

## Crouzon syndrome and the eye: An overview

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The current literature review aims to evaluate the ocular findings and associated ophthalmic features in Crouzon syndrome. Craniosynostoses are syndromes characterized by premature fusion of sutures of the skull and Crouzon syndrome is the most common of the craniosynostosis syndromes. Early fusion of sutures results in craniofacial anomalies, including abnormalities of the orbits. To prepare this review of the ophthalmic findings in this disorder, an organized search on online databases such as PubMed, Scopus, Cochrane Library, and Ovid was carried out. The key terms searched were “Crouzon”, “craniosynostosis”, “eye” and “ophthalmic”, and 51 research items were found. A total of 17 articles were included after scrutiny of the databases and a further 25 articles were added after augmented search. A detailed review was performed from the final 42 articles. A comprehensive description of associated anomalies is given along with the author’s own technique of surgical management in cases with Crouzon syndrome having bilateral luxation bulbi with exposure keratopathy. However, for optimum management of cranial and oculo-facial dysmorphisms, a multidisciplinary team of specialists is required.

**Key words:** Craniofacial dysmorphism, craniosynostosis, Crouzon, exorbitism

## Access this article online

## Website:

www.ijo.in

## DOI:

10.4103/ijo.IJO\_3207\_21

## Quick Response Code:



Craniosynostosis is the commonest inborn skull abnormality, resulting from untimely fusion of sutures of the cranium.<sup>[1]</sup> It can be divided into syndromic or non-syndromic, the latter being more common. Non-syndromic craniosynostoses are not associated with other body dysmorphisms and usually affect only one suture of the skull, while syndromic craniosynostoses are known to affect multiple skull sutures and are associated with craniofacial dysmorphisms, abnormalities of extremities, and other bony anomalies.<sup>[2]</sup> Over 150 syndromic craniosynostoses have been recognized in literature, the most common of which are Crouzon syndrome, Apert syndrome, Pfeiffer syndrome and Saethre–Chotzen syndrome, all being autosomal dominant.<sup>[3]</sup>

Crouzon syndrome (CS) is named after the French neurologist Octave Crouzon,<sup>[4]</sup> who was the first one to describe this condition. The incidence of this disease is 1.6 per 100,000 population, constituting 4.5% of all craniosynostosis patients.<sup>[5]</sup> Commonly, the fronto-sphenoidal and coronal sutures are involved, resulting in brachycephaly, mid-face hypoplasia, and a wider anterior skull base (Fig. 1a elucidates sutures in a normal neonatal skull and Fig. 1b shows the various cranial

anomalies due to craniosynostosis; Fig. 2 compares normal skull to a skull in Crouzon syndrome, showing increased antero-posterior diameter of skull, maxillary hypoplasia, and shallow orbits). Frontal bossing is seen due to compensatory growth of uninvolved sutures. Other common anomalies include hydrocephalus, parrot beak-nose, hypoplasia of maxilla, high arched palate but a typically normal axial skeleton (Fig. 3 shows a 3D CT reconstruction of a skull in Crouzon syndrome).<sup>[5]</sup> Orbital hypoplasia, combined with regressed orbital rims results in relative proptosis in almost all cases of CS.<sup>[5]</sup> A widened base of the skull results in hypertelorism. Other ocular findings include vision impairment,<sup>[6]</sup> strabismus,<sup>[7]</sup> nystagmus,<sup>[8]</sup> and glaucoma.<sup>[9]</sup> Few lesser found associations include abnormalities in corneal size (megalo/microcornea), keratoconus, aniridia, corectopia.<sup>[8]</sup> This review is aimed at studying the ocular associations in greater detail.

## Methods

A review of existing literature concerning the ophthalmic features of CS was performed utilizing online databases: PubMed, Scopus, Cochrane Library, and Ovid. A search of the term “Crouzon” brings up 1,289 articles, but specific articles relating to ophthalmic features were desired. A combined search was conducted using terms “Crouzon”, “craniosynostosis”, “eye”, and “ophthalmic” using Boolean operators AND and

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Received: 30-Dec-2021

Revision: 20-Mar-2022

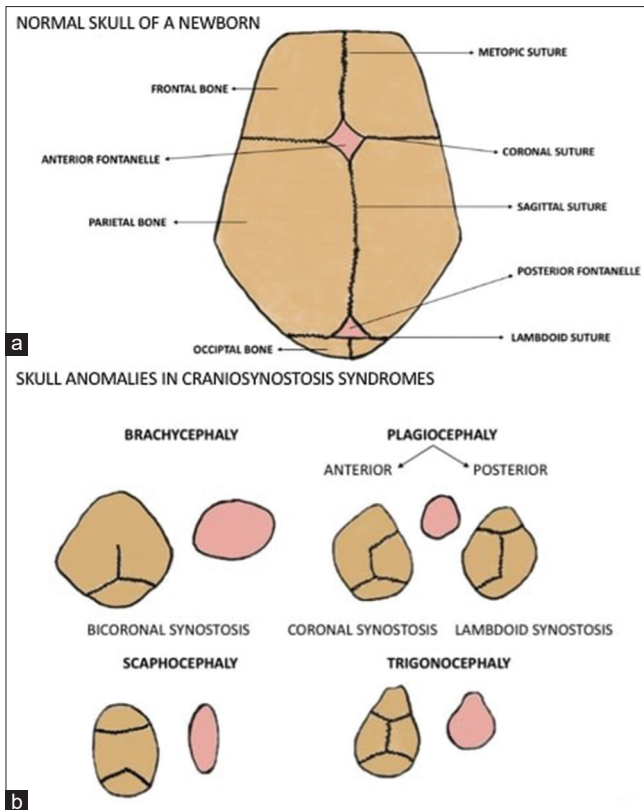
Accepted: 08-Apr-2022

Published: 30-Jun-2022

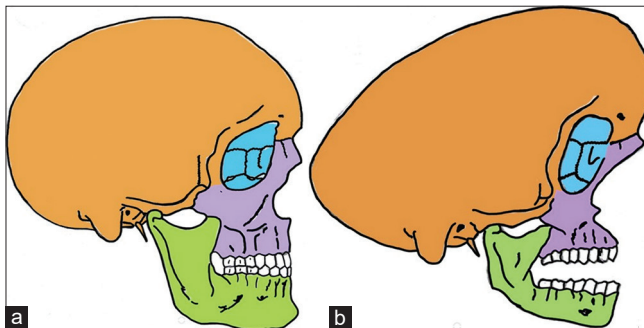
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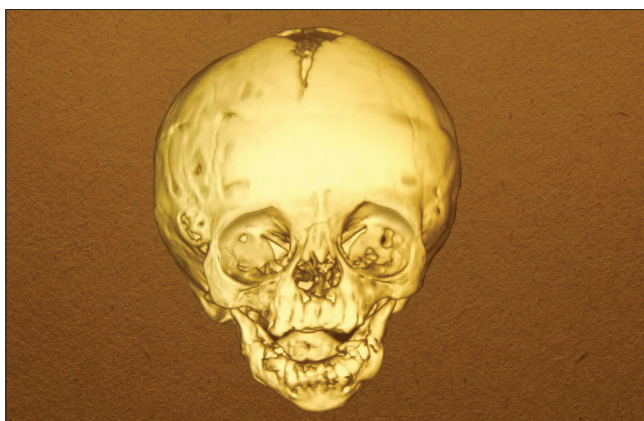
**Cite this article as:** Bhattacharjee K, Rehman O, Venkatraman V, Kikkawa D, Bhattacharjee H, Gogoi R, *et al.* Crouzon syndrome and the eye: An overview. Indian J Ophthalmol 2022;70:2346-54.



**Figure 1:** (a) Sutures in a normal skull of a newborn; (b) Skull anomalies in craniosynostosis



**Figure 2:** (a) A normal skull; (b) Increased antero-posterior diameter of skull, maxillary hypoplasia, and shallow orbits in Crouzon syndrome (CS)



**Figure 3:** Three-dimensional CT reconstruction of a skull in a patient with CS

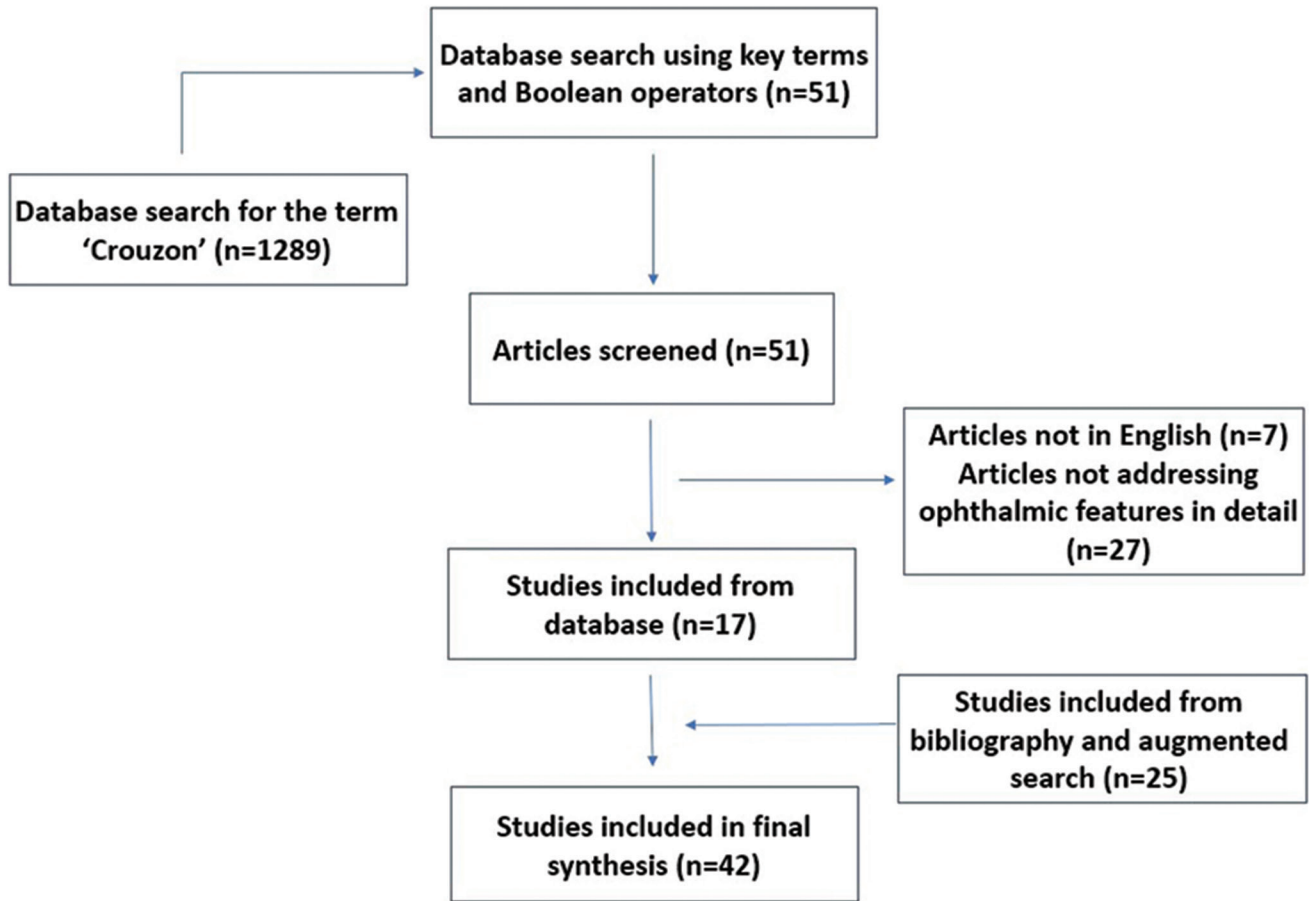
OR. In total, 51 research items were identified, dating back to 1975. Only English language manuscripts were considered. Articles not in the English language and those not pertaining to ocular findings in CS were not included. After the initial screening of these 51 research items, only 17 articles were found to be of interest. These were reviewed in detail and included 3 case reports, 11 research articles and 3 review articles. To further enhance the search, a manual search of other relevant articles and journals was also done, including the bibliography of selected articles. Finally, it was decided to include 42 articles in the study. The selection process is depicted in Fig. 4.

**Pathophysiology**

Crouzon syndrome is a congenital disease, inherited in an autosomal dominant (AD) manner. Fibroblast growth factor receptor (FGFR) is a family of four transmembrane proteins, out of which FGFR-1, 2 and 3 are responsible for signalling function involving cranial sutures. CS results from mutations in the transmembrane protein receptors FGFR-2 and FGFR-3, located on chromosome 10.<sup>[10]</sup> CS carries complete penetrance but expression in patients is variable. De novo mutations have also been noted in around 50% of patients with CS.<sup>[10]</sup> FGFR-2 and FGFR-3 proteins are required for differentiation of osteoblasts during embryogenesis. Mutations resulting in “gain-of-function” in these proteins results in rapid osteoblast differentiation, thus causing premature union of cranial sutures. To allow for continuous brain development, the remaining sutures show compensatory growth that occurs with increasing age. Commonly, fusion of bilateral coronal sutures causes brachycephaly (short, wide skull) in CS while other rarer presentations include trigonocephaly and scaphocephaly.<sup>[10]</sup> Facial abnormalities develop in coordination with anomalies involving the base of the cranium.<sup>[11]</sup> They typically start in the orbital area related to the anterior cranial base and then proceed toward the middle cranial base, with the resultant deformity being the worst in mid-facial region. Shallow orbits are a consequence of the concerted craniofacial abnormalities.

**Orbit**

The early anomalous fusion of sutures of the cranium and orbit affects orbital development in various ways. A study has suggested that the unusual orbital morphology is a central cause of globe protrusion in CS patients.<sup>[12]</sup> Regression of lateral and medial orbital walls, along with shallow orbits, results in exorbitism (Fig. 5 shows non-contrast computed tomography scan in sagittal section, illustrating regressed orbital walls and shallow orbit leading to luxation bulbi). Lu *et al.*<sup>[11]</sup> noted that the initial anomalies that appear in the face are reduced length of orbital floor and augmented globe prominence; these changes occur with a corresponding rise in the ratio of length of visual axis to orbital depth. It has been observed that the structure of the orbit in CS is markedly different from that in normal individuals in all three planes of space.<sup>[8]</sup> A higher orbital height is another anomaly detected in patients with CS. As for the globe position, patients with Crouzon have shortened distance between anterior pole of cornea and the facial plane, while the distance to the lateral rim of the orbit is increased.<sup>[8]</sup> As the sagittal depth decreases, an increased angle between the walls of the orbit is seen. The divergence between the orbits is a major contributor to globe subluxation seen in some patients with CS (Fig. 6 shows a child with subluxated right globe after a minor trauma with finger while playing). Yang *et al.*<sup>[13]</sup> reported



**Figure 4:** Selection process of articles for the study

a case of globe subluxation in a young child with CS, after an accidental fall. Edema of periorbital tissue in an already shallow orbit was the presumed cause for subluxation in this case. The report highlighted that minor trauma may trigger luxation of globe in CS patients.

#### Ocular alignment

Unusual orbital bone morphology and altered spatial arrangement of recti muscles may lead to specific strabismus disorders such as exotropia and V-pattern strabismus.<sup>[14]</sup> Several contributing factors to V-pattern strabismus have been noted that include overaction of inferior oblique<sup>[15]</sup> and underaction of superior oblique,<sup>[15]</sup> both of these resulting in excyclotorsion. Additionally, underdeveloped superior rectus and superior oblique can be present, another factor leading to V-pattern.<sup>[16]</sup> Dagi *et al.*<sup>[14]</sup> noted an association of increased excyclorotation of the recti with moderate-to-severe V-pattern, and also with a seesaw V-pattern in patients with syndromic craniosynostosis.

#### Vision

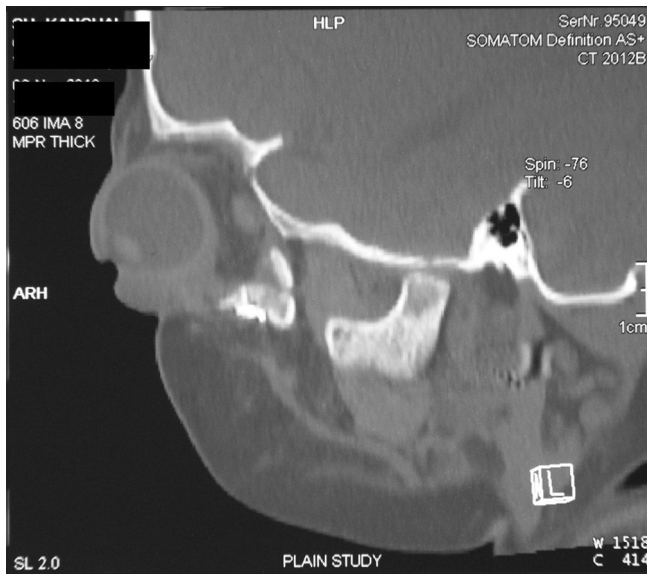
A recent study from Malaysia reported vision impairment in 32.1% of craniosynostosis patients, which is much higher than the normal population.<sup>[2]</sup> The most commonly reported causes in this study were amblyopia (25.0%), exposure keratopathy (3.6%), and optic atrophy (3.6%). The strongest risk factors for amblyopia were noted to be refractive errors and anisometropia. Gray *et al.*<sup>[17]</sup> also described amblyopia (21%) and

optic atrophy (7%) as two main causes of vision impairment in CS. Hertle *et al.*<sup>[18]</sup> also noted amblyopia (86%) as the leading cause of vision impairment in craniosynostosis, followed by optic atrophy (7%). Tay *et al.*<sup>[6]</sup> found an even higher prevalence of vision impairment (40%) in craniosynostosis syndromes. They reported that of these cases, 40% were due to potentially correctable causes such as amblyopia and ametropia. Similar results were noted by Khan *et al.*,<sup>[19]</sup> who found poor visual outcomes in 39.8% patients with craniosynostosis syndrome. They also reported astigmatism of 1 diopter or more in 40.3% of patients. Occurrence of squint in the primary position was also recognized as a major risk for amblyopia. A recent review by Hinds *et al.*<sup>[20]</sup> studied visual outcomes in 165 patients who were affected by syndromic craniosynostoses. They noted a higher percentage of patients attaining vision > 6/12 in the better eye but commented that poor vision remained a major source of morbidity in such patients. The higher proportion of eyes attaining good vision was attributed to the factor that children in the study were older in age as compared to previous studies and had become more adept at performing tests of vision. The prevalence of factors causing amblyopia was noted to be similar to the study by Khan *et al.*,<sup>[19]</sup> common ones being astigmatism, strabismus, and anisometropia.

#### Refractive errors

A high prevalence of refractive errors in individuals affected by craniosynostosis syndromes has been observed





**Figure 5:** Non-contrast CT scan in sagittal section showing regressed orbital walls, shallow orbit, and luxation bulbi



**Figure 6:** Globe subluxation on the right side in a patient with CS, post minor trauma with finger

by various researchers. Tay *et al.*<sup>[6]</sup> noted hypermetropia in 18.4% of patients and myopia in 2.6%, while Rafique *et al.*<sup>[2]</sup> observed hypermetropia in 20.6% and myopia in another 20.6%. The prevalence of anisometropia noted by Khan *et al.*<sup>[19]</sup> (16%) and Tay *et al.*<sup>[6]</sup> (18%) was similar in children with craniosynostosis, while Rafique *et al.*<sup>[2]</sup> noted even higher numbers (29.4%). The prevalence of astigmatism

was comparable in all three studies (40% by Khan *et al.*<sup>[19]</sup> and Tay *et al.*,<sup>[6]</sup> and 47.1% by Rafique *et al.*<sup>[2]</sup>). Refractive errors in these patients were attributable to many factors that included distorted corneal topography secondary to exposure keratopathy, ptosis, and unusual orbital shapes. As the prevalence of amblyopia is high in craniosynostosis patients, early detection and management of refractive errors is a key factor in management.

#### Anterior chamber

Anterior chamber (AC) anomalies have usually not been described in craniosynostosis syndromes but Okajima *et al.*<sup>[21]</sup> reported a case series of three patients with severe Crouzon or Pfeiffer syndrome having such anomalies. The same FGFR-2 mutation was noted in the 3 patients and all of them had AC dysgenesis. Other findings noted were midface hypoplasia, proptosis, and hydrocephalus, with two of the patients also having cloverleaf skull deformity. Two patients had features consistent with Peters anomaly, while the third had severe AC dysgenesis. This case series highlighted that FGFR-2 may be involved in AC formation during embryogenesis. McCann *et al.*<sup>[22]</sup> also implicated the role of FGFR-2 mutations in AC dysgenesis in their study.

#### Glaucoma

Glaucoma has rarely been reported in individuals having Crouzon syndrome. A 1983 case report had briefly outlined a case of glaucoma in an Indian male neonate with CS.<sup>[23]</sup> The child had an atypical head shape with closed fontanelles, along with parrot-beak deformity, and midface hypoplasia. Bilateral proptosis was noted along with high intraocular pressures (IOPs) and optic atrophy. The probable cause for glaucoma was attributed to AC developmental anomalies. Another recent report by Alshamrani *et al.*<sup>[9]</sup> described glaucoma in a 10-year-old female with CS. The patient had brachycephaly along with proptosis, exposure keratopathy, and congenital glaucoma. Shallow ACs with high axial lengths were noted in both the eyes, along with angle closure and advanced optic nerve cupping. Mutation for FGFR2 Ser351Cys was confirmed on genetic testing.

#### Optic nerve

Prevalence of papilledema has been described in craniosynostosis syndromes by different researchers: Rafique *et al.*<sup>[2]</sup> (8.3% incidence), Tay *et al.*<sup>[6]</sup> (9.5% incidence), and Sharma *et al.*<sup>[24]</sup> (5% incidence). Gray *et al.*<sup>[17]</sup> exclusively studied patients with CS and found a higher prevalence of papilledema than others (15%). The main mechanism behind papilledema is postulated to be high intracranial pressure (ICP), secondary to anomalous skull development. However, other contributing factors to papilledema development have been suggested, such as upper airway obstruction, intracranial venous anomalies, and obstructive sleep apnea.<sup>[25]</sup> As papilledema may be multifactorial in craniosynostosis, it represents general health status of the patient rather than just high ICP. Chronic papilledema over time may ultimately cause optic atrophy. The occurrence of optic atrophy was noted to be 11.4% by Rafique *et al.*<sup>[2]</sup> in syndromic craniosynostoses while Gray *et al.*<sup>[17]</sup> found it to be 13% in patients having CS. Few studies have reported disappearance of papilledema after craniofacial surgery,<sup>[2,6,26,27]</sup> but it may recur and may lead to optic atrophy even after surgery as growth of the brain occurs in the limited cranial space.

Association of extensive bilateral myelinated nerve fibers around the optic disc has been described by Garcia *et al.*<sup>[28]</sup> in a case of Crouzon syndrome. The role of FGFR-2 has been defined in oligodendrocyte growth<sup>[29]</sup> and overactivation of FGFR-2 has been linked to abnormal regulation of myelination.

### Management

Appropriate management begins with correct diagnosis and prompt management to prevent complications. Key distinguishing features that separate CS from other syndromic craniosynostoses are normal extremities (hands/feet), normal intellect, maxillary hypoplasia, parrot-beak nose, and exorbitism.<sup>[30]</sup>

Following factors should be considered during examination:

- Airway examination
- Cranial anomalies
- Cardiac anomalies
- Exposure keratopathy
- Papilledema/optic atrophy.

Three important functional problems in CS are raised ICP, corneal exposure as a result of extreme exorbitism, and maxillary hypoplasia leading to obstructive sleep apnea (OSA). Clinical diagnosis is based mainly on cranial anomaly and exorbitism. Needless to say, the anomalous facial effects may also have a deep psychosocial effect on the growing child.

### Imaging

Three-dimensional antenatal ultrasonography can reveal premature closure of skull sutures during gestational life. Plain films and computed tomography (CT) can detect craniofacial anomalies such as copper beaten appearance of skull, lacunae in the skull, shallow orbits, and maxillary hypoplasia in children. CT imaging can also detect premature fusion of skull sutures and assist with planning surgical intervention. Intracranial imaging is performed using magnetic resonance imaging (MRI) and CT scans to detect hydrocephalus and Chiari malformations.

### Genetic testing

Genetic testing can confirm diagnosis of CS, with over 50% of the cases exhibiting a gain-of-function mutation.<sup>[31]</sup> Almost all CS cases are localized to two exons of the gene immunoglobulin-like III (*Ig III*), namely IIIa and IIIc of *FGFR-2* gene; but a negative test for these mutations does not exclude the diagnosis.<sup>[31]</sup> Alterations in the amino acid sequence, due to deviations in nucleotides can be detected on chromosome 10q25-q26 in Crouzon syndrome [c.1030G>C (Ala344Pro)]. Several researchers have detected a number of mutations in diseased individuals, with an estimate of around 60 *FGFR-2* mutations identified.<sup>[13]</sup> *Ig III* mutations lead to an abnormally high activity of tyrosine kinase but similar activity has likewise been described in *IG I* mutations by Sharma *et al.*<sup>[32]</sup> in Cys62Ala mutation. A heterozygous missense mutation in exon 10 (c.1012G>C, p.G338R) of *FGFR-2* has recently been reported by Yang<sup>[13]</sup> *et al.* in family members of an individual affected with CS. de Ravel *et al.*<sup>[33]</sup> described a missense mutation in tyrosine kinase of *FGFR-2* gene in a family with Crouzon, who were negative for typical mutations in exons IIIa and IIIc. This

study highlighted the significance of looking for *FGFR-2* tyrosine kinase mutations in suspected CS but with negative screening for typical mutations.

### Treatment

A multidisciplinary approach is required while managing patients with Crouzon syndrome.

A pediatrician trained in dysmorphology can often act as the captain of the team, and coordinate care between the team of specialists.

#### i. Acute management

- Certain conditions may require acute or urgent management in CS.
- Severe mandibular/maxillary hypoplasia: may require tracheostomy
- Exposure keratopathy: tarsorrhaphy can be required
- Hydrocephalus with raised ICP: ventriculo-peritoneal shunting to decrease the
- high ICP might be required

#### ii. Surgical management

Surgical management remains the mainstay of treatment. Surgery may be planned in a staged manner or as a combined approach, depending on severity of malformations and the age of the patient.<sup>[30]</sup> Surgical treatment includes cranial vault remodeling and amendment of facial anomalies.

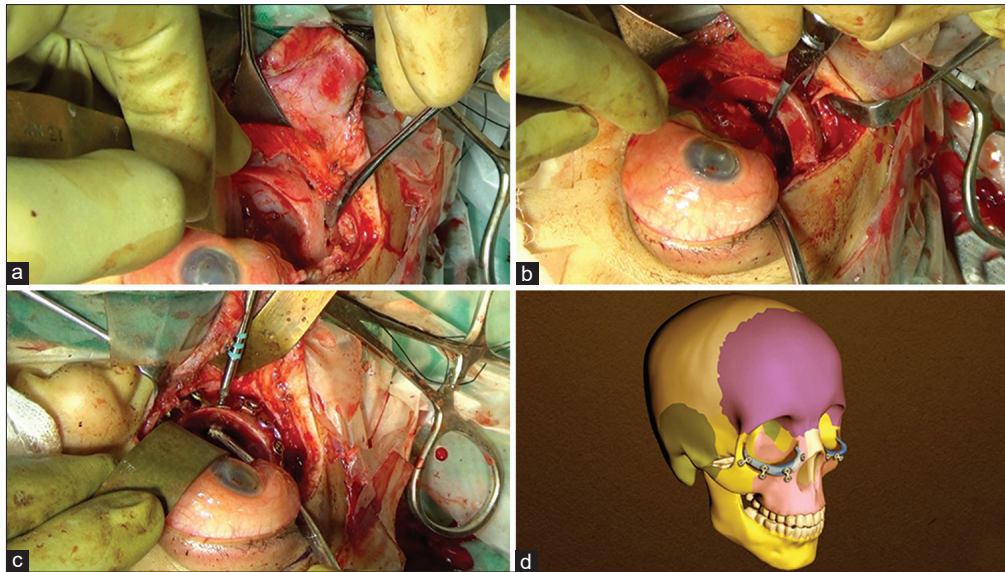
Staged surgical approach includes remodeling of the skull vault during infancy, surgery for facial and orbital correction at an age of 5–7 years, and advancement surgery for maxilla/mandible during teenage life.<sup>[5]</sup> For midfacial anomalies, surgical approaches to midface anomalies include Le Fort I, Le Fort III, Monobloc procedure, and combination surgeries.<sup>[30]</sup>

One notable surgical rehabilitation protocol is described by McCarthy *et al.*<sup>[34]</sup> Surgical management is divided into six different stages. The first stage (from birth up to six months) aims at decompression of the vault of the cranium and suture release using techniques like craniectomy, skull expansion, and skull fragmentation. The second stage (from six months up to an age of three years) involves reshaping of the fronto-orbital area plus advancement using techniques such as strip craniectomy or midface/monobloc distraction osteogenesis. Midface deformity correction and secondary vault procedures are done during the third stage (from four up to eight years of life), using the Le Fort III with distraction osteogenesis. Late correction of midface anomalies and 2° vault procedures may also be planned during the fourth stage (9 to 12 years). Orthodontic procedures are done during the fifth stage (from 13 years to 17 years) and include techniques such as rhinoplasty, canthopexy, and cranioplasty. The sixth stage (beginning after the child is 17 years old) involves orthognathic surgery for facial and cranial dysmorphisms. The abovementioned stages of management may vary depending upon the cosmetic or functional needs of the affected individual.

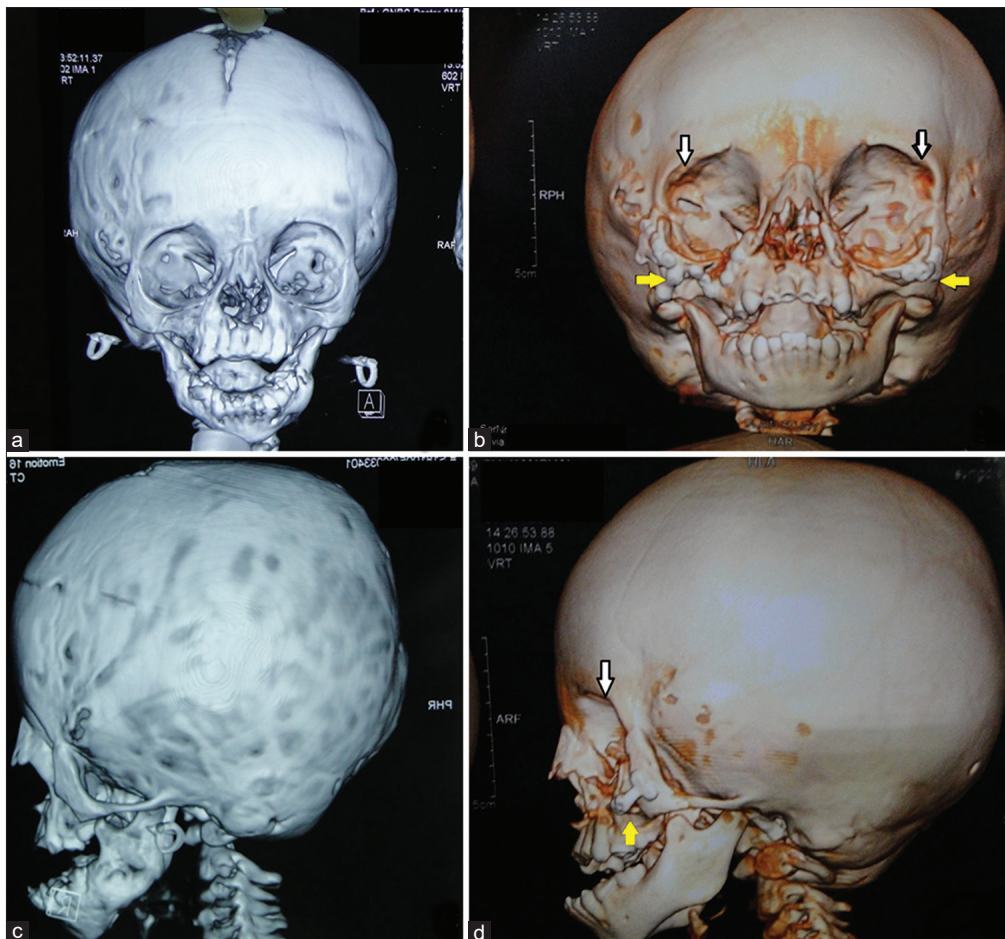
Computer-assisted approach has added an interesting and exciting dimension to surgical management in CS. The benefits of computer-assisted approach include shorter surgical time, more precise surgery and a near anatomical correction according to the patient's morphology.<sup>[35]</sup>

Distraction osteogenesis technique was first employed in treating craniofacial deformities in 1992.<sup>[36]</sup> The surgical





**Figure 7:** (a) Anterior maxilla being cut along a pre-marked delineation line; (b) Antero-superior rotation of the bone segment; (c) Fixation of the bone segment with plates and screws; (d) Digital reconstruction of the final outcome



**Figure 8:** (a) Preoperative 3D reconstructed CT scan in anterior view with shallow orbits; (b) Postoperative 3D CT scan image in anterior view with an increased orbital volume. White arrows point to the augmented space created around the orbital roof, and yellow arrows point to the titanium plates and screws; (c) Preoperative 3D CT scan in lateral view showing shallow orbit and maxillary hypoplasia; (d) Postoperative 3D CT scan in lateral view with enhanced orbital volume. White arrow shows the superior burr site, and yellow arrow shows the antero-superiorly rotated inferior orbital rim fixed with titanium plates and screws





**Figure 9:** (a) Preoperative picture of a patient with extreme exorbitism in downgaze; (b) Postoperative outcome of the same patient at six-month follow-up visit, now having no exorbitism in downgaze



**Figure 10:** (a) Canthal dystopia and ptosis in a 15-year-old patient; (b) Anatomical outcome post canthoplasty and bilateral levator surgery

procedure involves osteotomy with placement of the distraction device, a latency period for callous formation and organization, with gradual distraction and consolidation period for callous maturation and mineralization. A preoperative study of the 3D structure of the skull provides the required surgical simulation and the vectors needed for precise placement of the fixation device and appropriate segmental motion, ensuring the desired outcome in the minimum possible time frame.<sup>[37]</sup> The distraction device could be external, which might lead to inconvenience for the patient and family as the treatment spans over several months, or internal, wherein the device is fixed right onto the bone, alleviating the social distress and permitting longer periods of retention.<sup>[38]</sup> A composite technique involving the two may also be planned as it can make for a stable advancement arrangement. Notable advantages of this procedure include creation of superior advancement circumventing supplementary bone grafting along with concurrent new histogenesis as compared to conventional surgical modalities.<sup>[39]</sup> Relapse of deformity forms the most commonly encountered complication, which might necessitate a second procedure to take out the distractors. Infection, injury to teeth, hypertrophic scar formation, injury to adjacent nerves, CSF leak and non-union are also described.<sup>[40,41]</sup>

In this overview of CS and the eye, we would like to highlight the technique being used by the first author, which is an innovative strategy built on the principle of distraction osteogenesis. Although distraction osteogenesis yields successful surgical correction of exorbitism, it is tedious and thus, is a suitable management option for cases with no exigent vision-threatening presentation. In cases of exposure keratopathy, wherein tarsorrhaphy may not be possible due to extreme exorbitism, the surgical technique devised by the first author can serve as an ingenious single-step resort to address the luxation bulbi, thereby providing an apt alternative for vision and globe salvage. Additionally, distraction osteogenesis entails the risk of tract infection due to presence of externally fixed plates and screws, while the author's technique being a closed one bears a relatively lower predisposition to infection. Preoperatively, a thorough evaluation by a neurosurgeon should be performed, including measurement of the ICP by lumbar puncture method. In case ICP is raised, it should be addressed first. Our technique involves a transconjunctival inferior approach to the orbit after lateral canthotomy, lateral cantholysis, and medial full-thickness lid incision lateral to the punctum. Once the pre-periosteal soft tissue separation is performed meticulously, a periosteal incision is made, and it is reflected both anteriorly and posteriorly to achieve total visualization of the inferior orbital rim. A fragment of the inferior rim of the orbit is delineated using a surgical marker pen and then the bone is cut along this pre-determined incision line. This step is followed by separation of this bony fragment from the remaining maxilla using a bone separator. This leads to fashioning of a bone fragment having a posterior bone contact anchored medially and laterally but free for rotation antero-posteriorly. The segment is rotated antero-superiorly and fixed using plate and screws, yielding a dead space just inferior to it. This dead space is equivalent to the space created after fixing the distractors in case of distraction osteogenesis. This dead space acts as the cavity wherein callous formation can ensue. Once the bone is fixed, continuous traction is not necessary and thus, obviates the necessity for any secondary

surgical procedure. This newly generated space also deepens the available orbital space into which the globe can then be safely repositioned (Fig. 7 shows the intraoperative surgical steps and digital representation of the eventual outcome). Additionally, volume enhancement is supplemented by bony decompression of the orbital roof using a bone burr. Once adequate amount of depth in the cavity of the orbit is achieved, the eyeball is repositioned, and significant reduction in the proptosis is noted intraoperatively with this technique. Soft tissue closure is done in a layered fashion followed by esthetically conducted skin suturing and temporary tarsorrhaphy. The same procedure can be undertaken bilaterally (Fig. 8 depicts comparison of the preoperative and postoperative 3D reconstructed CT scan images). The postoperative outcomes are satisfactory and observed to be clinically stable both on immediate and long-term follow-up of up to 5 years. (Fig. 9a shows preoperative picture of a patient with extreme exorbitism in downgaze and Fig. 9b illustrates postoperative outcome of the same patient at six-month follow-up visit, now having no exorbitism in downgaze). The major advantage of this technique when compared to distraction osteogenesis lies in it being a one-step procedure that works on the identical principle to yield favorable long-term outcomes, unlike the latter which requires a two-step approach involving implantation and extraction of the distractors. Additionally, it can serve as a suitable rescue procedure in clinical presentations having severe exorbitism with exposure keratopathy and visual compromise.

Soft tissue repositioning is often required after bony alignment is completed. Treatment is directed to both the canthi. If telecanthus persists, Y-V plasty or transnasal wiring might be required. Lateral canthal dystopia with anti-mongoloid slant is very characteristic in individuals with CS and can be amended by using canthoplasty with anchoring of lateral canthal complex at a level above its existing level; in extreme cases, Z-plasty may also be employed. Finally, ptosis is also common and may require levator advancement or frontalis suspension in patients having poor levator function (Fig. 10 shows preoperative and postoperative pictures of a CS patient with ptosis and canthal dystopia).

## Conclusion

Crouzon syndrome is a compound craniofacial disorder that presents with a myriad of multisystem anomalies and bony abnormalities. Ophthalmologists should be aware of the many ophthalmic associations in Crouzon syndrome and must be alert toward conditions that may require early intervention. A multidisciplinary team (typically including a pediatrician with dysmorphology training, a craniofacial surgeon, a neurosurgeon, an oculo-facial plastic surgeon, a head and neck surgeon, and an oral maxillofacial surgeon) is needed for optimum management such that patients can achieve maximum functional and esthetic outcome.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## References

- Lajeunie E, Le Merrer M, Bonaiti-Pellie C, Marchac D, Renier D. Genetic study of nonsyndromic coronal craniosynostosis. *Am J Med Genet* 1995;55:500-4.
- Rafique Ali AA, Ismail F, May May C, Mohd Abdullah AA, Khaliddin N, Hariri F, *et al.* Ophthalmic features of craniosynostosis: A Malaysian experience. *Eur J Ophthalmol* 2021;11206721211030093. doi: 10.1177/11206721211030093.
- Cohen MM Jr, MacLean RE, editors. *Craniosynostosis: Diagnosis, Evaluation, and Management*. 2<sup>nd</sup> ed. New York: Oxford University Press; 2000.
- Crouzon LEO. Dysostose cranio-faciale hereditaire. *Presse Méd* 1912;20:737-9.
- Dicus Brookes C, Golden BA, Turvey TA. Craniosynostosis syndromes. *Atlas Oral Maxillofac Surg Clin North Am* 2014;22:103-10.
- Tay T, Martin F, Rowe N, Johnson K, Poole M, Tan K, *et al.* Prevalence and causes of visual impairment in craniosynostotic syndromes. *Clin Exp Ophthalmol* 2006;34:434-40.
- Rosenberg JB, Tepper OM, Medow NB. Strabismus in craniosynostosis. *J Pediatr Ophthalmol Strabismus* 2013;50:140-8.
- Kreiborg S, Cohen MM Jr. Ocular manifestations of Apert and Crouzon syndromes: Qualitative and quantitative findings. *J Craniofac Surg* 2010;21:1354-7.
- Alshamrani AA, Al-Shahwan S. Glaucoma with Crouzon syndrome. *J Glaucoma* 2018;27:e110-2.
- Conrady CD, Patel BC. Crouzon syndrome. [Updated 2021 Aug 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK51899>. [Last accessed on 2021 Dec 19].
- Lu X, Forte AJ, Sawh-Martinez R, Wu R, Cabrejo R, Steinbacher DM, *et al.* Orbit, zygoma, and maxilla growth patterns in Crouzon syndrome. *Int J Oral Maxillofac Surg* 2019;48:309-21
- Cruz AA, Garcia DM, Akaiishi PM, Arnaud E, Milbratz GH, Bertrand AL. Globe protrusion and interorbital divergence in syndromic faciocraniosynostoses. *J Craniofac Surg* 2015;26:1163-4.
- Yang J, Tao T, Liu H, Hu ZL. Inherited FGFR2 mutation in a Chinese patient with Crouzon syndrome and luxation of bulbus oculi provoked by trauma: A case report. *BMC Ophthalmol* 2019;19:209.
- Dagi LR, MacKinnon S, Zurakowski D, Prabhu SP. Rectus muscle exocyclorotation and V-pattern strabismus: A quantitative appraisal of clinical relevance in syndromic craniosynostosis. *Br J Ophthalmol* 2017;101:1560-5.
- Morax S, Pascal D, Barraco P. Significance of the "V" syndrome with double "up shoot". Insufficiency of the two superior oblique muscles in craniofacial malformations. *J Fr Ophthalmol* 1983;6:295-310.
- Greenberg MF, Pollard ZF. Absence of multiple extraocular muscles in craniosynostosis. *J AAPOS* 1998;2:307-9.
- Gray TL, Casey T, Selva D, Anderson PJ, David DJ. Ophthalmic sequelae of Crouzon syndrome. *Ophthalmology* 2005;112:1129-34.
- Hertle RW, Quinn GE, Minguini N, Katowitz JA. Visual loss in patients with craniofacial synostosis. *J Pediatr Ophthalmol Strabismus* 1991;28:344-9.
- Khan SH, Nischal KK, Dean F, Hayward RD, Walker J. Visual outcomes and amblyogenic risk factors in craniosynostotic syndromes: A review of 141 cases. *Br J Ophthalmol* 2003;87:999-1003.
- Hinds AM, Thompson DA, Rufai SR, Weston K, Schwiebert K, Panteli V, *et al.* Visual outcomes in children with syndromic craniosynostosis: A review of 165 cases. *Eye (Lond)* 2021. doi: 10.1038/s41433-021-01458-5.



21. Okajima K, Robinson LK, Hart MA, Abuelo DN, Cowan LS, Hasegawa T, *et al.* Ocular anterior chamber dysgenesis in craniosynostosis syndromes with a fibroblast growth factor receptor 2 mutation. *Am J Med Genet* 1999;85:160-70.
22. McCann E, Kaye SB, Newman W, Norbury G, Black GC, Ellis IH. Novel phenotype of craniosynostosis and ocular anterior chamber dysgenesis with a fibroblast growth factor receptor 2 mutation. *Am J Med Genet A* 2005;138A:278-81.
23. Krishnan M, Kantha R. Glaucoma in Crouzon's disease. *Indian J Ophthalmol* 1983;31:33-4.
24. Sharma N, Greenwell T, Hammerton M, David DJ, Selva D, Anderson PJ. The ophthalmic sequelae of Pfeiffer syndrome and the long-term visual outcomes after craniofacial surgery. *J AAPOS* 2016;20:315-9.
25. Marucci DD, Dunaway DJ, Jones BM, Hayward RD. Raised intracranial pressure in apert syndrome. *Plast Reconstr Surg* 2008;122:1162-8.
26. Bennett KG, Vick AD, Ettinger RE, Archer SM, Vercler CJ, Buchman SR. Age at craniosynostosis surgery and its impact on ophthalmologic diagnoses: A single-center retrospective review. *Plast Reconstr Surg* 2019;144:696-701.
27. Tuite GF, Chong WK, Evanson J, Narita A, Taylor D, Harkness WF, *et al.* The effectiveness of papilledema as an indicator of raised intracranial pressure in children with craniosynostosis. *Neurosurgery* 1996;38:272-8.
28. Garcia GA, Tian JJ, Apinyawasisuk S, Kim S, Akil H, Sadun AA. Clues from Crouzon: Insights into the potential role of growth factors in the pathogenesis of myelinated retinal nerve fibers. *J Curr Ophthalmol* 2016;28:232-6.
29. Fortin D, Rom E, Sun H, Yayon A, Bansal R. Distinct fibroblast growth factor (FGF)/FGF receptor signaling pairs initiate diverse cellular responses in the oligodendrocyte lineage. *J Neurosci* 2005;25:7470-9.
30. Sawh-Martinez R, Steinbacher DM. Syndromic craniosynostosis. *Clin Plast Surg* 2019;46:141-55.
31. Al-Namnam NM, Hariri F, Thong MK, Rahman ZA. Crouzon syndrome: Genetic and intervention review. *J Oral Biol Craniofac Res* 2019;9:37-9.
32. Sharma VP, Wall SA, Lord H, Lester T, Wilkie AO. Atypical Crouzon syndrome with a novel Cys62Arg mutation in FGFR2 presenting with sagittal synostosis. *Cleft Palate Craniofac J* 2012;49:373-7.
33. de Ravel TJ, Taylor IB, Van Oostveldt AJ, Fryns JP, Wilkie AO. A further mutation of the FGFR2 tyrosine kinase domain in mild Crouzon syndrome. *Eur J Hum Genet* 2005;13:503-5.
34. McCarthy JG, Warren SM, Bernstein J, Burnett W, Cunningham ML, Edmond JC, *et al.* Parameters of care for craniosynostosis. *Cleft Palate Craniofac J* 2012;49:1S-24S.
35. Laure B, Louisy A, Joly A, Travers N, Listrat A, Pare A. Virtual 3D planning of osteotomies for craniosynostoses and complex craniofacial malformations. *Neurochirurgie* 2019;65:269-78.
36. McCarthy JG, Schreiber J, Karp N, Thorne CH, Grayson BH. Lengthening the human mandible by gradual distraction. *Plast Reconstr Surg* 1992;89:1-8.
37. Hariri F, Abdul Rahman ZA, Bahuri NFA, Azmi MN, Abdullah NA, Ganesan D. Crouzon syndrome: A case series of craniomaxillofacial distraction osteogenesis for functional rehabilitation. *J Oral Maxillofac Surg* 2018;76:646.e1-12.
38. Rachmiel A, Shilo D. The use of distraction osteogenesis in oral and maxillofacial surgery. *Ann Maxillofac Surg* 2015;5:146-7.
39. Witherow H, Dunaway D, Evans R, Nischal KK, Shipster C, Pereira V, *et al.* Functional outcomes in monobloc advancement by distraction using the rigid external distractor device. *Plast Reconstr Surg* 2008;121:1311-22.
40. Wang JC, Nagy L, Demke JC. Syndromic craniosynostosis. *Facial Plast Surg Clin North Am* 2016;24:531-43.
41. Master DL, Hanson PR, Gosain AK. Complications of mandibular distraction osteogenesis. *J Craniofac Surg* 2010;21:1565-70.