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Tooth Agenesis in Clinical Practice: A review of Case Reports

Michael Dany[1], Ameta Primasari[2], Ervina Sofyanti[3*], Sry Suryani Widjaja[4], Thantrira Porntaveetus[5]

[1]*Faculty of Dentistry, Universitas Sumatera Utara, Medan, 20155 Indonesia*
[2]*Department of Oral Biology, Faculty of Dentistry, Universitas Sumatera Utara, Medan, 20155 Indonesia*
[3]*Department of Orthodontics, Faculty of Dentistry, Universitas Sumatera Utara, Medan, 20155 Indonesia*
[4]*Department of Biochemistry, Faculty of Medicine, Universitas Sumatera Utara, Medan, 20155 Indonesia*
[5]*Center of Excellence in Genomics and Precision Dentistry, Department of Physiology, Faculty of Dentistry, Chulalongkorn University, Bangkok 10330, Thailand*
[*]Corresponding Author: ervina.sofyanti@usu.ac.id

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ABSTRACT

Tooth agenesis (TA) relates to multiple congenital dental disorder and the most prevalent developmental disorders affecting approximately 200 million people globally. The management of TA require interdisciplinary dental approaches. Therefore, this study aimed to conduct a case report evaluation of TA based on population and ethnicity. This scoping reviews based on Preferred Reporting Items for Systematic Reviews and Meta-Analyses, has been registered in Open Science Framework. Relevant articles were retrieved from Proquest, Science Direct, PubMed, and SpringerLink databases with keywords comprising of 'Prevalence' AND 'Tooth Agenesis' AND 'Nonsyndromic or Syndromic'. From 2014 to 2024, there were only five non-syndromic tooth agenesis case reports were included to be reviewed. The review of multiple case reports of tooth agenesis demonstrated significant variability in clinical and radiography evaluation involving inheritance pattern. By early identification in mixed dentition, the comprehensive and individualized treatment approaches are required to address both esthetics and functional outcomes. Further population-based studies of genetic involvement in TA can contribute early detection of malocclusion.

Keywords: Prevalence, Tooth Agenesis, Non-syndromic

ABSTRAK

Agenesis gigi berkaitan dengan salah satu kelainan gigi bawaan dan memengaruhi sedikitnya 200 juta orang di seluruh dunia. Penatalaksanaan agenesis memerlukan pendekatan kedokteran gigi interdisipliner. Penelitian ini dilaksanakan untuk mengevaluasi laporan kasus agenesis gigi berdasarkan populasi dan etnis. Cakupan tinjauan berdasakan analisis PRISMA dan meta analisis, telah didaftarkan dalam Open Science Framework berdasarkan laporan kasus yang berhubungan dengan agenesis gigi. Pencarian artikel dilakukan menggunakan database Proquest, Science Direct, PubMed, dan SpringerLink dengan kata kunci yang terdiri dari 'Prevalensi' DAN 'Agenesis Gigi' DAN 'Nonsindromik atau Sindromik'. Dari tahun 2014 hingga 2024, hanya ada lima laporan kasus agenesis gigi non-sindromik yang disertakan untuk ditinjau. Tinjauan beberapa laporan kasus agenesis gigi menunjukkan variabilitas yang signifikan dalam evaluasi klinis dan radiografi yang melibatkan pola pewarisan. Dengan identifikasi dini pada gigi campuran, pendekatan perawatan yang komprehensif dan individual diperlukan untuk mengatasi hasil estetika dan fungsional. Studi berbasis populasi lebih lanjut tentang keterlibatan genetik dalam TA dapat berkontribusi pada deteksi dini maloklusi.

Kata kunci: Prevalensi, Agenesis Gigi, Non-sindromik

1. Introduction

Tooth agenesis (TA) is a multiple congenital dental disorder that remarkable esthetic challenging case and can be individual life-altering. This teeth anomaly is divided into hypodontia, oligodontia, and anodontia. The diagnosis of hypodontia occurs in cases of partial tooth loss, with one to six teeth absent, while oligodontia is used to describe the missing more than six teeth, exclude the third molar. The most severe is anodontia that characterized by total edentulism [1–3].

Clinical implications associated with tooth agenesis include cases of functional disturbances and malocclusion, often necessitating an interdisciplinary and multidisciplinary treatment approach. It is also important to consider potential secondary complications, such as bone loss, altered tooth migration during orthodontic treatment, and challenges in maintaining oral hygiene. The variable expression of the trait indicates a polygenic pattern of inheritance, influenced by epistatic gene interactions and environmental factors. Notably, some cases of anodontia may occur independently of any associated syndromic conditions [4,5]. Some TA diseases might manifest as either nonsyndromic or syndromic, constituting an important issue related to the quality of life. In addition, abnormal masticatory function, altered speech, and aesthetic issues, particularly the absence of anterior teeth have been reported. Other issues caused by TA include emotional disturbances [1,6–8].

As one of most prevalent growth disorders in humans, TA has been reported affecting approximately 200 million people globally. It affects both the primary and permanent dentition, with a higher frequency observed in permanent teeth [9]. The missing of distal or lingual proliferation of tooth bud cells partly originating from the dental lamina, related to biological basic of congenital missing of permanent teeth. Trauma, hormonal imbalance, irradiation, tumors, rubella infection, or exposure to thalidomide—as well as from hereditary genetic factors, or a combination of both, categorized as environmental factors. *MSX1* and *PAX9* genes are essential in the early 0stages of tooth development. *PAX9* as a paired domain transcription factor and plays a pivotal role in odontogenesis which link to nonsyndromic forms of tooth agenesis [10]. In permanent dentition, the third molars has become most frequently missing teeth, after the second mandibular premolars or maxillary lateral incisors that can unilateral or bilateral [11].

Kazanci et al. examined the prevalence of various developmental dental abnormalities among the population in North East Turkey and reported that the rates of hypodontia was 4.74%, oligodontia was 0.25%, and hyperdontia was 1.30% [12]. In a separate study involving 2,413 orthodontic patients in University hospital at Turkey demonstrated hypodontia prevalence was 7.54% [13]. Additionally, Altug Atac and Erdem reported that prevalence of hypodontia, oligodontia, and hyperdontia (affecting incisors and premolars) was 2.63%, 0.13%, and 0.36% respectively among Turkish children between 1978 to 2003[14]. Data for hypodontia worldwide, excluding the third molar, in both genders, vary from 0.3% in the Israeli population [15] to 11.3% in Slovenian [16], 6.3% in Kenyan [17], and 11.2% among Koreans [18] In orthodontic Mexican patients, there was a lower prevalence of hypodontia (2.7%) [19]. The different rates reported could be attributed to different measurement approaches, other methodologies, and ethnic backgrounds. Therefore, this study was conducted to a case report evaluation of TA based on population and ethnicity.

2. Materials and Methods

2.1. Study question

This scoping review was conducted to address following question:

What is the distribution and characteristic of TA case reports among different populations in several countries between 2014 and 2024?

2.2. Study design

A scoping review was conducted to obtain the list of prevalences in different countries associated with syndromic and non-syndromic TA.

2.3. Protocol

This review was carried out following PRISMA-ScR and the entire process was registered with the Open Science Framework to facilitate open access and ensure integrity and transparency. The structure of the

study question was conducted according to Population, Intervention, Comparison, and Outcome (PICO) method:

Table 1. PICO table of the research

P	Population	Individuals with nonsyndromic tooth agenesis
I	Intervention	Genetic screening
C	Comparison	Individuals affected or unaffected by non-syndromic tooth agenesis
O	Outcome	Prevalence of nonsyndromic tooth agenesis cases

2.4. Search strategy and eligibility criteria

Article searches were performed on June 25, 2024 using Proquest, Science Direct, PubMed, and SpringerLink databases with keywords comprising 'Prevalence' AND 'Tooth Agenesis' AND 'Non-syndromic or Syndromic'. The exclusion criteria were articles that could not be accessed, grey literature, articles considered irrelevant, and those with methodological design contrary to the inclusion criteria.

2.5. Study selection and data extraction process

All identified articles were exported to Mendeley, for easy removal of duplicates. The abstracts and titles were then selected and filtered. To assess eligibility according to the exclusion and inclusion criteria, full-text publications were downloaded, then the review was updated with the remaining articles. The inclusion criteria included TA ranging 2014 to 2024.

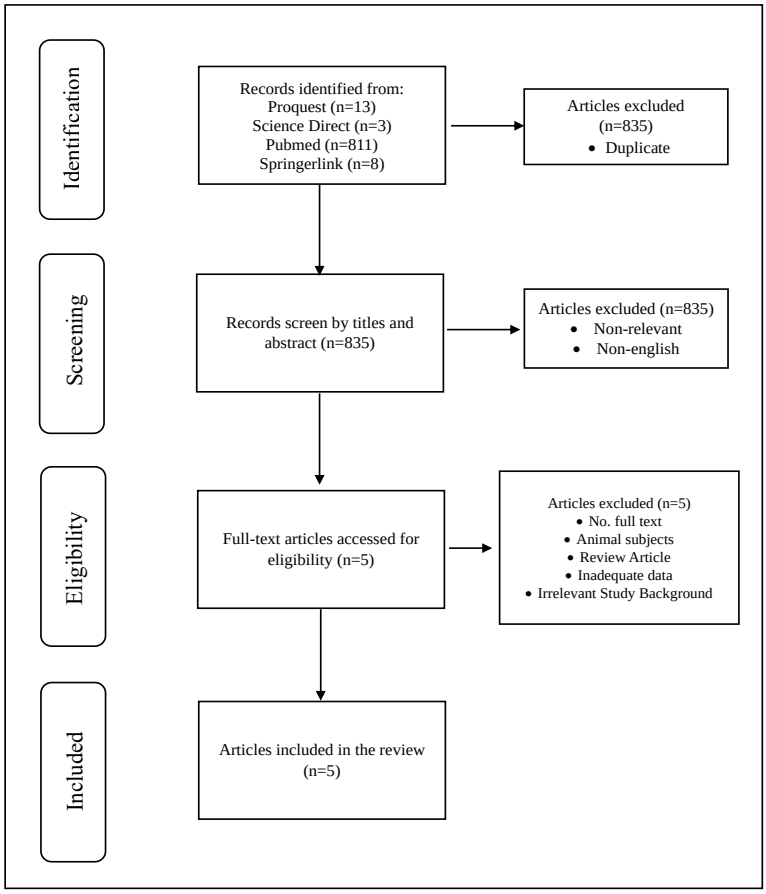


Figure 1. PRISMA Flowchart of the Scoping review

3. Results

There were only five articles were deemed eligible for qualitative review since 835 articles that were retrieved through the scoping review protocol using the PICO method and screened by two independent reviewers (MD and ES). The qualitative assessment was conducted independently, taking into consideration factors such as open-access status, duplication, PICO relevance, and reviewer subjectivity. A full-text assessment was carried out on these articles, leading to the inclusion of five articles reported about NSTA in China, Saudi Arabia, India, Germany, and Romania sub-population (Figure 1).

First case reported a 4 year old girl, Saudi sub-population diagnosed with nonsyndromic and nonfamilial oligodontia (Figure 2) [20]. Second case reported a 24 year old woman Indian subpopulation diagnosed with nonsyndromic and nonfamilial oligodontia (Figure. 3) [21] Third case reported about two brothers who are German sub-population diagnosed nonsyndromic and familial oligodontia. (Figure 4a and 4b) [22]. Fourth case reported a 5 year old boy who are Chinese sub-population diagnosed with nonsyndromic and nonfamilial oligodontia. (Figure 5) [23]. Fifth case reported a family in Romanian sub-population which are a 40 year old man diagnosed with nonsyndromic hypodontia a 12 year old daughter diganosed with nonsyndromic and familial hypodontia, and a 44 year old woman diagnosed with nonsyndromic and familial hypodontia. (Figure 6a-c) [24]

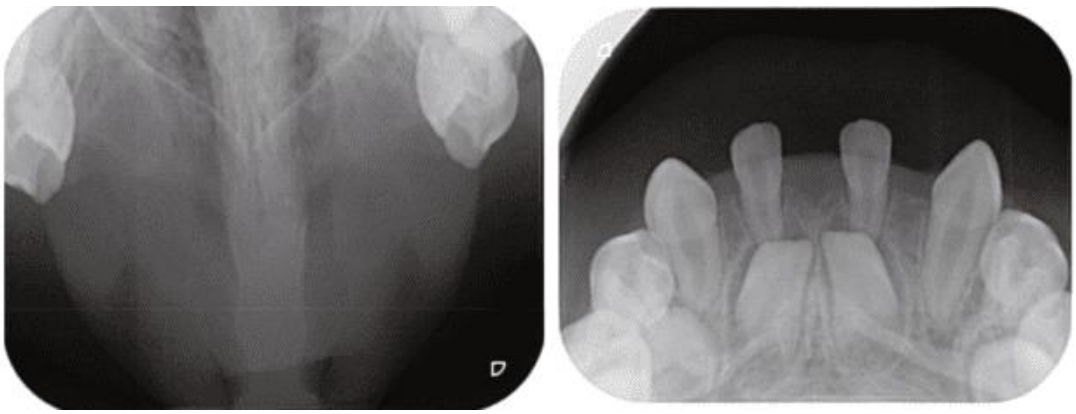


Figure 2. Occlusal view radiography of both the maxillary and the mandibular of the nonsyndromic oligodontia patient [20].

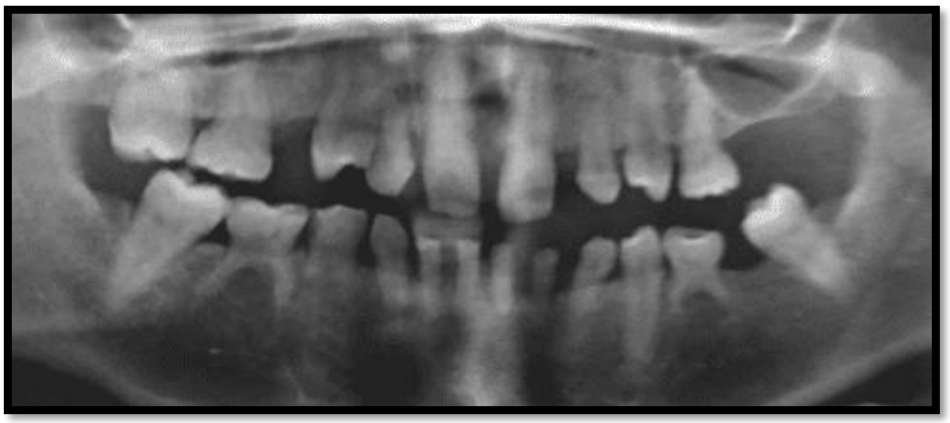


Figure 3. Radiography of nonsydromic oligodontia patient (teeth missing: 12, 13, 15, 17, 18, 22, 23, 25, 26, 27, 28, 31, 32, 33, 35, 37, 38, 41, 42, 43, 44, 45, 47, 48) [21]

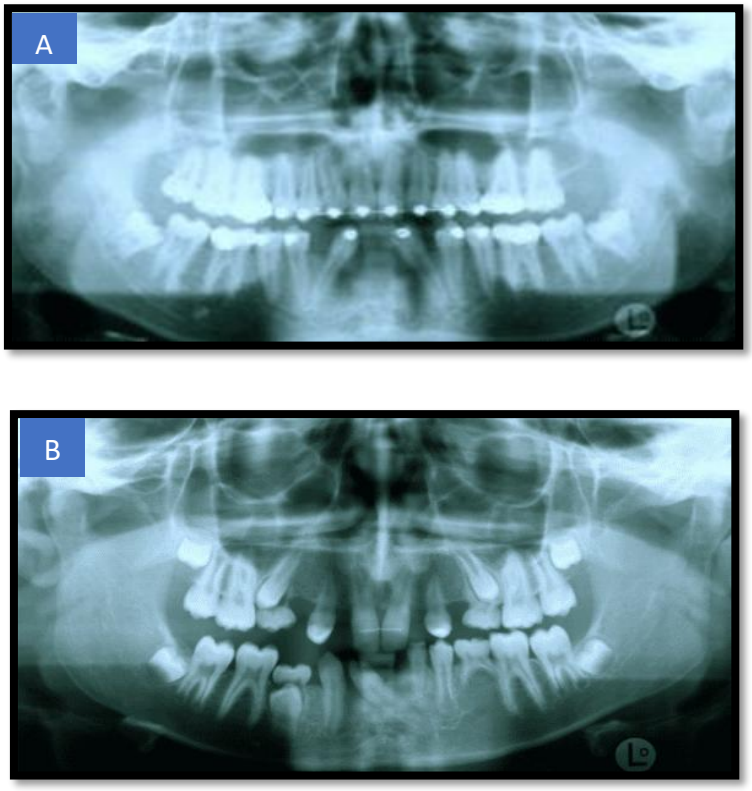


Figure 4. Radiographic of nonsydromic oligodontia patient. A. Missing permanent teeth: 12,13,14,22,23,24,32,35,42,45; B. Missing permanent teeth: 12,13,14,22,23,24,31,32,35,41,42,45 [22].

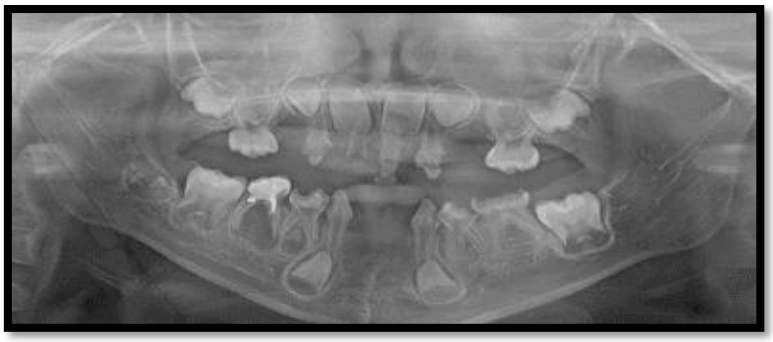
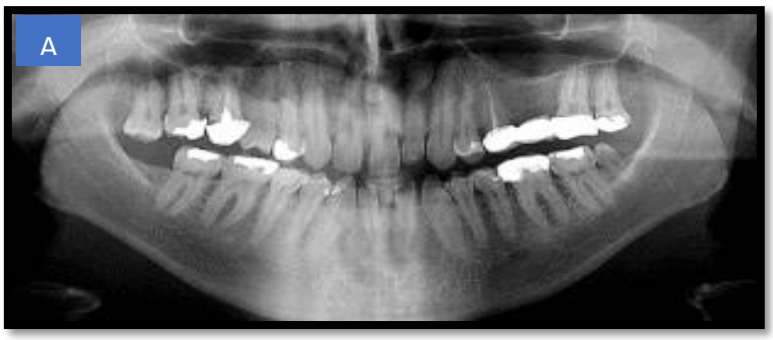


Figure 5. Radiography of nonsyndromic oligodontia patient with 16 permanent tooth germ absent [23]



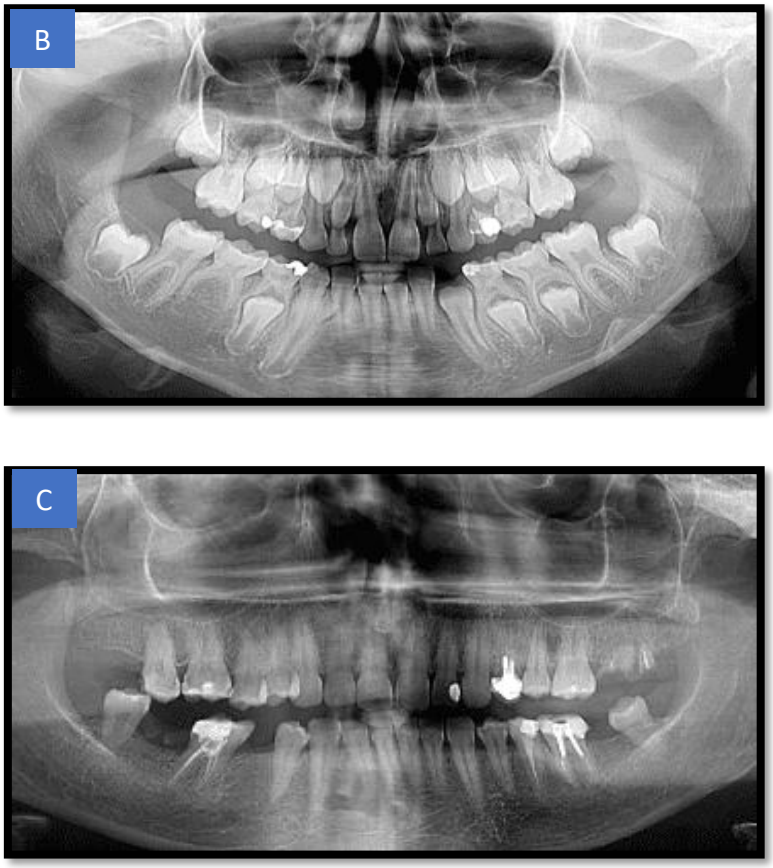


Figure 6. Radiographic of a Romanian sub-population family with unique case of tooth agenesis **A.**Radiograph of nonsyndromic hypodontia [24], **b.** Radiograph of nonsyndromic and familial hypodontia [24], **c.** Radiograph of nonsyndromic and familial hypodontia [24]

4. Discussion

This case report review can made as a starting point for developing new hypotheses or designing more comprehensive studies on the early detection of TA based on ethnicity. This review reported five cases on TA from Asia (Saudi Arabia, China, India), and then from Europe (Germany and Romania), with all cases being nonsyndromic oligodonti. with all cases being nonsyndromic oligodontia. Generally, the occurrence and types of missing teeth have been the subject of numerous studies in the literature. Since TA reports showed unique cases with variance diagnosis and treatment approaches. Even though there were also many case reports in the literature screening, five case reports met the eligibility criteria. There were 2 cases with nonsyndromic familial tooth agenesis and 3 with nonsyndromic nonfamilial tooth agenesis.

Among the five cases above, agenesis cases cannot be considered trivial, whether syndromic or nonsyndromic, unilateral or bilateral. In general, agenesis can affect the condition of the oral cavity comprehensively. Patients with TA problems experience difficulty with masticatory function, aesthetics, or psychology which example are disrupt bite alignment, affect speech, and lead to functional and aesthetic problems, impacting chewing, swallowing, and appearance. For the interdisciplinary management, treatment often requires the expertise of multiple specialists, including orthodontists for tooth movement, prosthodontists for restorations, and potentially surgeons for implant placement. Patient with TA need orthodontic treatment may involve closing spaces created by missing teeth or opening spaces for future restorations, and can be a crucial component of treatment for tooth agenesis. Some patients with TA require restorative options like bridges, dentures, or implants may be necessary to replace missing teeth and restore function and aesthetics. These review case reports also demonstrated a significant impact on a person's self-esteem and confidence, highlighting the importance of comprehensive treatment and psychological support. The adequate genetic assessment and counseling in accordance with the patient's consent related to dental treatment approaches. This is important for early detection and prevention as exemplified in case 3[25], and different comprehensive treatments including in first, second, third, and fifth case.

This review presents cases that show the probable congenital absence of teeth, specifically in the second lower premolars, mandibular central incisors, and maxillary lateral incisors. Five cases were examined to determine whether congenital dental disorders occur more often on one side (unilaterally) or on both sides (bilaterally). In some studies, a unilaterally elevated frequency of missing teeth has been reported, while a bilaterally elevated frequency has been reported in others. Differences can be attributed to racial disparities among the populations under analysis. The primary challenge in the management of congenital missing teeth is determining the most effective therapeutic protocol. To preserve the deciduous tooth in the dental arch and to protect it from occlusal trauma and abrasion, some studies recommend odontal care for missing solitary teeth. When a lower premolar is absent, other forms of treatment are recommended. The first course of action would be to remove the temporary molar and use orthodontic treatment to close the gap. An additional course of treatment includes maintaining the temporary molar in the dental arch for an extended period of time and a prosthetic or implant-based restoration. However, when complications arise with the temporary molar, such as resorption or ankylosis extraction, oral rehabilitation is required using alternative methods.

Among the five cases above, the cases of agenesis cannot be considered trivial, whether syndromic or non-syndromic, unilateral or bilateral. In general, agenesis can affect the condition of the oral cavity in a comprehensive way. Patients with TA problems experience difficulty with masticatory function, aesthetics, or psychology. Therefore, this condition must be handled seriously, both by anamnesis, complete examination, comprehensive treatment, and, when necessary, adequate genetic assessment and counseling according to the patient's consent. This is important for early detection and prevention, as exemplified in Case 3 [25], and different comprehensive treatments including Cases 1, 2, 4, and 5.

Previous studies, particularly those conducted before 2014 only reported the prevalence of agenesis taken from racial and ethnic demographics, but did not show diagnostic procedures and treatment strategies.In this review, after the search following prismSCR, only five case reports identified TA. Therefore, clinicians and specialists should consider reporting TA in the future to educate others who may encounter such cases.

The major limitation of several case report review is the absence of controlled experimental designs that related to proper case-report guidelines, which impedes the ability to attribute outcomes exclusively to a specific treatment or intervention. In the future, the systematic preparation of case report can emphasize a comprehensive anamnesis and meticulous clinical examination. It will be essential for the development of robust datasets to support research on genotype-phenotype correlations.

5. Conclusion

The review of multiple case reports of tooth agenesis demonstrated significant variability in clinical and radiography evaluation involving inheritance pattern. By early identification in mixed dentition, the comprehensive and individualized treatment approaches are required to address both esthetics and functional outcomes. Further population-based studies of genetic involvement in TA can contribute early detection of malocclusion. Recognizing the variability in TA is essential for developing appropriate interdisciplinary orthodontic management strategies and establishing effective treatment protocols. Further investigation into the genetic factors of TA across populations may contribute to the early malocclusion diagnosis.

6. Acknowledgements

We sincerely thank the authors for their willingness to share their case reports and be grateful to the Directorate of Internationalization and Global Partnerships of Universitas Sumatera Utara.

7. Conflict of Interest

The author declares that there is no conflict of interest.

8. Funding

Nil.

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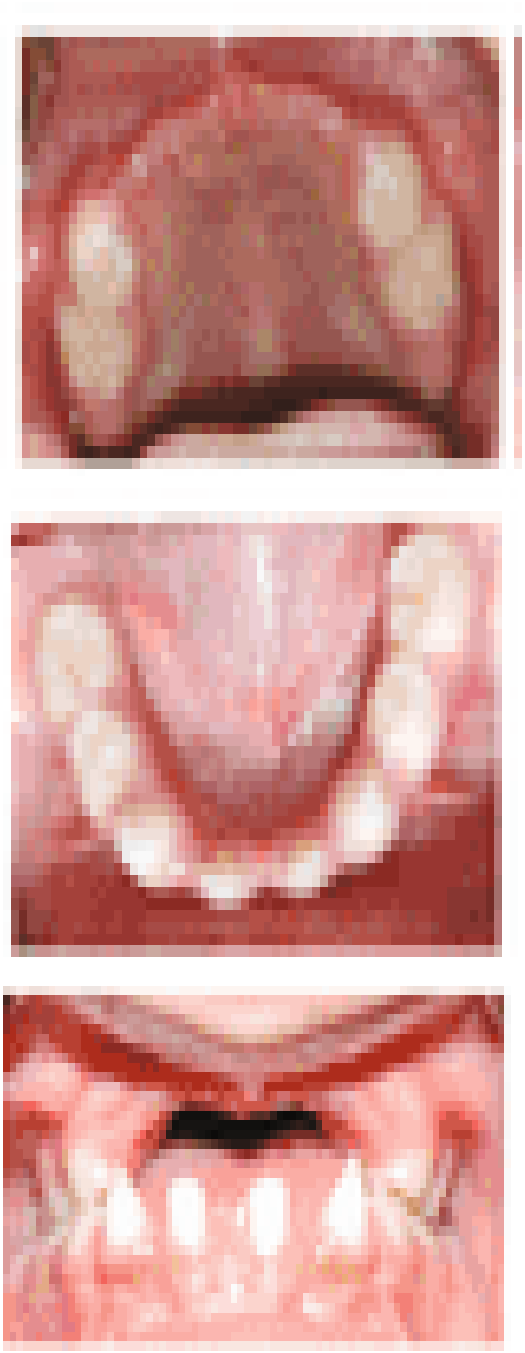
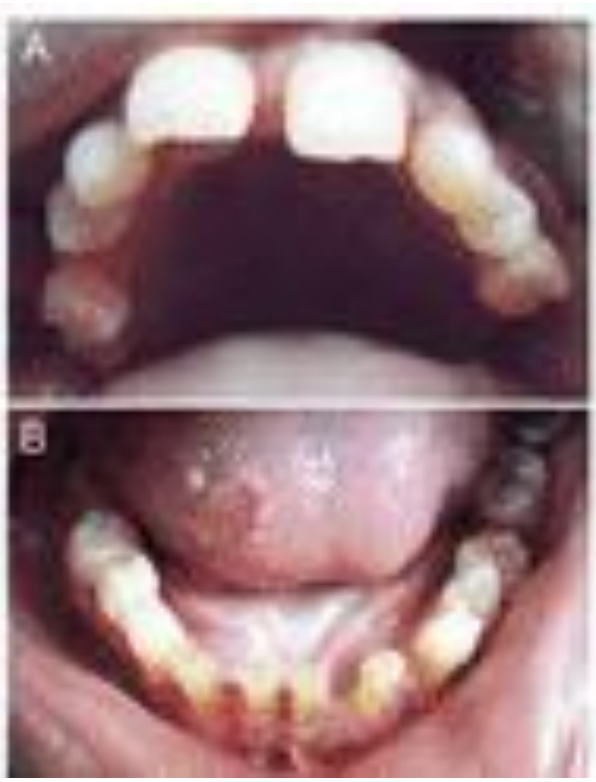
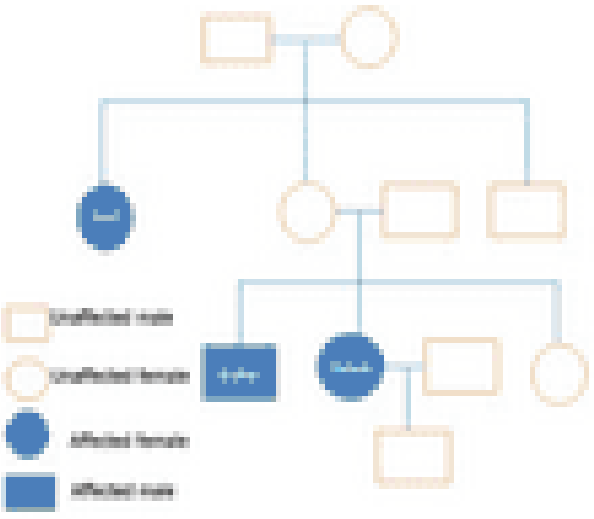
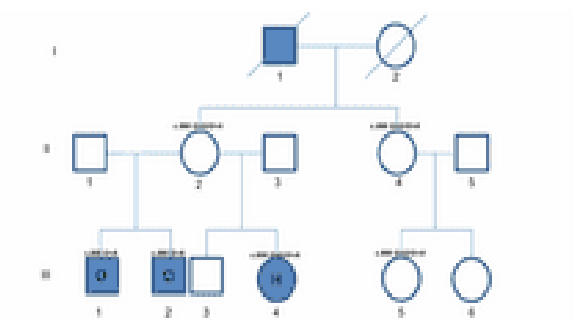
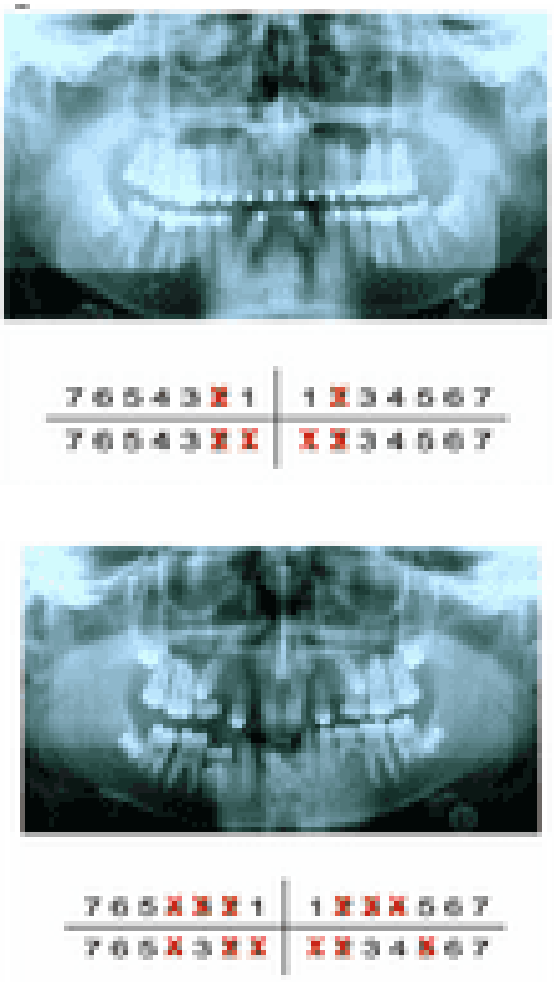
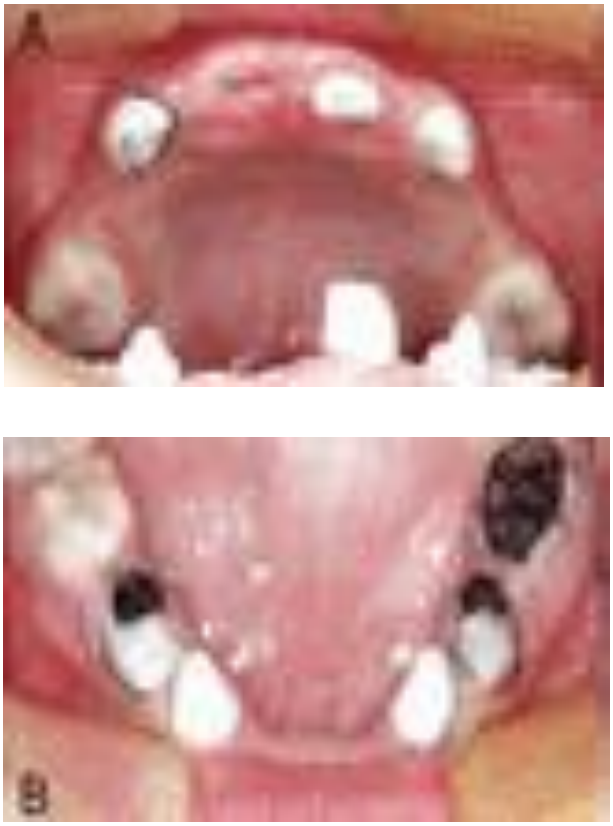
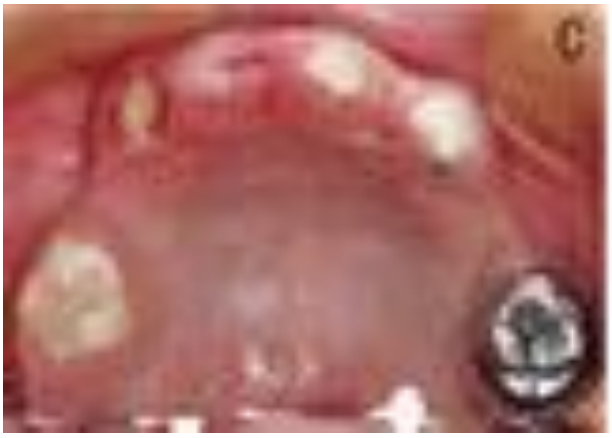
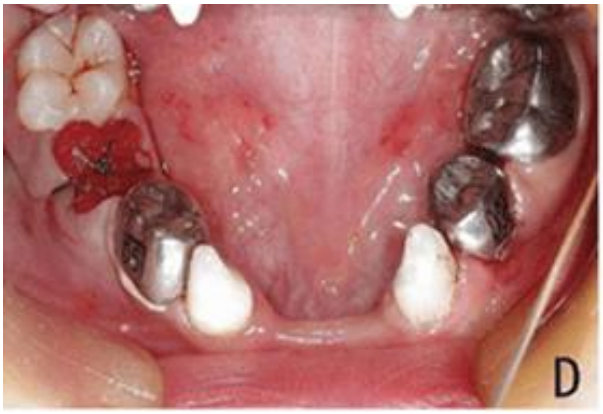
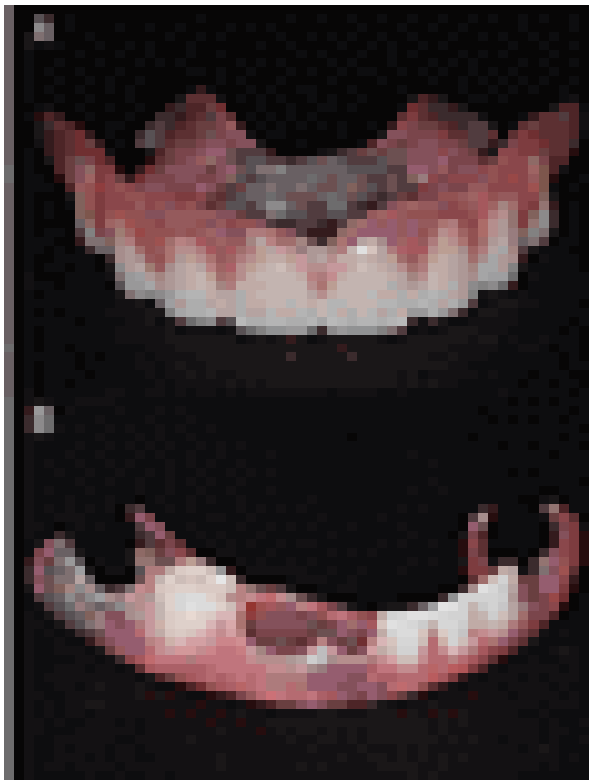
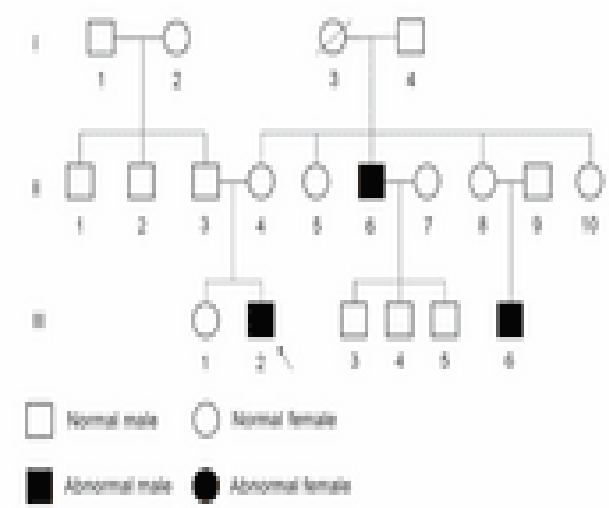
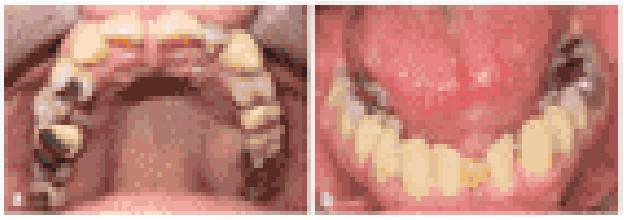
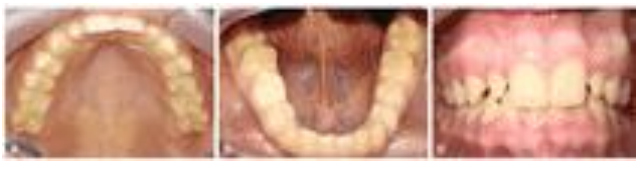
Appendix

No.	Case	Intraoral Photograph	Intervention
1.	Al-Ahmadi A, Assiry A, Khan S, Marya A, Venugopal A, Karobari M. Use of a Modified Nance Appliance for Esthetic Rehabilitation of a Child Patient with Rare Nonfamilial and Nonsyndromic Oligodontia. Case Rep Dent. 2021:1-6.		A modified fixed Nance appliance with artificial anterior teeth was planned for esthetic rehabilitation.

2.	Shaik Mohamed Shamsudeen SS, Nalin Kumar S, Sujatha G, Muruganandhan J. Non syndromic familial tooth agenesis-A case report and overview of genetic factors. J Oral Maxillofac Surg Med Pathol. 2015;27(1):140–2	 	No dental intervention
3.	Ruiz-Heiland G, Jabir S, Wende W, Blecher S, Bock N, Ruf S. Neue Missense-Mutation im EDA-Gen in einer von Oligodontie betroffenen Familie. Journal of Orofacial Orthopedics. 2016;77(1):31–8.		Genetic examination

			
4.	Ouyang T, Chen D, Ma Z, Li X, Cao G, Lin L, et al. Treatment strategy for patient with non-syndromic tooth agenesis: a case report and literature review. BMC Oral Health. 2024;24(1):80.		Tooth #51 was extracted under local infil tration anesthesia in the clinic. 10 affected teeth were treated under dental general anesthesia. Teeth #53, #61, #63, and #73 went for root canal therapy (RCT) and were filled with GIC. Tooth #55 was filled with composite resin.

		  	Tooth #65 had a large defect in the distal surface after caries removal, so we restored it with a stainless steel crown (SSC). Teeth #74, #75, and #84 were restored with SSC after RCT. Finally, tooth #85 was extracted due to poor prognosis after RCT. The patient came back to the clinic three months later with positive feedback. The Department of Prosthodontics recommended a transitional removable partial denture to restore the patient's oral functions. Ho Oral hygiene instructions were given.

		 	
5.	Margarit R. Nonsyndromic familial hypodontia: rare case reports and literature review. Rom J Morphol Embryol. 2019(4):1355–60.	  	No dental or medical intervention