

Ophthalmological findings in children with metopic craniosynostosis

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Abstract

Introduction: Trigonocephaly is a form of craniosynostosis resulting from premature fusion of the metopic suture. It is the second most common of single-suture craniosynostoses, yet ophthalmological manifestations associated with this condition remain under-reported. This study aimed to characterize ophthalmological outcomes of children with trigonocephaly and determine whether targeted visual screening is warranted.

Methods: We conducted a retrospective review of children with trigonocephaly managed in our institution between 2020 and 2024 who underwent a complete ophthalmological evaluation, including visual acuity testing, refraction, and oculomotor assessment.

Results: Twenty-eight children met the inclusion criteria. Median age at evaluation was 5.2 years (range: 0.3–11.7) with a male predominance (68%). The mean best corrected visual acuity was 0.07 ± 0.12 LogMAR, including five (18%) children with a history of amblyopia. Strabismus was documented in seven patients (25%), most commonly exotropia (57%). The mean refractive spherical equivalent was $+1.55 \pm 1.65$ diopters (D). Seventeen eyes (30%) demonstrated clinically significant astigmatism (> 1 D), with a mean cylindrical value of 0.91 ± 0.85 D. The astigmatism axis was with-the-rule in 71%, oblique in 26% and against-the rule in 3% of eyes. One child (3.3%) exhibited papilledema suggestive of intracranial hypertension. Two children (three eyes) presented congenital cataract.

Conclusion: Children with trigonocephaly exhibit a high prevalence of visual abnormalities, including refractive errors, strabismus, and in a very rare situations, signs of intracranial hypertension. These findings support the need of systematic, early, and longitudinal ophthalmological surveillance to facilitate prompt diagnosis and management of potential visual outcomes.

INTRODUCTION

Trigonocephaly is a form of craniosynostosis caused by premature fusion of the metopic suture (1). It is the second most common of single-suture craniosynostosis after scaphocephaly (sagittal synostosis) (2). Its prevalence is estimated at approximately 1 in 5,000 live births (3), and has risen markedly worldwide in recent decades (3–6). At Necker-Enfants Malades Hospital, the number of non-syndromic cases increased by 420% between 1988 and 2007 (2), although no definitive contributing factors have been identified to date (7). Reported risk factors include gestational age, foetal presentation at birth, birth weight, mode of delivery, external pressure on the fetal skull (8). Insufficient folic acid intake before pregnancy has also been implicated (5). Moreover, a severe form of trigonocephaly is described in fetal valproate syndrome (9, 10) with first-trimester, dose-dependent exposure to valproic acid representing a well-established teratogenic factor (11).

This premature fusion of metopic suture results in typical craniofacial abnormalities, including metopic ridge, deformation of the orbital roof, hypotelorism and upslanting palpebral fissures. The anterior cranial fossa is reduced, but without total skull volume restriction (12).

In general, craniosynostoses can be associated with neurological complications such as intracranial hypertension and developmental delay, as well as ophthalmological manifestations including optic neuropathy, refractive errors, strabismus and proptosis (13). The morphological severity of metopic synostosis is highly variable, ranging from a metopic ridge with mild forehead deformation and minor hypotelorism to major triangular foreheads with extreme bitemporal narrowing. Furthermore, a demonstration that trigonocephaly and metopic ridges have distinctive skull and orbital shapes, suggesting that metopic ridges are not a minor form of trigonocephaly (14). Even though prior studies suggest that the degree of frontal angulation seems to correlate with neurodevelopmental outcomes (15), there is currently no strong scientific argument for associating trigonocephaly with a specific risk of cognitive impairment (16).

PATIENTS AND METHODS

All medical records of children diagnosed with metopic synostosis (trigonocephaly) and followed in our tertiary referral center between January 2020 and March 2024 were retrospectively reviewed. Case identification was performed using the BaMaRa rare diseases database and Dr Warehouse search engine (20), screening for the French terms “*trigonocéphalie*”, “*synostose métopique*”, “*craniosynostose métopique*”. Syndromic, and secondary metopic synostoses were excluded. Children with incomplete ophthalmological evaluations were also excluded. Patients with a clinical diagnosis of trigonocephaly who did not undergo surgery were also excluded as well, unless surgery had been declined by the parents.

Clinical data

Medical records were reviewed to extract relevant clinical data and ophthalmological data. For each included child, the age at surgery was recorded. Ophthalmological assessment comprised the following parameters:

- Visual outcome: Best-corrected visual acuity (BCVA) reported in LogMAR scaling, the presence, history, laterality, and type of amblyopia; and presence of papilledema. Amblyopia was defined as an interocular BCVA difference of two more lines.
- Refractive outcomes: cycloplegic refraction including spherical error, cylindric error, axis of astigmatism and spherical equivalent. Refractive values were expressed in positive diopters and astigmatism axes in degrees.

Definition of significant refractive error: thresholds followed the 2020 recommendations of the *Association Francophone de Strabologie et d’Ophtalmologie Pédiatrique* (AFSOP) according to age (21). Before 18 months, the recommendations for optical equipment were: hyperopia $> +4.5D$, myopia $> -3D$, astigmatism $> 2.5D$ and/or anisometropia $> 1.75D$. Between 18 and 36 months, the recommendations for optical equipment were: hyperopia $> +3.5D$, myopia $> -1.5D$, astigmatism $> 1.5D$ and/or anisometropia $>$

1.25D. Finally, after 36 months, the recommendations for optical equipment were: hyperopia > + 3.25D, myopia > -1D, astigmatism > 1.25D and/or anisometropia > 1D.

- Strabismus outcomes: presence of any ocular motility disorder, type of strabismus and any alphabet pattern deviation. Assessment of ocular alignment was based on clinical examination using Hirschberg corneal reflex test, supplemented by orthoptic evaluation when needed. The most recent examination was used for analysis.
- Intra-ocular pressure: measured using air-puff tonometry or rebound tonometry.

Surgical technique

The surgical technique used to correct metopic synostosis has been standardized in the Necker-Enfants malades craniofacial unit for more than thirty years. The procedure consists in a fronto-orbital remodelling that included reshaping the supra-orbital bar to correct its abnormal angulation, followed by the placement of newly contoured, rounded, one-piece frontal bone segment harvested from the calvarial vault. The coronal bone flaps are carefully remodelled and repositioned, and fixation is achieved using resorbable suture and plates. Surgical indications are generally retained when the clinical presentation included a pronounced triangular forehead, bitemporal narrowing, and hypotelorism.

Statistical analysis

Data analyses were performed using RStudio (RStudio Inc., version 1.2.5033). Continuous quantitative variables were reported as mean $\pm$ standard deviation or as median with range, depending on their distribution. Categorical variables were summarized as frequencies (%). Comparisons of categorical variables were conducted using Chi-square or Fisher's exact tests. Continuous variables were compared using Student's *t*-test or the Mann–Whitney *U* test, as appropriate. Normality was assessed using the Shapiro–Wilk test.

For outcomes with paired measurements from both eyes, a mixed linear regression model was applied to account for the inclusion of bilateral data and intra-individual correlation. Statistical significance was set at $p < 0.05$ for all analyses.

The study was conducted in accordance with the Declaration of Helsinki. All patients and/or their legally authorized representatives were informed about the use of medical data for research purposes, and written consent for the use of clinical information and images was obtained.

RESULTS

A total of 28 children (56 eyes) were jointly followed in the cranio-facial unit and ophthalmology department for a trigonocephaly in Necker-Enfants Malades Hospital, allowing for complete ophthalmological assessment. Among these 28 patients, 19 were boys (68%) and 9 were girls (32%).

The median age at last visit was 5,2 [0.3; 11.7] years for a mean follow-up duration of 30 ± 31 months. Demographic characteristics of the series are available in Table 1.

Of the 28 children, 26 (93%) underwent a fronto-orbital remodeling at a median age of 10 months [3; 24]. Two (7%) patients did not undergo corrective cranial surgery due to parents' refusal. Only four patients had received an ophthalmological consultation prior to surgery.

Table 1
Demographic and clinical characteristics of the cohort.

Characteristics	Number
Demographical	
Patients	28
Median age [Range] years	5.2 [0.3; 11.7]
Female/male	9 / 19 (32% / 68%)
Median age at craniofacial surgery [Range] month	10 [3; 24]
Clinical	
Mean visual acuity (LogMAR)	0.07 +/- 0.12
Amblyopia	5 (18%)
Strabismus	7 (25%)
Papilledema	1 (4%)
Refractive disorders requiring optical correction	8 (29%)

Regarding visual outcomes, the mean BCVA was 0.07 ± 0.12 LogMAR. Five children (18%) exhibited amblyopia or a history of amblyopia: two strabismic, two secondary to congenital cataracts and one (14%) child had a complex form combining anisometropia, strabismus and stage 1 foveal hypoplasia with a normal electrophysiological testing. All amblyopia cases had been or were currently being treated with favorable outcomes.

Only one child (3%) exhibited signs of intracranial hypertension before surgery, with a Frisén grade 1 papilledema.

Strabismus was observed in seven (25%) patients: one esotropia (14%), four constant exotropia (57%) and two intermittent exotropia (29%). No alphabetical pattern strabismus was observed. Preoperative data were available for three patients; one patient developed an exotropia noted during postoperative

follow-up that had not been documented prior to surgery. No patient had demonstrated ocular motility restriction.

Refractive disorders requiring spectacle correction during the follow-up were documented in eight children (29%), including: four significant astigmatism, one hyperopia, two mixed myopia-astigmatism and one isolated anisometropia. The mean refractive spheric error was $+1,16 \pm 1.81$ D and the mean refractive spherical equivalent was $+1,55 \pm 1.65$ D.

Astigmatism ≥ 1 D was presented in 17 eyes (30%) from 11 children (39%). The mean cylindrical power in the cohort was $0,91 \pm 0,85$ D. Astigmatism axis distribution was as follows: with-the-rule in 71%, oblique in 26%, and against-the-rule in 3% of eyes. Astigmatism was further analysed according to two age subgroups (≤ 24 months and > 24 months) (Table 2).

The presence of a spherical anisometropia (defined as an interocular spherical difference ≥ 1 D) and cylindrical anisometropia (interocular cylindrical difference ≥ 1 D) was 11% (3/28) and 18% (5/28), respectively.

Table 2
Distribution of astigmatism and astigmatism axis in children with trigonocephaly aged ≤ 24 months and > 24 months

Group	≤ 24 -month-old	> 24 -month-old	P value
Astigmatism ≥ 1 D (%)	41,7%	37,5%	0.44
Astigmatism $\geq 1,5$ D (%)	29,2%	25%	0,55
Mean Cylinder (D)	0.84 D	1.0 D	0.65
(+/- SD)	± 0.68	± 1.1	
Axe (%)			
Direct	85%	50%	0.51
Indirect	0%	19%	0.08
Oblique	15%	31%	0.48

This series also revealed the presence of infantile cataract in two children (7%), affecting three eyes. One child had a non-surgical unilateral posterior polar cataract, successfully managed by patching the better eye. The second child presented a bilateral surgical cataract and underwent an initial lensectomy at the age of 3.5 years of age, followed by a secondary intraocular lens implantation. Long-term follow-up subsequently revealed secondary glaucoma in the left eye.

Only one patient presented a mild congenital ptosis, noted after cranial surgery, which resolved spontaneously before the age two years.

Overall, at least one ocular anomaly (strabismus, refractive error, or organic pathology) was identified in 36% of children with metopic craniosynostosis.

DISCUSSION

Only a few studies have specially examined ophthalmological findings in pediatric trigonocephaly (17–19, 22–25); their results are summarized in Table 3. The present work demonstrates that more than one-third of children with metopic craniosynostosis present at least one ocular anomaly, an observation that is not classically emphasized in this condition.

The reported incidence of amblyopia in trigonocephaly ranges from 8.8–17.1% (22, 23). In the present series, 18% of children were affected, with heterogeneous etiologies (organic, strabismic, or refractive).

Regarding strabismus, the incidence of strabismus in children with trigonocephaly varies between 0–15.8% (18, 19, 22–27), with a majority of esotropia (19). In contrast, this study identified oculomotor disorders in 25% of children, predominantly exotropia (57%). In the general population, the prevalence of strabismus in children is 2–3.3% (28–33). Denis et al. (16) hypothesized that fronto-zygomatic narrowing could exert a symmetrical traction on the lateral rectus muscles, inducing exotropia. This mechanism appears plausible and aligns with the pattern observed in our cohort.

Refractive disorders have been reported in 24.2–47.4% of children with trigonocephaly (19, 22, 23), predominantly hyperopia (19, 25) or astigmatism (22, 23). In our cohort, 29% of children required optical correction during follow-up, mainly due to astigmatism. The definitions of significant refractive errors, however, differ across studies. American cohorts (22, 23) used the definition of significant refractive errors of the American Academy of Ophthalmology (AAO) Preferred Practice Pattern (2017) age adjusted targets (≥ 2 D for astigmatism ; ≥ 4.5 D for hyperopia without deviation ; ≥ 1.5 D for hyperopia with deviation ; ≥ 3 D for myopia ; and a interocular difference ≥ 1.5 D for anisometropia), whereas our study relied on the 2020 French AFSOP recommendations (21). When AAO criteria are applied to our dataset, results remain consistent with the literature. The high refractive-error prevalence reported by Roider et al. (23) may be explained by the inclusion of children with concomitant deformational plagiocephaly or bradycephaly, conditions known to be associated with elevated rates of refractive anomalies.

Most studies report an increased prevalence of astigmatism in trigonocephaly (15.4–45%) (16, 20–22, 25). In our cohort, astigmatism was generally moderate (< 1.5 D), but 30% of eyes (17/56) had astigmatism ≥ 1 D, mostly in the with-the-rule orientation, unlike the predominantly oblique pattern described by Denis et al. (16). In the general pediatric population, astigmatism > 0.5 D is present in 14.9% of children (32); in our series, 42% exceeded this threshold. A Swedish study (22) comparing refractive status before and after cranial remodelling reported astigmatism > 1 D in 35–45% of eyes preoperatively, decreasing to 15.4–23.1% postoperatively, suggesting refractive modifications following fronto-orbital remodelling. Interpretation of early refractive data must also consider age, as significant astigmatism is common in infancy and decreases with maturation (33–35). In our cohort, no significant difference in astigmatism was found between children ≤ 24 months and > 24 months ($p = 0.44$).

Anisometropia > 1 D was present in 6/28 patients (21%): two mixed spherical-cylindrical, one spherical, and three cylindrical anisometropias. This rate is higher than those reported in previous studies (5–10.5%) (20–22), although prior definitions used a > 1.5 D threshold. Using the same > 1.5 D definition, the prevalence in our series was 7% (2/28). Astigmatic anisometropia > 1 D affected 18% of children (5/28), markedly higher than in the general population (1% at age six) (36) but lower than in unicoronal craniosynostosis (32%) (13). Aniso-astigmatism is strongly associated with amblyopia (OR 8.2, CI 1.4–47) (36).

Table 3

Summary of published findings on ocular abnormalities in children with trigonocephaly, including rates of amblyopia, strabismus and refractive errors

Study	n	Amblyopia	Strabismus	Astigmatism	Refractive errors	Anisometropia
MacIntosh et al. (2011)*	64	/	8/64 (15.6%)	/	28.13%	/
Nguyen et al. (2016)**	91	8/91 (8.8%)	8/91 (8.8%)	20.9% greater or equal 2D	24.2%	5.5% ≥ 1,5D
Roider et al. (2020)**	76	13/76 (17.1%)	12/76 (15.8%)	28.9% greater or equal 2D	47.4%	10.5% ≥ 1,5D
Ntoula et al. (2021)***	22	/	1/22 (4.5%)	35–45% before surgery and 15.4–23.1% after surgery more than 1D	/	5-7.7% ≥ 1D
Present series	28	5/28 (18%)	7/28 (25%)	30% greater or equal 1 D and 11% greater or equal 2D	29%	7% ≥ 1,5D

* Refractive status was reported when available. Significant refractive error was defined as > 1.0 D of astigmatism, > 2.5 D spherical equivalent hyperopia or > 1.0 D of spherical myopia.

** Significant refractive error was defined as ≥ 2.0 D of astigmatism, ≥ 4.5 D for hyperopia without manifested deviation, ≥ 1.5 D of hyperopia with deviation, ≥ 3.0 D for myopia, or an interocular difference ≥ 1.5 D for anisometropia.

***Significant refractive error was defined as ≥ 1.0 D of astigmatism or > 1.0 D of anisometropia.

Only one patient in our series showed ocular signs of intracranial hypertension. Because most ophthalmological examinations were performed postoperatively, transient elevations in intracranial pressure may have gone undetected. Intracranial hypertension is considered extremely rare in

trigonocephaly, as overall cranial volume is typically preserved despite a reduced anterior cranial fossa (12). In a large cohort, Cornelissen et al. (37) reported raised intracranial pressure in 1.9% of patients preoperatively and 1.5% postoperatively. However, these findings likely reflect a heterogeneous population that could not be stratified into severity groups, given the current limited understanding of the underlying mechanisms driving trigonocephaly.

This study has several limitations. First, its retrospective design limits the availability of preoperative ophthalmological data, as systematic on-site ophthalmic evaluation was not part of routine care for trigonocephaly, given the historically low reported rates of ocular complications. Following this work, our protocol has been revised to include systematic preoperative ophthalmological assessment.

The elevated rate of paediatric cataracts in this series may reflect referral bias, as our institution is a national tertiary centre for rare ocular diseases. Nevertheless, the possibility of a genetic association between trigonocephaly and cataract warrants further exploration.

Finally, different craniofacial surgical techniques exist (fronto-orbital remodelling and endoscopic approaches for instance), performed at different ages, and evaluating their differential effects on ocular outcomes in a large, prospective cohort represents an important direction for future research.

CONCLUSION

This series demonstrates that visual disturbances are relatively frequent in children with trigonocephaly, underscoring the need for systematic ophthalmological evaluation in all patients with metopic synostosis. The prevalence of strabismus and refractive errors—many of them amblyogenic—is markedly higher than in the general pediatric population. Early ophthalmic screening within the first months of life is therefore recommended to ensure timely detection and management of amblyopia and refractive disorders in this group.

Declarations

Competing Interests

None authors have a competing interest

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Author Contribution

A.C , R.T and E.A wrote the main manuscript texte and A.C prepared tables 1-3. All authors reviewed the manucript.

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Available data

describing ophthalmological findings in trigonocephaly remain limited, and updated evidence is needed (17–19). The objective of this study was to characterize the ophthalmological consequences of trigonocephaly and determine whether these children require targeted visual screening.

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