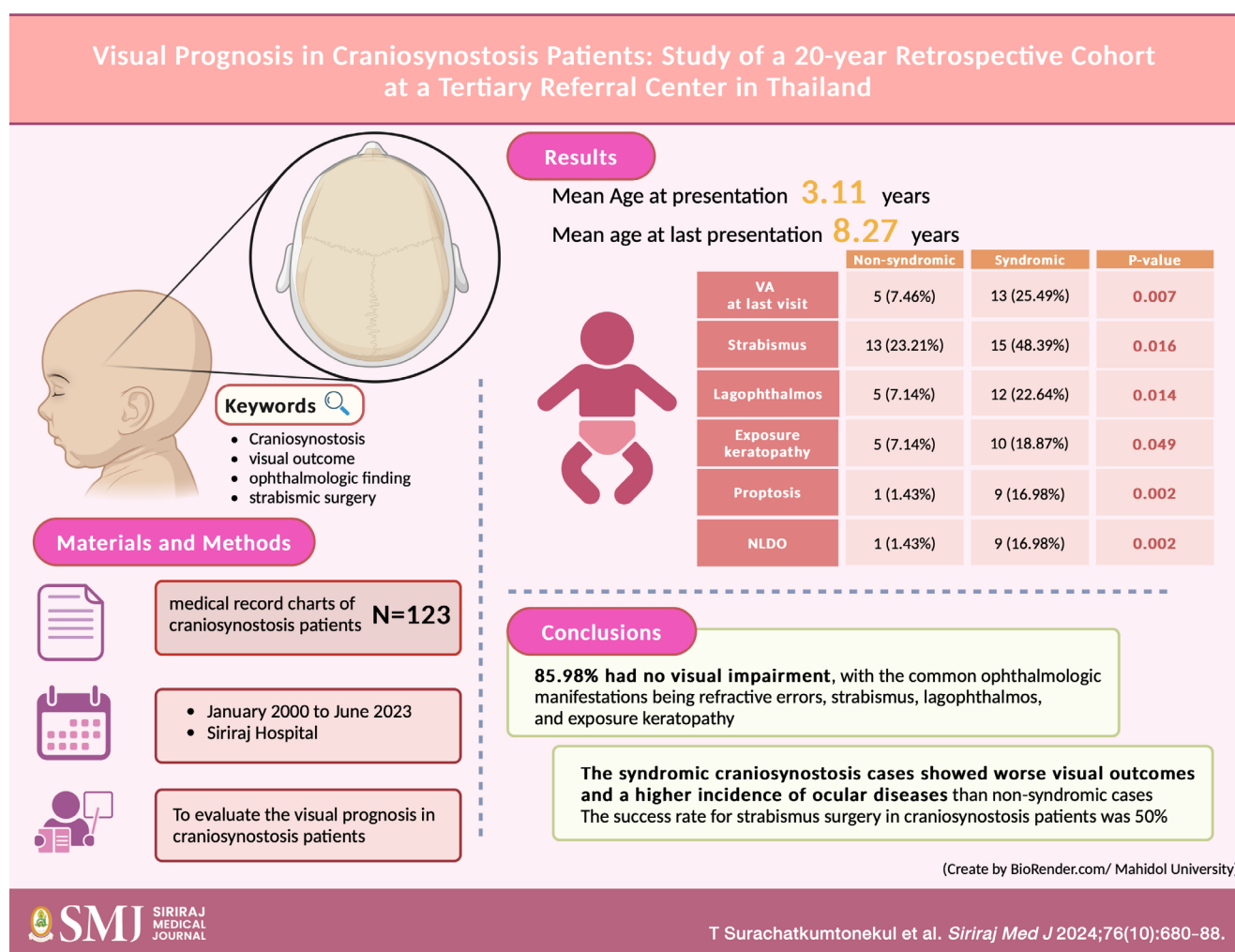


# Visual Prognosis in Craniosynostosis Patients: A 20-year Retrospective Cohort Study at a Tertiary Referral Center in Thailand

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**ABSTRACT**

**Objective:** This study aims to evaluate the visual prognosis in craniosynostosis patients in order to identify ophthalmologic manifestations in craniosynostosis patients and strabismus surgery outcomes in these patients.

**Materials and Methods:** The medical records craniosynostosis patients were reviewed retrospectively from January 2000 to June 2023. All the relevant patient data, such as age, sex, visual acuity, ophthalmologic examinations, and strabismus surgery outcomes were recorded.

**Results:** In total, 123 patients were included in the study, among whom 65 (52.84%) were male. Overall, there were 70 cases (56.91%) of non-syndromic craniosynostosis, and 53 cases of syndromic craniosynostosis, comprising Crouzon syndrome (15 cases), Apert syndrome (8 cases), Pfeiffer syndrome (2 cases), and other syndromes (28 cases). The mean age at first examination was 3.11 years old. Out of 107 cases with visual impairment at the first visit, 92 (85.98%) showed no visual impairment at the last visit. Among the 87 patients with strabismus, 28 (32.18%) had strabismus at the primary position, with exotropia being the most common type (18 cases). Eight cases underwent strabismus surgery, and 4 cases achieved success (deviation < 10 prism diopters). Other ophthalmologic manifestations were lagophthalmos (17 cases, 13.82%), exposure keratopathy (15 cases, 12.2%), ptosis (11 cases, 8.94%), proptosis (10 cases, 8.13%), and nasolacrimal duct obstruction (10 cases, 8.13%). The syndromic group exhibited higher rates of visual impairment, strabismus, lagophthalmos, exposure keratopathy, proptosis and nasolacrimal duct obstruction compared to the non-syndromic group.

**Conclusion:** Among the craniosynostosis cases, 85.98% had no visual impairment, with the common ophthalmologic manifestations being refractive errors, strabismus, lagophthalmos, and exposure keratopathy. The syndromic craniosynostosis cases showed worse visual outcomes and a higher incidence of ocular diseases than non-syndromic cases. The success rate for strabismus surgery in craniosynostosis patients was 50%.

**Keywords:** Craniosynostosis; visual outcome; ophthalmologic finding; strabismus surgery (Siriraj Med J 2024; 76: 680-688)

**INTRODUCTION**

Craniosynostosis is a medical condition marked by the premature fusion of one or more cranial sutures. There are two main types: non-syndromic craniosynostosis and syndromic craniosynostosis. Syndromic craniosynostosis is associated with other anomalies, especially bone irregularities in the hands and feet.<sup>1</sup> Crouzon, Apert, and Pfeiffer syndromes are the most common syndromic craniosynostosis types from autosomal dominant inheritance. Non-syndromic craniosynostosis, which is more common, typically presents with a defect in a single growth stream, or suture. Normally, non-syndromic craniosynostosis is not associated with other anomalies.<sup>2</sup> The prevalence of craniosynostosis was reported to be 5.2–5.9 per 10,000 live births.<sup>3</sup>

Hinds AM et al. found in their study that 76.7% of patients had normal visual acuity but that amblyopia, refractive error, and strabismus were common in syndromic craniosynostosis.<sup>4</sup> Khan et al. found that craniosynostosis patients had visual impairment in almost 40% of cases.<sup>5</sup> Moreover, Rafique Ali AA et al. reported that the other ophthalmologic manifestations in craniosynostosis included ptosis, proptosis, lagophthalmos, exposure keratopathy, papilledema, and optic atrophy.<sup>6</sup> Infantile

nystagmus syndrome and cataract were also reported in some craniosynostosis patients.<sup>7</sup>

Craniosynostosis has not been comprehensively studied in Asia or South-East Asia yet, and there is a lack of research on this condition in Thailand. Consequently, the primary objective of this study was to assess the visual prognosis of craniosynostosis in a Thai population. Additionally, we aimed to evaluate ocular deviation, the results of strabismus surgery, and other ophthalmologic manifestations associated with craniosynostosis.

**MATERIALS AND METHODS**

This study was approved by the Siriraj Institutional Review Board (Certificate of Approval no. Si 714/2023). In this retrospective descriptive cohort study, the medical records of craniosynostosis patients treated at Siriraj Hospital between January 2000 and June 2023 were reviewed retrospectively. Eligible patients for inclusion were those diagnosed with craniosynostosis, confirmed by computed tomography (CT) scans evaluated by a radiologist and clinical examination. Patients were included if an ophthalmologic examination was available. Conversely, those without an ophthalmologic examination were excluded from the study. All of the included patients

underwent ophthalmologic examination at least once. The collected data included the first and last age of ophthalmologic examination, sex, the classification of craniosynostosis (syndromic or non-syndromic), best-corrected visual acuity (BCVA), intraocular pressure, refraction, ocular alignment, and eye movement.

Other recorded ocular findings comprised ptosis, proptosis, nasolacrimal duct obstruction, nystagmus, and anterior and posterior segment examination results. Data on the history of craniofacial surgery and strabismus surgery were also collected. The postoperative strabismus surgery results, including BCVA, ocular alignment, and extraocular movement, were recorded at 2 weeks, 1–2 months, and 6 months postoperatively. The patients who had not been ophthalmologic examination were excluded.

BCVA was measured using a method appropriate for the patient age, cooperation, and underlying diseases. Visual acuity was converted to logMAR and analyzed. According to the definition of visual impairment by the World Health Organization (WHO), visual impairment (VI) refers to vision in the better eye worse than 6/12. Mild VI is defined as visual acuity  $\leq 6/18$ , moderate VI as  $\leq 6/60$ , severe VI as  $\leq 3/60$ , and blindness VI as  $\leq 1/60$ . For preverbal children, visual impairment is defined as the inability to fixate and follow in the better eye.<sup>8</sup>

Refraction was measured for each eye. The refractions of each eye were calculated to the spherical equivalent. Myopia was defined as  $\geq -0.5$  diopters, while hyperopia was defined as  $\geq +2.0$  diopters. Significant astigmatism was defined as  $\geq -0.75$  diopters.

Ocular alignment was measured by the alternate prism cover test at both distance and near, with BCVA in the primary position. The Krimsky test was employed to measure ocular alignment in non-cooperative patients. Ocular deviation was recorded in prism diopters (PD). The success of strabismus surgery was defined as a deviation of  $\leq 10$  PD.

### Statistical analysis

In this study, descriptive statistics were utilized to summarize both the demographic data and clinical characteristics of the patients. For categorical data, we presented the data as frequencies and percentages. In cases where continuous data adhered to a normal distribution, we reported the mean and standard deviation (SD); alternatively, for non-normally distributed data, the median and interquartile range (IQR) were utilized. Visual acuity data were transformed into logarithm minimal angle of resolution (logMAR) units for the purpose of the statistical analysis.

Descriptive outcomes were expressed as numbers and percentages with the corresponding 95% confidence intervals (CIs). Ocular findings in different subgroup analyses were compared using either the chi-squared or Fisher exact test, depending on the number of findings in each group. The chi-squared test was used when sample sizes in all categories were adequate while Fisher's exact test was employed otherwise, when the expected frequencies in any cell of the contingency table fell below five. A p-value less than 0.05 was considered statistically significant in these comparisons. All analyses were conducted using STATA version 16 (StataCorp, Lakeway, TX, USA).

## RESULTS

There were 123 craniosynostosis patients, and their medical records were reviewed. Of these, 65 (52.84%) cases were male and 58 (47.15%) cases were female. There were 70 cases (56.91%) diagnosed as non-syndromic craniosynostosis and 53 cases (43.08%) diagnosed as syndromic craniosynostosis. The syndromic craniosynostosis cases comprised Crouzon syndrome (15 cases), Apert syndrome (8 cases), Pfeiffer syndrome (2 cases), and other syndromes (28 cases). The mean age at first visit was 3.11 years old, with a median age of 1 year old (ranging from 3 days to 43 years old). Table 1 presents the data.

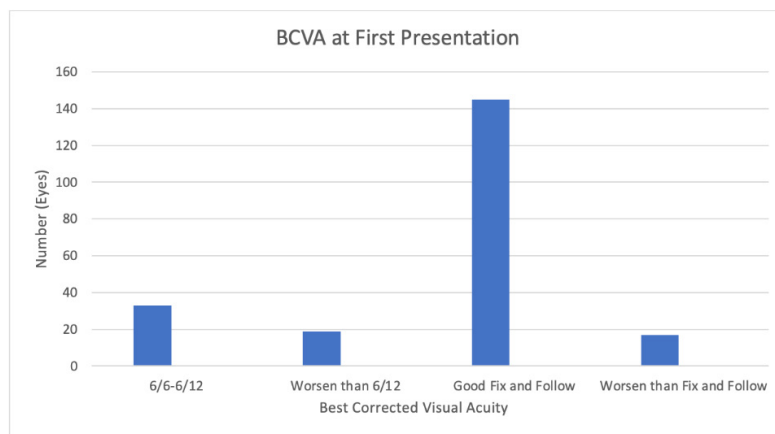
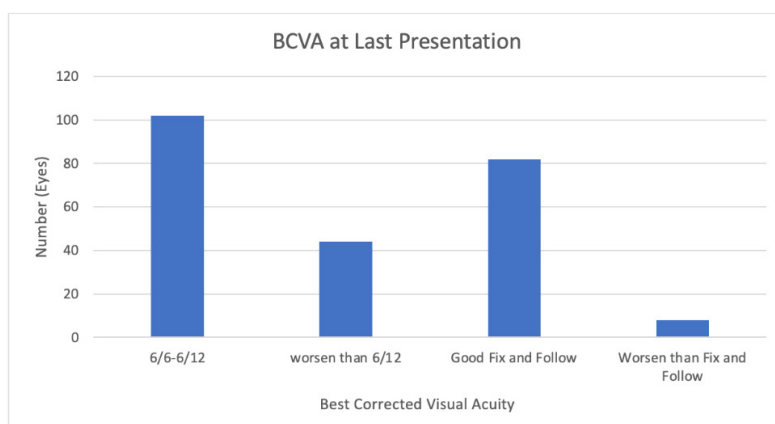
### Visual acuity

The best-corrected visual acuity (BCVA) at first visit can be recorded in logMAR units for 51 eyes. Overall, the cases were classed as good fix and follow (145 eyes), fair fix and follow (3 eyes), fixation but not follow (4 eyes), not fix and follow (10 eyes), no light perception (1 eye), and missing data due to uncooperative patients or immature visual development (32 eyes) (Fig 1). The average BCVA at first visit was 6/12–6/15 (logMAR 0.335). Of the 246 eyes total in the study, 145 eyes (72.36%) had a visual acuity of 6/12 or better and were classed as good fix and follow. Out of 107 patients with visual impairment at the first visit, 92 (85.98%) had no visual impairment at the last visit, while the other 15 (14.02%) still had visual impairment, with 8 out of these latter 15 patients having mild visual impairment (Fig 1).

The mean duration of follow-up was 5.16 years. The mean BCVA was 6/9.5–6/12 (logMAR 0.25) for 143 eyes, and good fix and follow was observed in 82 out of 93 eyes. Additionally, there were 8 eyes that did not fix and follow, 1 eye with hand motion, 1 eye with finger count, 1 eye with no light perception, and 10 eyes with missing out data due to uncooperative patients. The visual acuity recorded during the last visit examination included 236 eyes with visual acuity  $\geq 6/12$  and good fix

**TABLE 1.** Demographic data of the craniosynostosis patients (n = 123 patients).

| Characteristics                 | Number (%)                   |
|---------------------------------|------------------------------|
| Sex                             |                              |
| Male                            | 65 (52.84%)                  |
| Female                          | 58 (47.15%)                  |
| Category                        |                              |
| Non-syndromic craniosynostosis  | 70 (56.91%)                  |
| Syndromic craniosynostosis      | 53 (43.08%)                  |
| Crouzon syndrome                | 15 (12.20%)                  |
| Apert syndrome                  | 8 (6.50%)                    |
| Pfeiffer syndrome               | 2 (1.63%)                    |
| Other syndromes                 | 28 (22.76%)                  |
| Age at first presentation; year |                              |
| Mean ( $\pm$ SD)                | 3.11 ( $\pm$ 6.01)           |
| Median (Range)                  | 1 (range 3 days – 43 years)  |
| Age at last presentation; years |                              |
| Mean ( $\pm$ SD)                | 8.27 ( $\pm$ 8.06)           |
| Median (Range)                  | 6 (range 11 days – 43 years) |

**Fig 1.** Visual acuity at first visit (N=214 eyes)  
**Abbreviation:** BCVA = Best-corrected visual acuity.**Fig 2.** Visual acuity at last visit. (N=236 eyes)  
**Abbreviation:** BCVA = Best-corrected visual acuity.

and follow in 184 eyes (75.80%) (Fig 2). Also, 100 out of the 123 (81.30%) patients had no visual impairment at the last visit (Table 4).

### Ocular findings

Refraction errors were recorded for 144 eyes, while 102 eyes were unable to be recorded due to uncooperative patients. Among the recorded data, hyperopia was found in 25 eyes (17.36%), myopia in 18 eyes (12.5%), and astigmatism in 74 eyes (51.39%) (Table 2).

Ocular findings in the craniosynostosis patients included strabismus at the primary position in 28 out of 123 cases (22.76%), lagophthalmos in 17 cases (13.82%), and exposure keratopathy in 15 cases (12.2%). Corneal ulcer was observed in 5 cases and perforated cornea in 1 case, both of which were attributed to lagophthalmos and exposure keratopathy. The other findings were ptosis in 11 out of 123 cases (8.94%), proptosis in 10 cases (8.13%), nasolacrimal duct obstruction (NLDO) in 10 cases (8.13%), epiblepharon in 6 cases (4.88%), nystagmus and

entropion in 3 cases each (2.44%), glaucoma in 2 cases (1.63%), and optic disk atrophy, optic nerve hypoplasia, chronic dacryocystitis, euryblepharon, preceptal cellulitis, retinal dystrophy, entropion, and globe subluxation in 1 case each, as shown in Table 2.

### Strabismus and strabismus surgery outcomes

Twenty-eight of the 87 strabismus (32.18%) cases had strabismus confirmed at the primary position. We were not able to examine the other 36 patients due to uncooperation and visual immaturity. The most common strabismus was exotropia (18 cases). Among the 18 exotropia patients, two were found to have V pattern exotropia, and four patients were esotropia. The other six patients had combined strabismus, involving both exotropia and vertical deviation. Eight (5 cases exotropia and 3 cases esotropia) out of the 28 patients underwent strabismus surgery. The strabismus surgery details of the 8 patients are shown in Table 3.

The average BCVA preoperatively assessed in 12 eyes (6 cases) (in logMAR) was 6/12–6/15 and one case displayed good central, steady, and maintained (CSM) visual activity in both eyes. Postoperative BCVA evaluated in 14 eyes showed an average of 6/12, with one patient achieving good CSM in both eyes.

The average ocular deviations preoperatively for exotropia and esotropia were 38.75 PD (range 25–45 PD) and 46.67 (range 45–50 PD), respectively. Postoperatively, the mean ocular deviation was 3.2 PD (range 0–25 PD) in exotropia patients and 6.67 PD (range 0–20 PD) in esotropia patients. The success rate of strabismus surgery was 50%.

### Comparing syndromic vs. non-syndromic craniosynostosis

Visual acuity, refractive error and ocular diseases were analyzed to compare between syndromic and non-syndromic craniosynostosis. The number of cases with no visual impairment at first visit in non-syndromic craniosynostosis was better than for syndromic craniosynostosis, but this difference did not reach statistical significance. However, the visual impairment of the syndromic craniosynostosis group at the last visit was worse than for the non-syndromic group, with statistical significance ( $p$ -value = 0.007). The refractive errors did not differ between the two groups. To compare other ocular diseases, the incidences of strabismus, nasolacrimal duct obstruction, proptosis, lagophthalmos, and exposure keratopathy in the syndromic craniosynostosis group were higher than in the non-syndromic craniosynostosis group, with statistical significance, as shown in Table 4.

**TABLE 2.** Ocular findings.

|                               | Number (%)  |
|-------------------------------|-------------|
| Refractive error              |             |
| Hyperopia                     | 25 (10.16%) |
| Myopia                        | 18 (7.32%)  |
| Astigmatism                   | 74 (51.39%) |
| Strabismus                    | 28 (22.76%) |
| Lagophthalmos                 | 17 (13.82%) |
| Exposure keratopathy          | 15 (12.20%) |
| Corneal ulceration            | 5 (4.07%)   |
| Perforation of cornea         | 1 (0.81%)   |
| Ptosis                        | 11 (8.94%)  |
| Proptosis                     | 10 (8.13%)  |
| Nasolacrimal duct obstruction | 10 (8.13%)  |
| Epiblepharon                  | 6 (4.88%)   |
| Nystagmus                     | 3 (2.44%)   |
| Entropion                     | 3 (2.44%)   |
| Glaucoma                      | 2 (1.63%)   |
| Optic nerve atrophy           | 1 (0.81%)   |
| Optic nerve hypoplasia        | 1 (0.81%)   |
| Retinal dystrophy             | 1 (0.81%)   |
| Chronic dacryocystitis        | 1 (0.81%)   |
| Globe subluxation             | 1 (0.81%)   |
| Euryblepharon                 | 1 (0.81%)   |
| Preseptal cellulitis          | 1 (0.81%)   |

**TABLE 3.** Patients' data related to strabismus surgery.

| Patient | Pre-operative BCVA                 | Pre-operative alignment, PD              | Muscle surgery, mm                                                         | Post-operative BCVA              | Post-operative alignment, PD                                      |
|---------|------------------------------------|------------------------------------------|----------------------------------------------------------------------------|----------------------------------|-------------------------------------------------------------------|
| 1       | Could not evaluate                 | XT 25, IOOA OD                           | BLR rec 6<br>RIO myectomy 8                                                | 6/15 OU                          | Orthotropia                                                       |
| 2       | 6/12 OU                            | IOOA OS                                  | LIO rec 10                                                                 | 6/9 OU                           | ET 16, IOOA OU                                                    |
| 3       | 6/9 OU                             | XT 40                                    | BLR rec 8                                                                  | 6/12 OU                          | XT 12                                                             |
| 4       | 6/24, 6/9                          | ET 45, IOOA OU                           | BMR rec 5<br>IOAT OU                                                       | 6/12, 6/9                        | ET 20, IOOA OS                                                    |
| 5       | 6/24, 6/60<br>6/15, 6/30           | ET 45<br>XT 20                           | BMR rec 6<br>LLR rec 9                                                     | 6/15, 6/9<br>6/15, 6/30          | XT 8, DVD OU<br>Orthotropia,<br>DVD OD 14                         |
| 6       | 6/9, 6/7.5<br>6/9, 6/9             | XT 45<br>ET 30, LHT 14                   | BLR rec 8.5<br>Advancement LLR<br>to original insertion<br>LIO myectomy 10 | 6/6 OU<br>6/7.5, 6/9.5           | Orthotropia<br>E 5                                                |
| 7       | Good CSM OU                        | ET 50                                    | BMR rec 6                                                                  | Good CSM OU                      | Orthotropia                                                       |
| 8       | 6/12 OU<br>6/12, 6/9<br>6/15, 6/12 | XT 45<br>XT 30, IOOA OU<br>XT 25, RHT 12 | BLR rec 8<br>BMR res 5.5<br>BIO rec<br>RLR rec 4<br>RSR rec 5              | 6/9.5 OU<br>6/15, 6/12<br>6/9 OU | XT 30<br>XT 25, RHT 12,<br>V pattern<br>XT 25 IOOA OU,<br>SOUA OU |

**Abbreviations:** ET = esotropia, XT = exotropia, LHT = left hypertropia, RHT = right hypertropia

OU = both eyes, OD = right eye, OS = left eye, E = esophoria, IOOA = inferior oblique overaction, SOUA = superior oblique overaction, BMR = bilateral medial rectus muscle, BLR = bilateral rectus muscle, LLR = left lateral rectus, BIO = bilateral inferior oblique, RIO = right inferior oblique, LIO = left inferior oblique, RSR = right superior rectus, IOAT = inferior oblique anteriorization, DVD = dissociated vertical deviation, rec = recession, BCVA = best-corrected visual acuity, CSM = central, steady, and maintained, PD = prism diopter, mm = millimeters.

## DISCUSSION

Our study investigated both syndromic and non-syndromic craniosynostosis in Thailand over the past 20 years, examining a total of 123 cases in our medical records. The majority of the patients experienced good visual outcomes. When comparing the non-syndromic and syndromic craniosynostosis groups, the non-syndromic group exhibited good visual outcomes during the last visit and a lower incidence of other ocular diseases compared to the syndromic group.

Hind AM et al. evaluated 165 cases and reported that 76.7% achieved a final best-corrected visual acuity

(BCVA) better than 6/12 in the better eye.<sup>4</sup> Khan SH et al. conducted a 21-year review involving 141 children with syndromic craniosynostosis (Crouzon, Pfeiffer, Apert, and Saethre–Chotzen syndromes), revealing that 61.2% achieved a visual acuity of 6/12 or better.<sup>5</sup>

Rafique Ali AA et al. conducted a retrospective study over 6 years of 37 craniosynostosis patients in Malaysia, finding a 32.1% prevalence of visual impairment.<sup>6</sup> Additionally, Tay T et al. explored the prevalence of visual impairment in syndromic craniosynostosis over 22 years, reporting a 35.5% prevalence for bilateral visual impairment and 9.1% for unilateral visual impairment.<sup>7</sup>

**TABLE 4.** Ocular findings in syndromic and non-syndromic craniosynostosis.

| Characteristics                            | Non-syndromic<br>craniosynostosis |                           | Syndromic<br>craniosynostosis |                           | p-value | Percent Difference<br>(95% CI) |
|--------------------------------------------|-----------------------------------|---------------------------|-------------------------------|---------------------------|---------|--------------------------------|
|                                            | Total<br>patients                 | Number of<br>patients (%) | Total<br>patients             | Number of<br>patients (%) |         |                                |
| Visual acuity at first visit               |                                   |                           |                               |                           |         |                                |
| No visual impairment                       | 65                                | 58 (89.23%)               | 42                            | 34 (80.95%)               |         |                                |
| Visual impairment                          | 65                                | 7 (10.77%)                | 42                            | 8 (19.05%)                | 0.228   | 8.28 (-23.54, 5.09)            |
| Visual acuity at last visit                |                                   |                           |                               |                           |         |                                |
| No visual impairment                       | 67                                | 62 (92.54%)               | 51                            | 38 (74.51%)               |         |                                |
| Visual impairment                          | 67                                | 5 (7.46%)                 | 51                            | 13 (25.49%)               | *0.007  | 18.03 (-32.06, -4.72)          |
| Refractive errors                          |                                   |                           |                               |                           |         |                                |
| Hyperopia                                  | 40                                | 9 (22.50%)                | 31                            | 6 (19.35%)                | 0.747   | 3.15 (-16.60, 21.27)           |
| Myopia                                     | 40                                | 6 (15.0%)                 | 31                            | 6 (19.35%)                | 0.627   | 4.35 (-23.04, 13.01)           |
| Astigmatism                                | 40                                | 22 (55.0%)                | 31                            | 20 (64.52%)               | 0.418   | 9.52 (-30.41, 13.13)           |
| Strabismus                                 | 56                                | 13 (23.21%)               | 31                            | 15 (48.39%)               | *0.016  | 25.18 (-44.27, -4.51)          |
| Lagophthalmos                              | 70                                | 5 (7.14%)                 | 53                            | 12 (22.64%)               | *0.014  | 15.50 (-29.01, -2.98)          |
| Exposure keratopathy                       | 70                                | 5 (7.14%)                 | 53                            | 10 (18.87%)               | *0.049  | 11.73 (-24.86, 0.15)           |
| Ptosis                                     | 70                                | 4 (5.71%)                 | 53                            | 7 (13.21%)                | 0.149   | 7.50 (-19.64, 2.97)            |
| Proptosis <sup>+</sup>                     | 70                                | 1 (1.43%)                 | 53                            | 9 (16.98%)                | *0.002  | 15.55 (-27.85, -5.58)          |
| Nasolacrimal duct obstruction <sup>+</sup> | 70                                | 1 (1.43%)                 | 53                            | 9 (16.98%)                | *0.002  | 15.55 (-27.85, -5.58)          |
| Epiblepharon                               | 70                                | 4 (5.71)                  | 53                            | 2 (3.77%)                 | 0.621   | 1.94 (-7.69, 10.47)            |
| Nystagmus <sup>+</sup>                     | 70                                | 1 (1.43%)                 | 53                            | 2 (3.77%)                 | 0.404   | 2.34 (-11.40, 4.46)            |

\* Statistically significant (p-value &lt; 0.05)

<sup>+</sup> Fisher's exact tests

Our study revealed that 85.98% of patients showed no visual impairment during their initial visit, while 14.02% exhibited visual impairment. With a mean follow-up duration of 5.16 years, the percentage of patients with a last recorded visual acuity of  $\geq 6/12$ , with good fixation and follows was 75.80%. Notably, the incidence of visual impairment in our study was lower than in other comparable studies. The observed improvement in visual outcomes during the final visit may be attributed to the early treatment of amblyopia and refractive errors.

A number of previous studies have documented ocular findings in craniosynostosis. Hind AM et al. reported a prevalence of astigmatism of 67.2%.<sup>4</sup> Khan SH et al. identified astigmatism as the most common

refractive error, at 40.3%.<sup>5</sup> Rafique Ali AA et al. reported the common refractive errors were astigmatism (45.6%), hyperopia (18.2%), and myopia (13.5%), respectively.<sup>6</sup> In our study, abnormal refractive errors included astigmatism at 30.08%, followed by hyperopia at 10.16% and myopia at 7.32%. Astigmatism was the most common refractive error, which correlated with previous studies.<sup>4-6</sup>

In Hind AM et al.'s research, nearly half of their patients exhibited exotropia with a V pattern.<sup>4</sup> The other ocular findings were optic disk swelling and/or pallor (18.2% of eyes), signs of corneal exposure (9.6%), and corneal scar (2.9%). Khan SH et al. reported a 70% prevalence of strabismus in syndromic craniosynostosis.<sup>5</sup> Rafique Ali AA et al. found that strabismus occurred

in 50.6% of craniosynostosis patients, often alongside other ocular manifestations, such as proptosis in 78.6% of cases, lagophthalmos in 53.3%, exposure keratopathy in 30.6%, and optic disc atrophy in 13.7%.<sup>6</sup>

In our study, strabismus was found in 23% of cases, with exotropia being the most common type. Eight patients underwent strabismic operations. Although the mean postoperative ocular deviation in both exotropia and esotropia groups was within 10 PD, three patients required more than one surgery. One patient showed the absence of the right superior oblique in our study. Strabismus surgery is performed after craniofacial surgery. Furthermore, strabismic surgeries are complicated due to abnormal orbits and anomalies of extraocular muscles.<sup>9</sup> Surgical success in craniosynostosis patients was 50%, compared to 60.2% in normal subjects.<sup>10</sup> The lower surgical success in craniosynostosis patients was attributed to the thinner and weaker extraocular muscles and abnormal orbital structure.<sup>9-11</sup>

Craniosynostosis patients are at risk of developing lagophthalmos and exposure keratopathy. Our study identified 5 patients with corneal ulcers, and 1 patient with corneal perforation due to a corneal ulcer. Ophthalmologists need to be aware of these serious findings and prescribe lubricating medications to prevent exposure keratopathy. In our study, one patient required permanent tarsorrhaphy due to severe exposure keratopathy.

Rostamzad P et al. conducted a systematic review on the prevalence of ocular anomalies in craniosynostosis. They reported proptosis in 86% of cases, optic atrophy in 8%–29%, entropion in 2%–50%, and nasolacrimal duct obstruction (NLDO) in 60%<sup>12</sup>; while our study found lower prevalence rates for proptosis, optic atrophy, entropion, and NLDO compared to Rostamzad's research.

We conducted a comparison of visual acuity, refractive errors, and ocular diseases associated with craniosynostosis between non-syndromic and syndromic groups. The visual outcomes in the syndromic group were worse than those in the non-syndromic group. Additionally, syndromic craniosynostosis patients exhibited significantly higher rates of strabismus, proptosis, NLDO, exposure keratopathy, and lagophthalmos compared to the non-syndromic craniosynostosis patients. The increased prevalence of ocular diseases in syndromic craniosynostosis patients can be attributed to the presence of multiple sutures abnormalities, mid-face abnormalities, and developmental issues, which are more pronounced than in non-syndromic craniosynostosis patients.<sup>13</sup>

This study offers insights into visual prognosis in craniosynostosis, which is valuable for counseling purposes. It lists the high incidence of ophthalmologic findings,

providing a guideline for other ophthalmologists to consider when dealing with craniosynostosis. Early detection and treatment of manageable ophthalmologic conditions can prevent additional diseases and complications, including amblyopia from strabismus and refractive errors, as well as corneal complications from lagophthalmos and exposure keratopathy.

However, it is essential to note the limitations of this study, as it involved a retrospective review of medical records. Many data points were missing due to the challenges associated with conducting complete ocular examinations in craniosynostosis patients which most were infant of children. Ocular manifestations like visual acuity, strabismus, and amblyopia are believed to result from various mechanical processes. For example, the underlying neurodevelopmental disorders prevented a comprehensive ophthalmologic examination from being conducted in a single session. The visual acuity test in uncooperative children provides qualitative data only, making it challenging to compare directly with the visual acuity of adults or cooperative children. Interestingly, the number of patients with recorded visual acuity measurements at both the initial and final visits was inconsistent. Therefore, we assumed that younger children have a different normal range of visual acuity compared to older children, which gradually becomes similar to that of adults with normal vision. Older children typically cooperate well during visual acuity tests and eye examinations. However, allowing the visual acuity measured at the last visit to affect results might lead to unclear outcomes. Moreover, childhood eye exams and the results of strabismus surgery varied depending on the individual ophthalmologist. Our study examined medical records and surgical outcomes from multiple ophthalmologists, introducing some degree of bias. Future studies could provide more comprehensive data on eye exams and the accuracy of strabismus surgery results when conducted by a single ophthalmologist and surgeon.

To overcome these limitations, future studies should aim to include larger sample sizes to enhance the statistical power and improve the generalizability. Nevertheless, we believe that our study presents real-life statistics and highlights the fact that with proper methodology it is possible to significantly improve the reliability and validity of research findings.

In summary, our findings indicate a higher prevalence of visual impairment among patients with craniosynostotic syndromes. Notably, the majority of these visual impairments are amenable to treatment with timely intervention, particularly through strabismic therapy. Although

the prevalence of abnormal ophthalmologic findings is relatively low, their impact on visual impairment remains significant. Therefore, regular ophthalmologic evaluations are essential for patients diagnosed with craniosynostosis to facilitate early detection of abnormalities and prompt management. Further research, including genetic evaluations, is warranted to enhance the diagnostic accuracy and overall understanding of craniosynostotic syndromes.

## CONCLUSION

The visual outcomes in the craniosynostosis patients were good. The majority of the patients did not have visual impairment. Common ophthalmologic manifestations were refractive error, strabismus, lagophthalmos, and exposure keratopathy. Syndromic craniosynostosis patients had poor visual outcomes and ocular findings more often than the non-syndromic patients. The success rate for strabismus surgery in craniosynostosis patients was about half. A multidisciplinary team is necessary to treat craniosynostosis patients. Early ocular examination should be provided to craniosynostosis patients to prevent serious ocular complications.

## Conflict of Interest

The authors declare that they have no conflicts of interest related to the publication of this research.

## Author Contributions

SS: general research process, framework of the study, supervision, conceptualization, methodology, writing-original draft preparation, review and editing; TS: general research process, framework of the study, supervision, review and editing WS: methodology, data analysis, review and editing. All authors have read and agreed to the final version of the manuscript.

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