

Treacher Collins Syndrome (TCS) and Pierre Robin Sequence — Treatment and Life Expectancy

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Treacher Collins syndrome is characterized by the congenital hypoplasia of the zygomatic and mandible bones. It is a syndrome with a concise clinical presentation and mostly surgical treatment. Pierre Robin disorder, on the other hand, is a sequence and not a syndrome, i.e., in Pierre Robin sequence, micrognathia leads to glossoptosis. Glossoptosis, on the other hand, is responsible for the airway obstruction seen in infants with Pierre Robin sequence.



Definition of Treacher Collins Syndrome and Pierre Robin Sequence

Treacher Collins syndrome

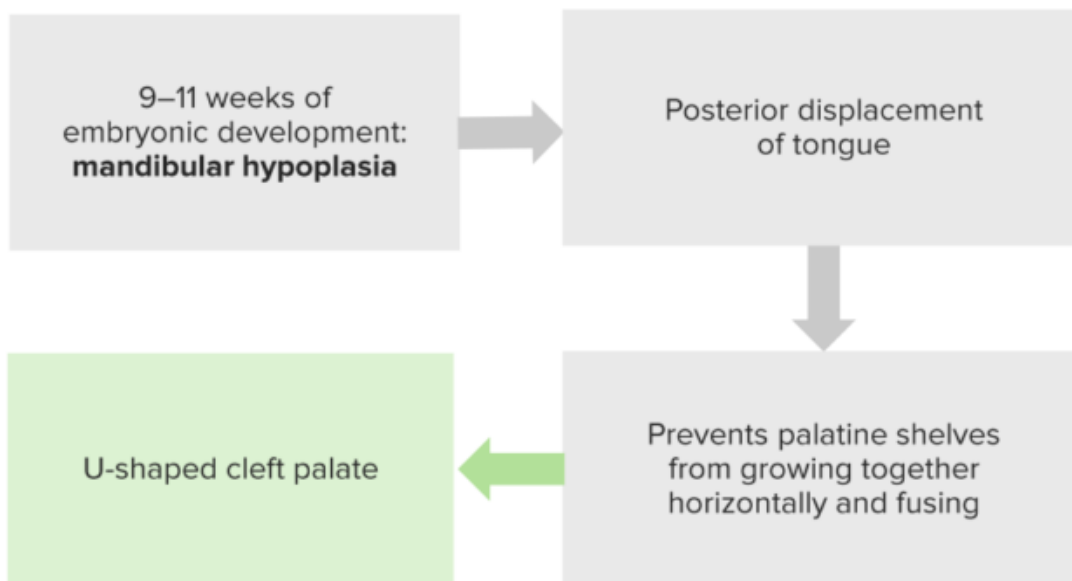
Treacher Collins syndrome is characterized by the **congenital hypoplasia of the zygomatic and mandible bones**. **External ear abnormalities, coloboma, absence of lower eyelashes, and preauricular hair displacement** are also common findings in patients with Treacher Collins syndrome. Patients with this syndrome typically have

conductive hearing loss due to ankylosis, hypoplasia or absence of the ossicles and middle ear structures. Inner ear abnormalities are typically absent.

Pierre Robin sequence

Pierre Robin sequence is a **triad of congenital micrognathia, glossoptosis, and airway obstruction**. Patients with this syndrome also have mandible hypoplasia, but the exact affected bones, size of defects, and severity of the condition are different from Treacher Collins syndrome.

Pierre Robin disorder is a sequence and not a syndrome. The difference between a sequence and a syndrome is that **in a sequence disorder, one malformation is responsible, i.e., leads to the formation of a subsequent malformation**. In Pierre Robin sequence, micrognathia leads to glossoptosis. Glossoptosis, on the other hand, is responsible for the airway obstruction seen in infants with Pierre Robin sequence.



Epidemiology of Treacher Collins Syndrome and Pierre Robin Sequence

Treacher Collins syndrome

The estimated prevalence of Treacher Collins syndrome is between 1 per 10,000 and 1 per 50,000. A family history of Treacher Collins syndrome is described in a significant number of patients; therefore, genetic studies were performed and **several genes have been linked to the syndrome**. Consanguinity marriages might increase the risk of Treacher Collins syndrome in a family with a positive history of the syndrome.

Pierre Robin sequence

Pierre Robin sequence incidence in the United States range between 1 per 8,500 to 1 per 14,000 live births depending on the definition and diagnostic criteria used. A family history of Pierre Robin sequence puts other relatives' offspring at an increased risk of Pierre Robin sequence, cleft lip, and palate. Like Treacher Collins syndrome, **several genes and chromosomal loci have been linked to Pierre Robin sequence**.

Etiology and Genetic Basis of Treacher Collins Syndrome and Pierre Robin Sequence

Treacher Collins syndrome

Genetic testing has identified **three genes as associated with Treacher Collins syndrome**. These genes include:

1. TCOF1
2. POLR1C
3. POLR1D

A few infants with Treacher Collins syndrome do not have a mutation in any of these three genes. Whether an unknown locus is causing the syndrome in those patients is yet to be discovered.

TCOF1 mutations are responsible for up to **71% of the cases** of Treacher Collins syndrome. Mutations in this gene can be either **sequence variants or deletions**; therefore, sequence analysis and deletion/duplication analysis are the two main methods used to look for mutations in this gene in an infant who meets the clinical diagnostic criteria of Treacher Collins Syndrome.

POLR1D and POLR1C mutations account for **8% of Treacher Collins syndrome** cases. POLR1D mutations are usually of sequence variants type. Deletion or sequence variant mutations are not seen in the POLR1C gene in patients with Treacher Collins syndrome.

Pierre Robin sequence

The **first clue that genetic predisposition plays a role** in Pierre Robin sequence was gained **from monozygotic twin studies** which showed a high concordance. Deletions in the loci 4p, 4q, 6q, and 11q have been associated with micrognathia which is believed to be the first step in this sequence of malformations. Duplications in loci 10q and 18q have also been linked to micrognathia. Some external factors during intrauterine life, like oligohydramnios, may play a role in micrognathia that, in turn, results in glossoptosis and a sequence that results in Pierre Robin sequence.

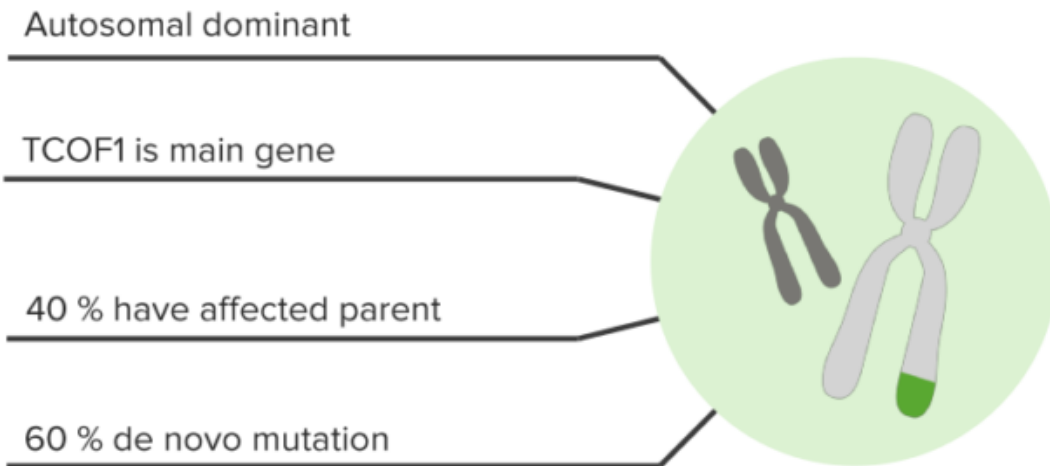
Clinical Characteristics of Treacher Collins Syndrome and Pierre Robin Sequence

Treacher Collins syndrome

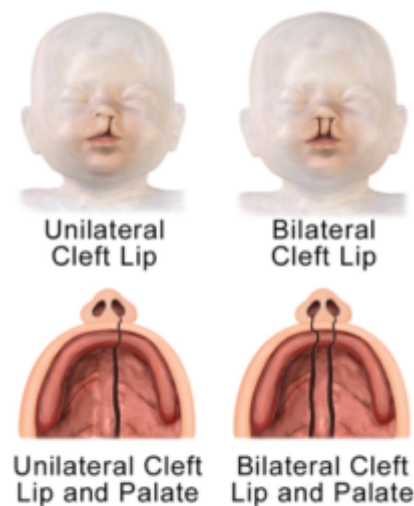
The clinical features of Treacher Collins syndrome have been categorized into **major and minor clinical features**. These features can be used to make the diagnosis of Collins syndrome more objective and decide who needs genetic testing looking for mutations in the three associated genes TCOF1, POLR1C and POLR1D.

The major clinical features of Treacher Collins syndrome include **hypoplasia of the zygomatic bones and mandible**. Typically, midface hypoplasia is the main clinical manifestation of this abnormality. **Micrognathia** is found in 78% of the cases. **External ear abnormalities** include absent ears, small ears, or rotated ears. Such abnormalities

are found in 77% of the cases. **Coloboma** and **absent lower eyelid lashes** are found in half of the cases. Family history is usually elicited in 40% of the cases. The abnormality in shape is usually bilateral and symmetric.



The minor clinical features of Treacher Collins syndrome include other external ear



[Image](#): "Unilateral and Bilateral Cleft Lip and Palate" by BruceBlaus. License: [CC BY-SA 4.0](#)

abnormalities rather than the ones mentioned for major features and conductive hearing loss:

- Cleft palate, pharyngeal hypoplasia, results in difficulty in swallowing
- Parotid glands are absent or ill-formed
- Hypoplastic or retro-positioned tongue
- Preauricular hair displacement
- Tracheostomy
- Unilateral or bilateral choanal stenosis or atresia

are found in approximately one fifth up to one-fourth of the cases.

Pierre Robin sequence

Pierre Robin sequence consists of a **triad of micrognathia, glossoptosis, and airway obstruction**.

Glossoptosis is characterized by the abnormal placement of the tongue in the posterior part of the mouth. The main reason behind glossoptosis is micrognathia.

Micrognathia is caused by the hypoplastic abnormalities seen in the mandible in infants with this sequence.

The abnormal position of the tongue is responsible for the **airway obstruction** seen in the triad of Pierre Robin sequence. Suprasternal retractions and the use of accessory muscles of respiration are common findings in infants with Pierre Robin sequence which are activated in an attempt to forcefully relieve the airway obstruction. Severe airway obstruction may result in hypoxia, cerebral impairment and failure to thrive. Pierre Robin sequence is also commonly associated with feeding difficulties. There is a U-shaped or V-shaped cleft palate.

Diagnostic Workup for Treacher Collins Syndrome and Pierre Robin Sequence

Treacher Collins syndrome

The main diagnostic test to be ordered in an infant born with clinical features suggestive of Treacher Collins syndrome is a **radiographic evaluation of the facial bones**. The type of abnormalities seen on radiography increases the certainty of the diagnosis.

Radiographic findings

The main manifestations on conventional radiography employing the occipitomeatal projection (Waters' view) are **hypoplasia or aplasia of the zygomatic arch**. Malar hypoplasia is also seen when computed tomography scanning of the orbital and zygomatic bony structures is performed. **Mandibular retrognathia** is the main abnormality seen on radiography in infants with Treacher Collins syndrome.

Patients with two major features of Treacher Collins syndrome, or three minor features of Treacher Collins syndrome, should undergo genetic testing **to confirm the diagnosis**.

Sequence analysis and deletion or duplication analysis

Sequence analysis and deletion or duplication analysis of the TCOF1 gene is performed first because it is the most commonly affected gene in this syndrome. Patients with a normal TCOF1 gene should undergo POLR1D sequence analysis. If the previous two genes are normal, or there is a family history of multiple siblings affected with Treacher Collins syndrome, POLR1C should be tested via sequence analysis. Once the mutation is identified, **future prenatal diagnosis can be offered and antenatal diagnosis can be offered**.

Pierre Collins sequence

The diagnosis of Pierre Collins sequence is based on the **clinical assessment and radiographic findings**. Mandibular hypoplasia and/or zygomatic hypoplasia are the main radiologic features seen in this sequence.

Management of Treacher Collins Syndrome and Pierre Robin Sequence

Treacher Collins syndrome

The management of the clinical manifestations of Treacher Collins syndrome is **dependent on the anomaly being repaired**. Patients with airway or feeding difficulties due to cleft palate might get surgical repair any time between birth and two years of age depending on the severity.

Surgical Treatment

Zygomatic and orbital reconstruction surgery is typically performed in children aged between 5-7 years in patients with Treacher Collins syndrome. **Maxillomandibular reconstruction surgery** is also indicated for patients with Treacher Collins syndrome. Mild and moderate malformations of the mandible are typically repaired when the child is aged between 13 and 16 years. More severe malformations might be repaired in patients as young as 6 years of age. **External ear reconstruction** is typically performed after six years of age. Hearing aids are important for the developmental growth of the child. **Middle ear reconstruction surgery** is indicated in patients with bilateral microtia.

Pierre Robin sequence

Patients with Pierre Robin sequence may be treated **non-surgically**. The placement of the **infant in the prone or lateral position** will resolve the airway obstruction in two-thirds of the cases. Sometimes, a **nasopharyngeal tube** is inserted to avoid frequent oxygen desaturation.

Patients who do not respond to these conservative measures should undergo a surgical procedure for airway obstruction. **Tongue-lip adhesion, distraction osteogenesis, and tracheostomy are the main procedures** performed in non-syndromic and syndromic Pierre Robin sequence for airway management.

Prognosis

All neonates with significant Pierre Robin sequence are at risk of developing sudden death due to a compromised airway.

References

Gangopadhyay N., Mendonca D.A., Woo A.S. "[Pierre Robin Sequence](#)." Seminars in Plastic Surgery. 2012;26(2):76-82. doi:10.1055/s-0032-1320065. Available at: <https://www.scholars.northwestern.edu/en/publications/pierre-robin-sequence>

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