INTERNATIONAL JOURNAL OF HEALTH & MEDICAL RESEARCH

ISSN(print): 2833-213X, ISSN(online): 2833-2148

Volume 05 Issue 09 September 2026

DOI : 10.58806/ijhmr.2026.v5i9n02

Page No. 877-880

Mandibulofacial Dysostosis (Treacher Collins Syndrome): Aetiopathogenesis, Clinical Features and Multidisciplinary Management

Güldeste AYDIN[1], Betül YAZMACI[2], Mehmet Sinan DOĞAN[3]

[1,2,3]Harran University, Faculty of Dentistry, Pediatric Dentistry

ABSTRACT

Treacher Collins syndrome (TCS) is a rare genetic disorder caused by mutations in TCOF1, POLR1C, POLR1D or POLR1B, which trigger neural crest cell apoptosis and bilateral craniofacial malformations of the branchial arches. Key clinical manifestations include malar and mandibular hypoplasia, microtia, hearing impairment, and severe dental anomalies such as tooth agenesis, malocclusions, and elevated caries risk. The resulting anatomical narrowing frequently causes severe upper airway obstruction and complicates anesthetic airway management. Optimal outcomes rely on an early, coordinated multidisciplinary approach—integrating vital airway interventions, staged reconstructive surgeries, mandibular distraction osteogenesis, and proactive pediatric dental care to restore function, aesthetics, and long-term quality of life.

KEYWORDS: Mandibulofacial Dysostosis; Treacher Collins Syndrome; Multidisciplinary Care.

INTRODUCTION

Treacher Collins syndrome (TCS) is rare, genetically caused condition that adversely affects bone development in the head and face. First described in the medical literature in 1889 by the ophthalmologist Edward Treacher Collins in a case report of a patient with lower eyelid anomalies, the condition was clinically characterised in detail by Adolphe Franceschetti and David Klein in 1940. This syndrome, which is primarily characterised by underdevelopment of the jaw and facial bones, is also known as Franceschetti–Klein syndrome in recognition of the contributions of these researchers (1,2) . Occurring in roughly 1 per 50,000 live births, the condition shows an equal gender distribution, with spontaneous mutations accounting for 60% of instances and the remainder following an inherited familial pattern. (3,4).

Pathogenic variants underlying TCS, predominantly transmitted via an autosomal dominant pattern, disrupt first and second pharyngeal arch morphogenesis bilaterally. While TCOF1 represents the predominant causative gene, mutations in POLR1C and POLR1D also contribute to its clinical manifestation (5). Treacher Collins syndrome, which exhibits a genetically heterogeneous structure, has four distinct subtypes described in the literature. The clinical forms of the syndrome are classified according to the underlying mutations: TCS1 is caused by pathogenic variants in the *TCOF1* gene, TCS2 by those *in the POLR1D gene*, and TCS3 by those in the *POLR1C* gene. It has been shown that mutations in the *POLR1B* gene, identified in recent years, are responsible for the most recent form of the syndrome, the TCS4 subtype (6).

The basis of the pathogenesis, however, lies in the haploinsufficiency of the TCOF1 gene, located at 5q32-q33.1, which plays a critical role in the survival of neural crest cells. Deficiency of the Treacle protein disrupts the biogenesis of mature ribosomes. It has been reported that this is essential for craniofacial growth, particularly the fusion of the frontonasal protrusions and the branchial arches in the embryo. Mutations in the TCOF1 gene, which forms part of the rRNA biogenesis mechanism, lead to the early apoptosis of neural crest cells—a multipotent, migratory cell population that gives rise to bone, tendon, neuron, glial, melanocyte, connective, endocrine and adipose tissue—and result in the development of the syndrome (7,8) .

In Treacher Collins syndrome, genetic diagnosis can be established with over 95% accuracy through linkage analysis in families with multiple affected members. For postnatal diagnosis, a blood sample is taken from the affected individual for DNA analysis. During the antenatal period, in addition to blood samples from the family, invasive procedures are also utilised. DNA is isolated from foetal cells via chorionic villus sampling in the 10th–11th weeks of pregnancy or via amniocentesis in the 16th–17th weeks (9) .

Craniofacial manifestations in TCS typically present as bilateral, symmetrical hypoplasia originating from defective first and second pharyngeal arch morphogenesis (3). Clinically, these features are categorized into major and minor manifestations based on their prevalence. Major characteristics, seen in roughly 78% of patients, prominently feature downward-slanting palpebral fissures (89–100%), zygomatic/malar underdevelopment (81–97%), bilateral conductive auditory deficits (83–92%), and micrognathic/retrognathic mandibular hypoplasia (78–91%). This structural jaw defect imparts a characteristic "bird-like" facies

and increases the vulnerability of neonates to posterior upper airway compromise. Less frequent (secondary) findings occur in 24–77% of cases and encompass external auditory canal stenosis/atresia (68–71%), microtia (10–77%), lower lid colobomas (54–69%), and expressive language delays (57–63%), whereas cognitive capacity is characteristically preserved (10–12) .

In cephalometric and radiological assessment, an increased frontonasal angle and a pronounced mandibular antegonial notch are considered characteristic findings of the syndrome. The mandible is hypoplastic in the ramus, body and jaw projection, and the jaw, which is rotated inferiorly with a wide gonial angle, gives the mandible a bow-shaped appearance(13) . In computed tomography (CT) scans, hypoplasia or aplasia of the condyles and coronoid process, marked curvature of the lower border of the mandible, and the concave curvature of the horizontal ramus—which is considered pathognomonic—are notable; the maxilla is narrow, and the palate is high or narrow (5). Consequently, temporomandibular joint (TMJ) dysfunction is prevalent in this population and frequently manifests as restricted mandibular mobility and limited mouth opening (14). The associated intraoral spectrum is broad, frequently featuring generalized dental diastemas, crowding and tooth malalignment, enamel hypoplasia, and TMJ dysplasia. Furthermore, affected individuals often present with dental midline discrepancies, Angle Class II or Class III malocclusions, and cranial-base-related maxillary retrognathism or prognathic discrepancies (6) .

Dental anomalies are reported in approximately 60%of children with TCS, and an average of 1–8 anomalies may be observed per patient. Hypodontia represents the most prevalent dental anomaly, occurring in approximately 33% of patients, with mandibular second premolars most commonly missing, followed by maxillary second premolars, lateral incisors, and maxillary canines. Other documented odontogenic variations include impacted maxillary hyperdontia, ectopic eruption of first permanent molars in the maxilla, and structurally defective, malpositioned maxillary central incisors. In addition to limiting mastication, speech and mouth closure functions, these anomalies may also be accompanied by systemic conditions such as hearing, vision and respiratory problems, as well as obstructive sleep apnoea. Additional systemic manifestations, such as cardiac defects, thumb anomalies and cryptorchidism, have also been reported in this syndrome (10,15,16) . Insufficient bone mass leads to dental crowding and malocclusion, whilst delayed tooth eruption and multiple caries-like lesions are also documented in recent case series. Furthermore, reduced salivary flow resulting from salivary gland pathology is observed in these patients. This factor, together with other contributing factors such as mouth breathing, malocclusion and a soft diet, creates a predisposition to a high incidence of dental caries (6,9,12) . These patients may have physiological limitations regarding swallowing and chewing; furthermore, the presence of inflamed and painful oral tissues associated with periodontitis can further complicate adequate calorie intake and oral hygiene practices, thereby reducing quality of life. Furthermore, children with special needs frequently use paediatric medicines containing high levels of sugar, which also poses a serious cariogenic threat. For all these reasons, it is reported that this group of patients requires regular and early dental care to prevent the observed pathologies and limit their severity (17) .

Airway obstruction in TCS is multi-level and complex; it has been reported that approximately 46% of individuals with the syndrome have airway obstruction ranging from mild obliteration to life-threatening obstructive sleep apnoea. Three-dimensional analyses have shown that the total upper airway volume is reduced by approximately 30%, with the most pronounced narrowing occurring in the retroglossal region; mandibular projection has been found to show a negative correlation with airway volume(2,3) . In children, obstructive sleep apnea syndrome (OSAS) is documented to cause developmental delay and cognitive dysfunction, resulting in compromised executive functions and poorer academic performance relative to unaffected controls. Furthermore, untreated apneic episodes drive significant cardiometabolic morbidities irrespective of patient age, making timely diagnosis and structured therapeutic interventions essential (18) .

The primary issue with TCS in anaesthetic management is a difficult airway; difficulties with visualisation may be encountered during mask ventilation and endotracheal intubation, and it has been reported that the Cormack-Lehane score deteriorates with age. A review comprising the anaesthesia records of 240 patients from various centres reported that 40% of patients required a technique other than direct laryngoscopy for endotracheal tube placement; supraglottic airway devices were found to be effective without any ventilation failures, and video laryngoscopy was reported to improve the Cormack-Lehane score (19) . High scores for mandibular retrusion and ramus hypoplasia show a strong correlation with difficult airway management; in severe cases, tracheostomy dependence may develop(20) . It has been reported that airway management is the priority at birth. In severe cases where the airway is compromised, a tracheostomy may be required to overcome obstruction secondary to glossoptosis and mandibular retrognathia. The tracheostomy may need to remain in place until adequate mandibular growth is achieved or distraction osteogenesis is performed to allow airflow through the oral cavity (21) .

In dentistry, this situation necessitates planning treatment under general anaesthesia, particularly in non-cooperative paediatric patients. The literature emphasises that, due to limited mouth opening, fibre-optic intubation is preferred over a laryngeal mask and GlideScope, and that dyspnoea and cyanosis may develop during recovery (22) . It is therefore reported that a comprehensive perioperative assessment and airway management plan must be carried out prior to any dental procedure in patients with TCS (19) . Patients with TCS must undergo audiological testing and early hearing assessment by a specialist. It is recommended that speech therapy, bone-conduction amplification and the use of hearing aids be initiated at an early age to facilitate the development of communication skills. Reconstruction of the orbital and zygomatic complexes is typically undertaken between the ages of 5 and 7.

Nonetheless, invasive skeletal remodeling carries substantial risks of morbidity and perioperative complications. As an alternative strategy, less invasive aesthetic modalities can be employed to partially disguise mandibular retrognathia and midfacial hypoplasia (23) .

Successful TCS management relies on sustained, multi-specialty intervention involving craniofacial and plastic surgery, otolaryngology, orthodontics, medical genetics, speech therapy, and psychology. Treatment regimens incorporate diverse surgical procedures, including cleft palate closure, zygomatic bone augmentation, and auricular/auditory canal reconstruction, working in tandem with soft-tissue cosmetic surgery and extensive orthodontic therapy (24). Lower eyelid notches or colobomas predispose patients to ocular dryness and elevated infection risks, frequently necessitating corrective surgical procedures. Furthermore, reconstructive operations may be indicated to augment zygomatic volume, correct nasal or mandibular deficiencies, or rebuild the external ear (25) .

As distraction osteogenesis—the preferred method in TCS treatment, which provides a better quality of life—is carried out in conjunction with pre- and post-operative orthodontic treatment, an experienced, multidisciplinary team comprising orthodontists and maxillofacial surgeons is essential to achieve successful outcomes. Indeed, the improvement in cosmetic appearance offers these patients the opportunity to lead a more fulfilling social life (26) . Based on their clinical experience, craniofacial surgeons prefer to perform the initial distraction surgery between the ages of 8 and 10, followed by definitive orthognathic surgery in late adolescence where possible. The primary reason for this preference is that mandibular distraction osteogenesis (MDO) performed at an early stage in patients with TCS is associated with high relapse rates and the need for repeated distraction (20) .

CONCLUSİON

Treacher Collins syndrome presents a complex clinical picture, affecting craniofacial structures, airway patency and orofacial functions in a multifaceted manner due to genetically based neural crest cell pathologies. In the management of the syndrome, each stage—ranging from vital airway stabilisation in the neonatal period through to early hearing and speech rehabilitation, and from staged reconstructive and distraction surgeries to preventive dental follow-ups—is of critical importance. In particular, dental procedures planned under general anaesthesia—due to the high risk of caries, anatomical limitations and potential difficult airway conditions—require a meticulous perioperative assessment. Consequently, optimising functional competence, aesthetic appearance and psychosocial quality of life in individuals with TCS is only possible through the adoption of a long-term, multidisciplinary treatment protocol involving coordinated collaboration between paediatric dentists, orthodontists, surgeons and relevant medical specialists.

REFERENCES

1) Guo P, Pan B, Jiang H, Yang Q, He L, Lin L. Prevention methods for Treacher Collins syndrome: A systematic review. International Journal of Paediatric Otorhinolaryngology. 2020 Jul;134:110062. doi:10.1016/j.ijporl.2020.110062
2) Ulhaq ZS, Nurputra DK, Soraya GV, Kurniawati S, Istifiani LA, Pamungkas SA, et al. A systematic review on Treacher Collins syndrome: between molecular geneticand clinical severity. . Clinical Genetics. February 2023;103(2):146–55. doi:10.1111/cge.14243
3) Aljerian A, Gilardino MS. Treacher Collins Syndrome. Clinics in Plastic Surgery. April 2019;46(2):197–205. doi:10.1016/j.cps.2018.11.005
4) Marszałek-Kruk BA, Wójcicki P, Dowgierd K, Śmigiel R. Treacher Collins syndrome: genetics, clinical features and management. Genes. 2021 Sep 9;12(9):1392. doi:10.3390/genes12091392
5) Khatiwada A, Thapa B, Pandit R, Bhandari D, Kc S. Imaging of Treacher Collins syndrome: A case report. Radiology Case Reports. 2025 Jan;20(1):593–6. doi:10.1016/j.radcr.2024.10.042
6) C D, Cardoso I L. Treacher Collins syndrome and its implications for the oral cavity. Clin Res Trial. 2019;5(5). doi:10.15761/CRT.1000278
7) Dixon J, Jones NC, Sandell LL, Jayasinghe SM, Crane J, Rey JP, et al. Tcof1- /is required for neural crest cell formation; deficiencies in proliferation lead to craniofacial abnormalities. Proc Natl Acad Sci USA. 5 September
8) School of Dentistry/ University of Sulaimani, Sulaimanya, 053 Iraq, Gataa I. Oral and Dental Malformations Associated with Treacher Collins Syndrome. jmscr. 2015 Oct 5. doi:10.18535/jmscr/v3i10.02
9) Nassar JY, Kefi F, Alhartani MM, Sultan AA, Al-Khatib T, Safdar OY. Treacher Collins syndrome: A comprehensive review on clinical features, diagnosis, and management. Journal of Family Medicine and Primary Care. 2024 Oct;13(10):4165–72. doi:10.4103/jfmpc.jfmpc_851_24
10) Bartzela TN, Carels C, Maltha JC. Update on 13 syndromes affecting craniofacial and dental structures. Front Physiol. 2017 Dec14;8:1038. doi:10.3389/fphys.2017.01038
11) Pan Z, Xu H, Chen B, Tian Y, Zhang L, Zhang S, et al. Treacher Collins syndrome: : A and retrospective analysis of Chinese patients. . Molec Gen & Gen Med. 2021 Feb;9(2):e1573. . doi:10.1002/mgg3.1573

12) Camarillo-Benitez S, Mendez-Catala CF, Chima-Galan MDC, Rivera-Yañez CR, Negrete-Torres N, Arrieta TA, et al. Genetic and Molecular Characterisation of Treacher Collins Syndrome in Three Mexican Families. IJMS. February 16;27(4):1891. doi:10.3390/ijms27041891
13) Singh G, Verma S, Tandon P, Mehrotra D. Increased frontonasal angle and surface area of the mandibular antegonial ; reliable signs of Treacher Collins syndrome. J Cleft Lip Palate Craniofac Anomal. 2014;1(1):65. doi:10.4103/2348-2125.126579
14) Takegoshi H, Kaga K, Kikuchi S, Ito K. Mandibulofacial dysostosis: CT evaluation of the temporal bones for surgical risk assessment in patients with bilateral aural atresia. International Journal of Paediatric Otorhinolaryngology. August 2000;54(1):33–40. doi:10.1016/S0165-5876(00)00344-X
15) Lamzouri A, El Rherbi A, Ratbi I, Laarabi F, Chahboune R, Elalaoui S, et al. Misdiagnosis of Tracher-Collins syndrome initially attributed to drug teratogenicity: a Moroccan case report. Balkan Journal of Medical Genetics. 1 December
16) Kadakia S, Helman SN, Badhey AK, Saman M, Ducic Y. Treacher Collins Syndrome: genetics of a craniofacial disorder. International Journal of Paediatric Otorhinolaryngology. June 2014;78(6):893–8. doi:10.1016/j.ijporl.2014.03.006
17) Campos PSSL, Taitson PF, Pinto Da Silva LC, Leão LL. Dental and health aspects in the co-occurrence of Treacher Collins and Down syndromes: A case report. Special Care in Dentistry. January 2023;43(1):94–8. doi:10.1111/scd.12735
18) Damlar İ, Altan A, Turgay B, Kiliç S. Management of obstructive sleep apnoea in a patient with Treacher Collins syndrome using mandibular distraction osteogenesis. J Korean Assoc Oral Maxillofac Surg. 2016;42(6):388. doi:10.5125/jkaoms.2016.42.6.388
19) Mohan S, Del Rosario TJ, Pruett BE, Heard JA. Anaesthetic management of Treacher Collins syndrome in an outpatient surgical centre. Am J Case Rep. 28 July 2021;22. doi:10.12659/AJCR.931974
20) Rein LE, McQuitty A, Nguyen T. Multidisciplinary airway management and postoperative planning in a paediatric patient with unrepaired Treacher-Collins syndrome: a case report. Cureus. 10 July 2025. doi:10.7759/cureus.87655
21) Pierse J, McSwiney T. Treacher Collins syndrome: , , clinical features and multidisciplinary management. . 2 February
22) Soğukpinar A, Erkmen Almaz M. Dental treatment of a patient with Treacher Collins syndrome under general anaesthesia: A case report. Cumhuriyet Dental Journal. 13 March 2019;22(1):136–9. doi:10.7126/cumudj.475374
23) Kolsi N, Boudaya F, Ben Thabet A, Charfi M, Regaieg C, Bouraoui A, et al. Treacher Collins syndrome: A case report and review of the literature. . Clinical Case Reports. December 2022;10(12):e6782. . doi:10.1002/ccr3.6782
24) Fraszczyk-Tousty M, Jankowska A, Tousty J, Tousty P, Łoniewska B. Treacher Collins syndrome – a case report. Case Reports in Perinatal Medicine. 27 January 2023;12(1):20200009. doi:10.1515/crpm-2020-0009
25) Mohan RPS, Verma S, Agarwal N, Singh U. Treacher Collins syndrome: a case report. BMJ Case Reports. 24 May 2013;2013:bcr2013009341. doi:10.1136/bcr-2013-009341
26) Martelli-Junior H, Coletta RD, Miranda RT, de Barros LM, Swerts MS, Bonan PR. Orofacial features of Treacher Collins syndrome. . Med Oral Patol Oral Cir Bucal. 2009.