Amelogenesis imperfecta: a literature review based guide to diagnosis and management

Amelogenesis imperfeita: um guia baseado em revisão de literatura para diagnóstico e tratamento

Amelogénesis imperfecta: una guía basada en la revisión de la literatura para el diagnóstico y el tratamiento

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ABSTRACT
Amelogenesis imperfecta (AI) is a hereditary disorder which alters the enamel formation of the teeth by exhibiting the changes in quality and quantity of the enamel. The varieties of clinical presentations range from hypoplastic, hypomaturation to hypocalcified with the combination of different genetic mutations. It can present in both deciduous and permanent dentitions. The diagnosis of AI depends on clinico-pathological correlation by excluding other structural disorders of enamel such as fluorosis and chronological hypoplasia. Therefore, the knowledge of AI is related to its clinical features, radiological and histological findings, genetic mutations and treatment options are utmost important during the management of AI. The following review article will address the diagnostic and management perspectives of AI.

KEYWORDS: Amelogeneses. Dental enamel. Dentistry.

RESUMO
A amelogênese imperfeita (AI) é uma desordem hereditária que altera a formação do esmalte dos dentes, exibindo as mudanças na qualidade e quantidade do mesmo. As variedades de apresentações clínicas variam de hipoplásica, hipomaturação a hipocalcificada com a combinação de diferentes mutações genéticas. Pode se apresentar tanto na dentição decídua quanto na permanente. O diagnóstico de AI depende da correlação clínico-patológica, excluindo outras desordens estruturais do

esmalte, como fluorose e hipoplasia cronológica. Portanto, o conhecimento da AI está relacionado às suas características clínicas, achados radiológicos e histológicos, mutações genéticas e opções de tratamento são de extrema importância durante o manejo da AI. O seguinte artigo de revisão abordará as perspectivas de diagnóstico e gerenciamento da AI.

PALAVRAS-CHAVE: Amelogênese. Esmalte dentário. Odontologia.

RESUMEN

La amelogénesis imperfecta (AI) es un trastorno hereditario que altera la formación del esmalte de los dientes al exhibir los cambios en la calidad y cantidad del esmalte. Las variedades de presentaciones clínicas van desde hipoplásicas, hipomaturación hasta hipocalcificadas con la combinación de diferentes mutaciones genéticas. Puede presentarse tanto en dentición temporal como permanente. El diagnóstico de AI depende de la correlación clínico-patológica al excluir otros trastornos estructurales del esmalte como la fluorosis y la hipoplasia cronológica. Por lo tanto, el conocimiento de la AI está relacionado con sus características clínicas, los hallazgos radiológicos e histológicos, las mutaciones genéticas y las opciones de tratamiento son de suma importancia durante el manejo de la AI. El siguiente artículo de revisión abordará las perspectivas de diagnóstico y manejo de la AI.

PALABRAS CLAVE: Amelogénesis. Esmalte dental. Odontología.

INTRODUCTION

A fundamental knowledge with regard to improving the diagnosis and management of AI is uttermost important to achieve the good clinical outcomes. The aim of this study was to review the literature on diagnosis and management of AI. The following electronic flat forms were used to search the literature from 1945-2018: the Scientific Electronic Library Online, biomedical journal literature of the National Library of Medicine (MEDLINE/PubMed), Research gate, and Google scholar. The search was limited to the articles in English language. Out of 315 articles, only 77 articles were included to carry out this review. Rest of the other articles were excluded due to minimize the repetition of some findings.

LITERATURE REVIEW

AI is defined as an inherited disorder which affects the quality and quantity of the enamel which is ectodermally derived portion of the teeth with the absence of systemic manifestations. The prevalence varies approximately from 1:700 to 1:14,000, according to the populations studied[1-2]. AI is also known as hereditary enamel dysplasia, hereditary brown enamel and hereditary brown opalescent teeth[3].

AI has been classified according to its clinical presentations and genetic manifestations. These four major phenotypes have been further divided into 15 subtypes based on the mode of inheritance. In addition, many classifications have been proposed by different scientists based on its phenotype[4-5], based on the phenotype and mode of inheritance[2,6-10], based on the clinical, microradiographic and histopathological findings[11], based on molecular defect, biochemical result, mode of inheritance, phenotype[12-13], and based on molecular defect sub-classification of the AMELX conditions[14].

Hypoplastic type has been identified as the most common type representing 60-73% of all cases[15] (Figure 1). This type of AI occurs as a result of a defect in the first stage of enamel matrix formation. Due to lack of enamel matrix deposition, clinically it mimics the thin enamel with yellowish-brown, rough or smooth, flat occlusal surfaces of the posterior teeth due to attrition, and with/without grooves and/pitting[16]. Although the enamel is thin it will be mineralized properly. Radiographically it reveals thin enamel with normal radio-density with clear demarcation from dentine[17]. Histologically the hypoplastic type shows a disturbance in differentiation or viability of ameloblasts and it is reflected as defects in matrix formation or total absence of matrix[18-19]. Different types of hypoplastic AI are described in Figure 2.

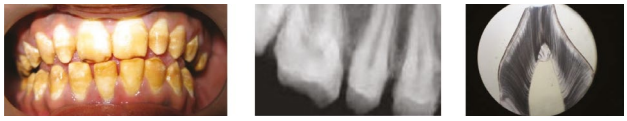

Figure 1 - Clinical, radiographical and histological features of hypoplastic AI.

Type	Variant	Mode of inheritance	Characteristic features	Radiographic features
IA	Generalized pitted	AD	Pinpoint to pinhead-sized pits which are scattered across the surface of the teeth affecting buccal surface more severely, stained and arranged in rows or columns. The enamel between the pits is of normal thickness, hardness, and coloration and normal contact between teeth	Normal radiographic contrast of enamel and dentin
IB	Localized pitted	AD	The affected teeth may demonstrate either horizontal rows of pits, a linear depression or one large area of hypoplastic enamel surrounded by a zone of hypocalcification. Middle third of the buccal surfaces of the teeth is mainly affected, leaving incisal and occlusal surface intact	Normal radiographic contrast of enamel and dentin
IC	Localized pitted	AR	It is more severe and typically demonstrates the involvement of all teeth in both dentitions	Normal radiographic contrast of enamel and dentin
ID	Diffuse smooth	AD	The crown with thin, hard, glossy and smooth enamel, altered shape, opaque white to translucent brown color, anterior open bite and open contact between teeth	The teeth exhibit a thin peripheral outline of radiopaque enamel
IE	Diffuse smooth	XLD	Male: Diffuse thin, smooth and shiny enamel in both dentitions, yellowish brown, altered the shape of crown, open bite and open contact between teeth Female: Vertical furrows of thin hypoplastic enamel, alternating between hands of normal thickness	Male: A peripheral outline of radiodense enamel Female: The banding often is detectable with dental radiographs
IF	Diffuse rough	AD	The thin enamel denser then smooth type, hard and rough-surfaced, white to yellow-white, taper teeth toward the incisal-occlusal surface, open contact points and anterior open bite	Thin peripheral outline of-radio-dense enamel
IG	Enamel agenesis		Total absence of enamel, causing shape of crown by rough dentin, yellow-brown hue which taper toward the incisal-occlusal surface, open contact points and anterior open bite	No peripheral enamel overlying the dentin with absence of eruption of many teeth with significant resorption

AD: Autosomal dominant, AR: Autosomal recessive, XLD: X-linked dominant, XLR: X-linked recessive, AI: Amelogenesis imperfecta.

Figure 2 - Variation of hypoplastic.

Hypomaturation type of AI has been reported 20-40% out of all AI cases[15] (Figure 3). Unlike in hypoplastic type, the enamel matrix protein is normal in this type. However, the maturation process of the enamel crystal structure is defective. Therefore the enamel matrix is immature. Clinically it manifests as mottled yellowish-brown with opaque discoloured/snow coloured crown. The crown is normal in size and shape. Since the enamel is poorly mineralized, the enamel can be easily penetrated if it is probed by a dental probe. Radiographically it shows the normal thickness of the enamel and radiodensity is less than that of dentin[17]. Histologically it appears with altered enamel rod and rod sheath structures[18-19]. Different types of hypoplastic AI are described in Figure 4.

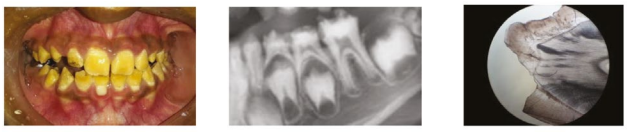

Figure 3 - Clinical, radiographical and histological features of hypomaturative AI.

Type	Variant	Mode of inheritance	Characteristic features	Radiographic features
IIA	Diffuse pigmented	AR	The enamel surface is mottled, agar-brown and soft enough to be punctured by a dental explorer	The affected enamel exhibits a radiodensity that is similar to dentin
IIB	Diffuse pigmented	XLD	Male: The deciduous teeth are opaque with translucent mottling while the permanent teeth are opaque yellow-white and may darken with age The enamel tends to chip and often call be pierced with a dental explorer point Female: Vertical bands of white opaque, translucent enamel are random and asymmetric	Male: The contrast between enamel and dentin is reduced Female: The bands are not detectable
IIC	Snow-capped	XLD/XLR	Features are similar in male and female, i.e., a zone of white opaque enamel on the incisal or occlusal one-quarter to one-third of the crown affecting both deciduous and the permanent dentitions	The contrast between enamel and dentin is reduced
IID	Snow-capped	AD	Similar to snowcapped X-linked	The contrast between enamel and dentin is reduced

AD: Autosomal dominant, AR: Autosomal recessive, XLD: X-linked dominant, XLR: X-linked recessive, AI: Amelogenesis imperfecta.

Figure 4 - Variation of hypomaturative AI.

Hypocalcified type can occur due to deficient calcification processes in amelogenesis. However, the enamel matrix is laid down appropriately. Therefore, clinically, the erupted teeth are in proper shape with very soft and friable enamel. With the age, coronal enamel is chipped off more than a cervical portion. During the early stages, the tooth will appear in yellowish-brown or in orange colour. With time the colour of teeth changes to brown or black with the deposition of calculi. Hypocalcified type represents about 7% of AI cases reported in literature[15] (Figure 5). Radiographically enamel is less radiopaque then dentin[17-19].

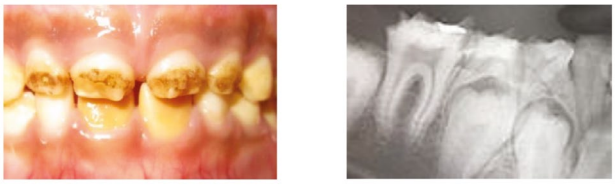

Figure 5 - Clinical, radiographical and histological features of hypocalcified AI.

Hypomaturation-hypoplastic with taurodontism, cases exhibited thin, mottled yellow to brown, and pitted enamel. While molar teeth show taurodontism, other teeth have enlarged pulp chambers[18-19](Figure 6). Different types of hypoplastic-hypomaturation AI are described in Figure 7. Furthermore, Tricho-dento-osseous (TDO) syndrome is a rare, autosomal dominant disorder principally characterised by curly hair at infancy, severe enamel hypomineralization and hypoplasia and taurodontism of teeth, sclerotic bone, and other defects[20].

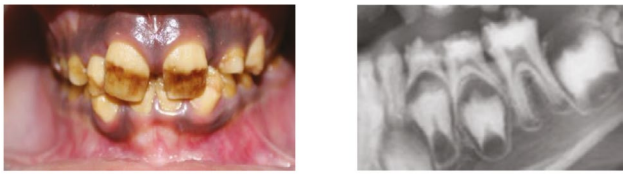

Figure 6 - Clinical, radiographical and histological features of hypomaturation-hypoplastic AI.

Type	Variant	Mode of inheritance	Characteristic features	Radiographic features
IVA	Hypomaturation-ypoplastic with taurodontism	AD	Hypomaturation is a major defect than hypoplastic The enamel appears as mottled yellow-white to yellow-brown with pits on the buccal surfaces	The enamel appears similar to dentin in density. Large pulp chambers with varying degrees of taurodontism can be seen
IVB	Hypoplastic-hypomaturation with taurodontism	AD	Hypoplasia is a major defect	Decrease in the thickness of the enamel remaining similar to the hypomaturationy-poplastic variant

AD: Autosomal dominant, AR: Autosomal recessive, XLD: X-linked dominant, XLR: X-linked recessive, AI: Amelogenesis imperfecta.

Figure 7 - Variation of hypomaturative AI with taurodontism.

Patterns of Genetic Mutations in AI

The genes which can be mutated are summarized in Figure 8. The different types of AI phenotypes can be manifested as a result of several modes of genotypes[58-60]. They can be represented as an AD: autosomal dominant, AR: autosomal recessive, XLD: X-linked dominant, XLR: X-linked recessive or sporadic inheritance (Figures 2, 4 and 7).

Gene	Mutation of the gene results (References)
Amelogenin (AMELX)	X-linked AI[21-28]
Enamelin (ENAM)	AD AI[29-33]
Ameloblastin (AMBN)	AD hypoplastic AI[34-36]
KLK4	AR AI[37]
MMP20	AR AI[38-42]
DLX3	AD AI hypoplastic-hypomaturation with taurodontism[43]
WDR72	AR hypomaturationamelogenesis[44-45]
FAM83H	Hypocalcified AI with AD AI[46-49]
C4orf26	AR AI[50]
SLC24A4	AR hypomaturation AI[51-52]
ITGB6	AR AI, pitted hypomineralized AI[53-55]
LAMB3	Hypoplastic AD AI[56-57]

Figure 8 - Different gene mutation in AI.

Other Clinical Manifestation of AI

According to the literature AI can be associated with other dental and skeletal abnormalities such as agenesis of teeth, anterior open bite, attrition, crown and root resorption, delayed eruption, dens in dente, microdontia, pulp stones, taurodontism and tooth impaction[61-63].

Furthermore, concluded that there was a significant acceleration of dental age in AI children about 1.13 ± 0.78 years compared with normal children and a six-fold increase in the tendency of impaction of the permanent teeth and follicular cysts[61]. Further, had found that the main complaints of AI patients were dissatisfaction with the appearances of their teeth, extreme dental sensitivity, the presence of dental caries and other orthodontic problems[63].

AI with taurodontism is found to be associated with tricho-dento-osseous syndrome with hypoplastic enamel that occurs with hypomaturation/hypocalcification defects[64].

Clinical Management of AI

The clinical management can be divided into four phases as an emergency, prevention, stabilization and definitive treatments. The clinical diagnosis of AI can be obtained by asking four questions according as follows[65].

1. Has anyone else in the family had anything like this?
2. Has there been anything in the patient's medical history which might have caused sufficient metabolic disturbance to affect enamel formation?
3. Are all the teeth affected in a similar manner?
4. Is there a chronological distribution to the appearance of the defect?

The investigations and treatment planning are depending on the clinical complaints of the patients and the restorative challenges in related to the AI patients such as psychosocial problems, low self-esteem, poor oral hygiene, chronic gingivitis, dentine sensitivity, caries, discolouration, loss of occlusal vertical dimension, large pulp to crown ratio and decreased bond strength of resin to enamel[66].

Most of the AI patients are reported to the dentists when dental caries or sensitivity is severely affected[16]. Considering all the aspects, if the patient is presented with pain or discomfort, priority should be given to relieve them during the emergency phase. Sometimes, the solution may be a restoration as a first step[16].

In the prevention phase attention should be focused on habit intervention, dietary advice/counseling, introducing fluoridated mouthwashes and topical fluoride, and to improve oral hygiene. Maintaining good oral hygiene is a challenge for the patients due to sensitivity while brushing and therefore they can be advised to use warm water for tooth brushing[67-71].

During the stabilization phase, emphasis should be to prevent or minimize further damage to the existing dentition. It could be included temporary restorations, fissure sealant or necessary extractions.

Definitive treatment depends on the age of the patient, type of the dentition, the severity of the condition and other associated dental problems. Definitive restorations are basically provided to improve the current condition and aesthetics as well as stop the further deteriorations. They can be range from minimal intervention to invasive procedures. The treatment options include bleaching and micro-abrasion, crown lengthening, direct or indirect composites, porcelain veneers, crowns, metal onlays, removable dentures, implants and orthodontic treatments[16,66-72]. Some of the reported clinical diagnosis and management of AI in literature are summarized in Figure 9.

Research/case study	Number of patients	Type of AI	Clinical management
Koruyucu et al. 2014[68]	31	All types	Prevention Restorations Orthodontics
Ortiz et al. 2019[73]	1	Hypomaturation	Diagnostic and provisional phase (pediatric dentistry and orthodontics) Restorative phase (prosthodontics, orthodontics, endodontics, and periodontics) Maintenance (prosthodontics and periodontics)
Cantekin et al. 2016[74]	1	Hypoplastic	Correction of OVD (SS crowns) Anterior aesthetics (Composites) Maintenance
Dursun et al. 2016[75]	2	Hypocalcified	Pain managements Endodontics Stainless steel crowns (molars) Anterior aesthetics (Composites)

Figure 9 - Literature summary of AI clinical management.

DISCUSSION

AI is a developmental, often inherited disorder, affecting dental enamel and usually occurs in the absence of systemic features. It comprises of diverse phenotypic entities like extrinsic disorders of tooth formation, chronological disorders of tooth formation and localized disorders of tooth formation[76]. Therefore, that should be considered in the differential diagnosis. The commonest differential diagnoses are dental fluorosis, chronological enamel hypoplasia and tetracycline stains.

The radio-graphical and histopathological investigations along with the clinical appearance lead to rule out the other conditions from AI. According to the literature the all genetic diseases, the final classification will be based on genetic mutation and the resulting biochemical abnormality in each family. Several investigators have suggested a classification system based on the phenotype and pedigree, combined with a scanning electron microscopic examination, biochemical methods, and molecular genetics.

The varying etiology of AI conjures a wide array of clinical features whose restorative management poses a challenge for dentists. As both esthetics and function are compromised in these patients, their management usually involves complete oral rehabilitation by way of full coverage crowns, direct and indirect veneers, and bonded esthetic restorations, depending on the condition of the individual tooth and the age of the patient[36].

AI can have an extremely negative functional and emotional impact on Patients that may include pain and difficulty in eating as well as social avoidance, distress and low self-respect. Dental care can be challenging and prolonged[77]. The prime goal of treatment is to approach each concern as it presents with an overall comprehensive plan that outlines anticipated future treatment needs. It is essential that clinicians treating children and adolescents with AI understand and solve the clinical and emotional demands of these disorders with understanding.

CONCLUSION

AI directly affects the appearance of enamel and cause dentin sensitivity which will lead to patients being unable to maintain good oral hygiene. Thus, these patients' psychological wellbeing and quality of life will deteriorate. Therefore, to fix back their smile a proper clinical and radiological evaluation, genetic mapping, and proper treatments planning are mandatory. For that, dental professionals must be aware of all the possible and available treatment options for AI patients.

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