rise to the central nervous system, peripheral nervous system (eye, ear, and nose sensitive epithelia), sweat glands, hair, skin, nails, teeth, and enamel.[1, 2, 4–6] The EDA gene codes for the ectodysplasin protein, a critical signaling unit involved in the interaction between the ectoderm and the mesoderm 5; this embryological interaction is crucial for the production of several structures that arise from the ectoderm, such as the skin, sweat ducts, nails, hair, and teeth.[1, 5]

Early detection is very important for the management of individual symptoms and to potentially prevent morbidity and mortality associated with hypohidrosis. Additionally, an early diagnosis might prove beneficial during counseling, particularly in light of the clinical trials that are aimed toward improving the treatment of XLHED in-utero.[1]

Manifestations and Types of ED

The extraoral and intraoral manifestations of ED include the following: tooth agenesis (hypodontia and anodontia) with lack of alveolar bone development; conical teeth; hair dystrophy (sparse or absent hair and hypotrichosis); nail dystrophy; a lack of or abnormal functioning of the sweat glands (hypohidrosis); skin problems such as a smooth, dry skin or hyperkeratosis; cranial abnormalities such as a short face, unusual facial concavity, frontal bossing; a depressed nasal bridge (saddle nose); maxillary retrusion and relative mandible protrusion; visual problems; and respiratory issues[1, 4, 7] as shown in Figure 1–10.

***Corresponding author:**
Yasemin Yavuz
Department of Restorative Dentistry, Faculty of Dentistry, Harran University, Sanlıurfa, Turkey
E-mail: yyavuz-21@hotmail.com

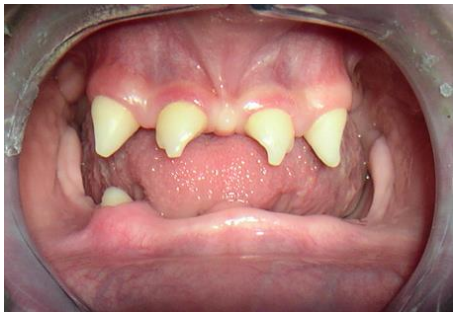

FIGURE 1. Ectodermal dysplasia is characterized by the absence and/or malformation of teeth (from hypodontia to anodontia with conically shaped teeth)

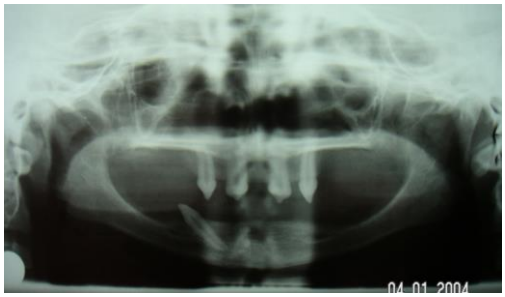

FIGURE 2. Panoramic radiography showing the absence of some permanent teeth and/or malformed conically shaped teeth

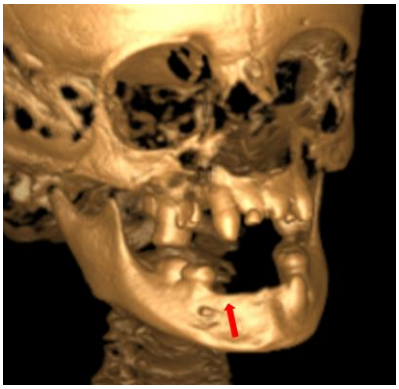

FIGURE 3. Absences of teeth along with the lack of alveolar crest development in the maxillae and mandible in a patient with ectodermal dysplasia

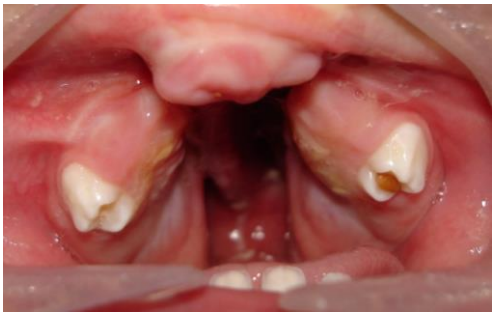

FIGURE 4. Ectrodactyly, ectodermal dysplasia, and cleft lip/palate is characterized by the presence of a cleft lip and palate.

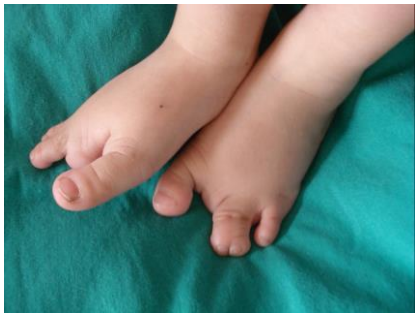

FIGURE 5. Ectrodactyly, ectodermal dysplasia, and cleft lip/palate with syndactyly of the fingers in the feet

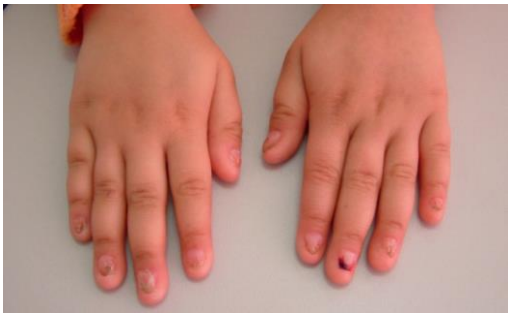

FIGURE 6. An ectodermal dysplasia patient with abnormal nails in the hand

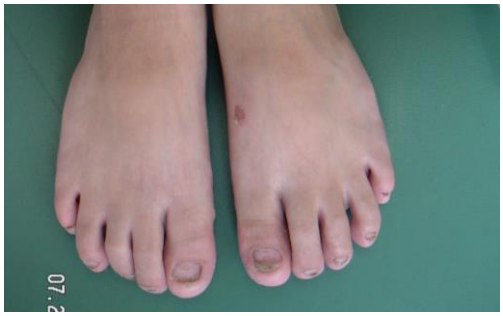

FIGURE 7. An ectodermal dysplasia patient with abnormal foot nails

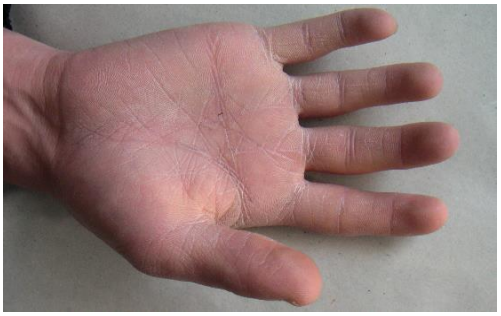

FIGURE 8. Ectodermal dysplasia is characterized by abnormal skin in the hand (dry and cracked).

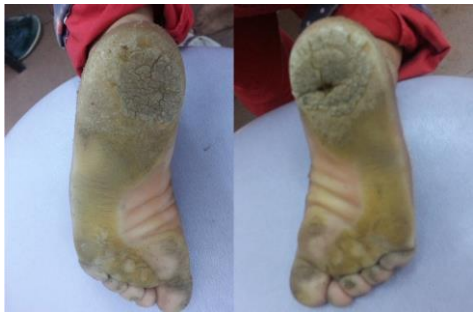

FIGURE 9. An ectodermal dysplasia patient with dry and cracked skin in the feet

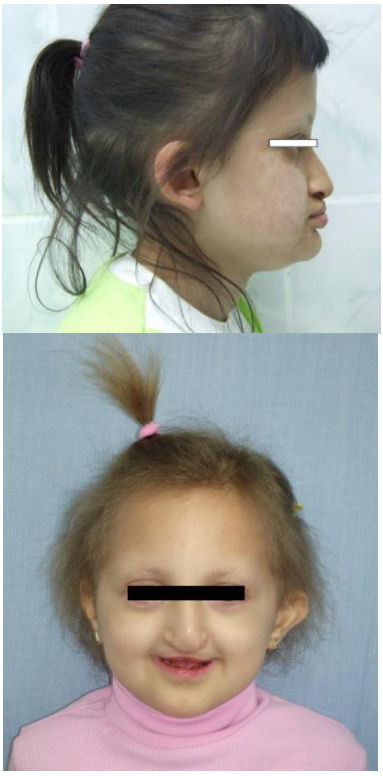

FIGURE 10. Extraoral aspects of patients with ectodermal dysplasia

The earliest recorded cases of ED were described in 1792. Since then, nearly 170–200 different pathological and clinical conditions have been recognized and defined.[1–3] These disorders are considered to be relatively rare with an incidence rate of 1 in 10,000 to 1 in 100,000 births.[2, 8, 9]

The diagnosis of ED is based on the episodes of type of hair, absence of teeth and tooth buds, and tooth morphology. Peeling of the skin at birth, eczema, asthma, and frequent respiratory infections might be additional indications of this disorder. Furthermore, other criteria such as dermatoglyphic analysis, characteristics of lacrimal secretion, and the distribution and pattern of hair in the scalp have been used to diagnose ED. ED is primarily characterized by a partial or complete absence of certain sweat glands (eccrine glands), which results in the lack of or diminished sweating leading to heat intolerance and fever (anhidrosis or hypohidrosis).[1, 2, 4–6]

Classification of Ectodermal Dysplasia

Different forms of ED have been classified according to the functions of the causative genes.[8] Nevertheless, this classification is limited by the relatively low number of causative genes discovered to date and could appear to be somewhat arbitrary because some proteins may be involved in several cellular functions.[8] Genes responsible for at least 30 different types of ED have been identified over the past few decades.[8]

In an attempt to classify the 170–200 different types of EDs, different subgroups have been created on the basis of the presence or absence of the four primary defects[8, 10–12]: ED1, trichodysplasia (hair dysplasia); ED2, dental dysplasia; ED3, onychodysplasia (nail dysplasia); and ED4, dyshidrosis (sweat gland dysplasia). The well-known list of familiar EDs is provided by Ectodermal Dysplasia Society.[13]

The present study included all the major signs observed in patients with ED, such as the presence of sparse hair (trichodysplasia), teeth abnormalities (conical shape and absence); smooth skin (hypohidrosis), abnormal fingers and toenails; skull and facial abnormalities; and pedigree of the patients.[1, 2, 4, 5]

Diagnosis and Treatment of ED

ED is a genetically transmitted rare multisystem disorder. The basic modes of inheritance include new mutations, autosomal dominant, autosomal recessive, and X-linked recessive. According to the medical history and pedigree of the families, it was found that some of the patients were related to each other and presented with similar features, thus confirming the hereditary nature of this disorder. A clinical diagnosis of ED is difficult because the identification of the precise type could be challenging, particularly in the absence of any collaboration between the patient and the different medical specialties.

Steiner's cephalometric analyses have proven useful for examining the presence of maxillary reduction, labial retrusion, chin prominence, nasolabial reinforcement, facial height reduction, and facial concavity. Nevertheless, it should be noted that these measures might be unreliable during tooth agenesis. Partial or total dental agenesis could curb bone growth in the chin.

Due to lack of partial or total bone growth unfortunately, dental implants cannot be used in children.[14–16] They can

be placed only after the bones of the jaw have completed their growth. Discrepancies between the alveolus and the implant are generally due to dentoalveolar growth. The placement of dental implants during the growth period will impede jaw growth and the movement of the teeth into their natural positions within the oral cavity. The earliest recommended ages for dental implants are as follows: at least 15 years for females and 17 years for males.

Implants can be placed in the anterior region of the mandible to support the overdenture from the age of 6 years when the median sutures of the mandible are closed. In adult patients, they can be placed via zygomatic fixation to support the denture in the maxilla, when the dentoalveolar growth is insufficient. Zygomatic surgery can be considered to be a viable and safe alternative to conventional treatment modalities for oral rehabilitation. Nevertheless, clinicians must be aware that zygomatic implant insertion is a difficult procedure and is not risk-free. A highly experienced surgeon with prior special training must perform this procedure for a successful outcome.[5]

Genetic Variabilities in ED

ED is characterized by facial abnormalities, including a prominent forehead, depressed nasal bridge (saddle nose), unusually thick lips, and darkly pigmented skin around the eyes (periorbital and hyperpigmentation). Ectrodactyly–ED–clefting (EEC) is characterized by the presence of a cleft lip and palate, stenosis or atresia of the lacrimal duct systems, ocular complaints (particularly, dry eye symptoms), and syndactyly of the fingers in the hands and toes. EEC is a rare entity associated with mutations in genes that express the protein p63.[17] Patients with ED can present with the following features: prematurely aged appearance; underdeveloped mucous glands of the respiratory tracts; and decreased lung capacity and function, which can potentially increase their susceptibility to recurrent respiratory infections and/or allergic conditions. However, despite the various types of ED described so far, fewer than 30 types have been explained genetically (at the molecular level with the identification of the causative gene).[18]

A multidisciplinary approach and advanced equipment are required for the diagnosis and treatment of this condition. The molecular basis of ED in the light of the most recent advances in molecular biology and has provided a useful tool for diagnosis and research. Approaches to this disorder are based on the functional and molecular findings of genes and the clinical presentations of the related diseases. This clinical functional approach will help in accurately diagnosing the condition and identifying new causative genes. Additionally, it might aid in discovering new molecular interactions among proteins mutated in patients with ED.[19]

Yin *et al*. described a deletion mutation in exon 8 of the EDA (ectodysplasin A) gene as a cause for XLHED.[20] Mutations in the EDA, EDAR, and EDARADD genes result in faulty ectodysplasin A formation, which intercepts the normal interconnection between the ectoderm and the mesoderm and teeth. The improper formation of this ectodermal structure leads to the characteristic features observed in patients with ED.[21] EDA-A1 replacement with EDI200 has been demonstrated to be well tolerated and biologically active in mouse and dog models of XLHED.[22] EDI200, in the early neonatal period, may provide significant and sustained health benefits. A better understanding of the genetic variability in XLHED may relate to the therapeutic response; studies show that we are on the verge of converting a decade of preclinical studies into the first test of a novel paradigm for the rescue and permanent correction of a human developmental disorder.[22]

Role of Dentists

Several types of EDs remain unidentified. Dentists must have better knowledge and understanding of ED before treating the patient to improve their condition. Additionally, they should be aware and experienced regarding the main signs and symptoms of these disorders; moreover, carriers should be identified early for genetic transportation. The molecular diagnosis of a defined group of ED is expected to be feasible and more affordable in the near future. Previous studies, particularly reviews and case series, provide valuable insights into the prevalence, characteristics, and variabilities of the clinical features of ED.[6, 7] These publications provide the clinician with useful information that can be delivered to patients with ED, which could improve the diagnosis and clinical management of those with this disorder.

Dentists have a responsibility to rehabilitate these patients and improve their appearance, masticatory function, and speech. When confronted with multiple dental ageneses, the clinician should look for an association between the signs of ED, because new undedected ED case could also be detected.

CONCLUSIONS

The principal aim of this review was to get experiences for dentists for determine patients who are affected by ED. We believe that this and other similar studies will add to our knowledge and experiences in dealing with for clarity patients with ED. As a result dentists with their increasing knowledge could do diagnosis for undefined ED cases.

ETHICAL APPROVAL

For this study; Approval was obtained from the Harran University Clinical Research Ethics Committee with its decision dated 04.10.2021 and numbered HRU/21.17.21.

ACKNOWLEDGEMENT

The authors would like to thank Ektodermal Displazi Grubu – Türkiye for their contrubution.

CONFLICT OF INTEREST

The authors report no conflict of interest.

FUNDING

None declared.

Received: October 8, 2021 | Accepted: November 18, 2021

REFERENCES

1. Anbouba GM, Carmany EP, Natoli JL. The characterization of hypodontia, hypohidrosis, and hypotrichosis associated with X-linked hypohidrotic ectodermal dysplasia: A systematic review. *Am J Med Genet A*. 2020;182:831–41.
2. Swathi G, Ramesh T, Sravani KB. Ectodermal dysplasia-a report of two cases. *Indian J Clin Dent*. 2020;1:10–3.
3. Itin PH. Etiology and pathogenesis of ectodermal dysplasias. *Am J Med Genet A*. 2014;164A:2472–7
4. Goncharuk-Khomyn M, Yavuz I, Cavalcanti A, Boykiv A, Nahirny Y. Key aspects of dental diagnostics and treatment specifics in ectodermal dysplasia patients: Comprehensive literature review. *J Stomatol*. 2020:73:342–50.
5. Goker F, Grecchi E, Mancini EG, Del Fabbro M, Grecchi F. Zygomatic implant survival in 9 ectodermal dysplasia patients with 3.5- to 7-year follow-up. *Oral Dis*. 2020;26:1803–9.
6. Callea M, Nieminen P, Willoughby CE, Clarich G, Yavuz I, Vinciguerra A, *et al*. A novel INDEL mutation in the EDA gene resulting in a distinct X- linked hypohidrotic ectodermal dysplasia phenotype in an Italian family. *J Eur Acad Dermatol Venereol*. 2016;30:341–3.
7. Yavuz I, Baskan Z, Ulku R, Dulgergil TC, Dari O, Ece A, *et al*. Ectodermal dysplasia: Retrospective study of fifteen cases. *Arch Med Res*. 2006;37:403–9.
8. Lamartine J. Towards a new classification of ectodermal dysplasias. *Clin Exp Dermatol*. 2003;28:351–5.
9. Itin PH. Ectodermal dysplasia: thoughts and practical concepts concerning disease classification - The role of functional pathways in the molecular genetic diagnosis. *Dermatol*. 2013;226:111–4.
10. Deshmukh S, Prashanth S. Ectodermal dysplasia: a genetic review. *Int J Clin Pediatr Dent*. 2012;5:197–202.
11. Priolo M, Laganà C. Ectodermal dysplasias: a new clinical-genetic classification. *J Med Genet*. 2001;38:579–85.
12. Wright JT, Fete M, Schneider H, Zinser M, Koster MI, Clarke AJ, *et al*. Ectodermal dysplasias: Classification and organization by phenotype, genotype and molecular pathway. *Am J Med Genet A*. 2019;179:442–7.
13. The Ectodermal Dysplasia Society. *Alphabetical List of Types of ED*. United Kingdom: The Ectodermal Dysplasia Society, 2021.
14. Kearns G, Sharma A, Perrott D, Schmidt B, Kaban L, Vargervik K. Placement of endosseous implants in children and adolescents with hereditary ectodermal dysplasia. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1999l;88:5–10.
15. Guckes AD, McCarthy GR, Brahim J. Use of endosseous implants in a 3-year-old child with ectodermal dysplasia: case report and 5-year follow-up. *Pediatr Dent*. 1997;19:282–5.
16. Percinoto C, Vieira AE, Barbieri CM, Melhado FL, Moreira KS. Use of dental implants in children: a literature review. *Quintessence Int*. 2001;32:381–3.
17. Meza Escobar LE, Isaza C, Pachajoa H. Síndrome de ectrodactilia, displasia ectodérmica y fisura de labio/paladar, informe de un caso con expresividad variable [Ectrodactyly, ectodermal dysplasia and cleft lip/palate syndrome, report of a case with variable expressivity]. *Arch Argent Pediatr*. 2012;110:e95–8.
18. García-Martín P,Hernández-Martín A, Torrelo A. Displasias ectodérmicas: Revisión clínica y molecular [Ectodermal dysplasias: A clinical and molecular review]. *Actas Dermosifiliogr*. 2013;104:451–70.
19. Priolo M. Ectodermal dysplasias: An overview and update of clinical and molecular-functional mechanisms. *Am J Med Genet A*. 2009;149A:2003–13.
20. Yin W, Ye X, Bian Z. The second deletion mutation in exon 8 of EDA gene in an XLHED pedigree. Dermatol. 2013;226:105–10.
21. Panda SP. Ectodermal dysplasia: An overview. Indian J Forensic Med Toxicol. 2020;14:9071–4.
22. Huttner K. Future developments in XLHED treatment approaches. *Am J Med Genet A*. 2014;164A:2433–6.