Craniosynostosis: To Study the Spectrum and Outcome of Surgical Intervention at a Tertiary Referral Institute in India

Charandeep S. Gandhoke, Simran K. Syal, Ajay Sharma, Arvind K. Srivastava, Daljit Singh

Original Article

Department of Neurosurgery, Maulana Azad Medical College, Lok Nayak Jai Prakash Narayan Hospital, Guru Nanak Eye Centre and Govind Ballabh Pant Institute of Postgraduate Medical Education and Research (GIPMER), New Delhi, India, 1Department of Paediatrics, Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar, Punjab, India

Aims and Objectives: This study aimed to analyze the spectrum and surgical outcome of cases of craniosynostosis operated at a tertiary referral institute in India

Design: This was a cross-sectional study.
Materials and Methods: We retrospectively examined 60 cases of craniosynostosis operated at our institute from 2008 to 2014 (with a minimum follow-up of 2 years). Data was collected including name, age, gender, involved sutures, other medical conditions, whether syndromic craniosynostosis or not, whether symptoms and signs of intracranial hypertension were present or not, associated findings on magnetic resonance imaging of brain and cervico-medullary junction, type of surgery performed, age at which surgery was performed, perioperative complications (if any), and findings on follow-up. To be able to analyze the surgical results, we used the seven category classification system used by Sloan et al.

Results: Craniosynostosis affected more men than women. The incidence of syndromic craniosynostosis was 11.67%. Mean age at first surgery was 3.85 years. Chiari malformation was present in 80% of the Crouzon’s syndrome cases, 62.5% of the oxycephaly cases, and 4.44% of the non-syndromic, non-oxycephaly cases. Intracranial hypertension was present in 80% of the Crouzon’s syndrome cases, 75% of the oxycephaly cases, and 6.67% of the non-syndromic, non-oxycephaly cases. Perioperative complications were present in 42.86% of the syndromic craniosynostosis cases, 50% of the oxycephaly cases, and 15.56% of the non-syndromic, non-oxycephaly cases. Compromised overall correction was present in 4 of 7 cases of syndromic craniosynostosis, 3 of 8 cases of oxycephaly, and 2 of 45 cases of non-syndromic, non-oxycephaly group.

Conclusion: The study highlights the importance of educating the masses so that cases of craniosynostosis present early. The incidence of Chiari malformation, intracranial hypertension, and perioperative complications was significantly higher in the syndromic craniosynostosis and oxycephaly groups than in single-suture craniosynostosis. The best surgical outcome and the least perioperative complications were seen in the trigonocephaly group. Compromised overall correction and reoperations were more common in the syndromic and complex craniosynostosis groups than in single-suture craniosynostosis.

Keywords: Chiari malformation, craniosynostosis, intracranial hypertension, perioperative complications, trigonocephaly

INTRODUCTION

Craniosynostosis is a condition in which one or more of the fibrous sutures in an infant skull prematurely fuse by turning into bone (ossification),
Craniosynostosis, and Muenke’s syndrome. Syndromes associated with craniosynostosis include Crouzon’s syndrome (coronal synostosis, midface hypoplasia, and exophthalmos), Apert’s syndrome (coronal synostosis, osseous syndactyly of the hands and feet, symphalangism, radiohumeral fusion, and mental retardation), Pfeiffer’s syndrome (coronal synostosis, broad fingers/toes, and partial soft-tissue syndactyly of the fingers and toes), Saethre–Chotzen syndrome, Carpenter’s syndrome, Jackson–Weiss syndrome, and Muenke’s syndrome. Imaging in a case of craniosynostosis should include X-ray skull, three-dimensional computed tomography scan of the skull and magnetic resonance imaging (MRI) of the brain, and craniovertebral junction to look for associated brain abnormalities such as corpus callosal agenesis, septum pellucidum cyst, ventriculomegaly, and tonsillar herniation with or without syringomyelia. As there is scanty literature available in Indian population regarding the spectrum and outcome analysis of surgical intervention in cases of craniosynostosis, this study concentrated on finding the frequency of different type of synostosis in Indian population, male or female preponderance, mean age at surgery, whether syndromic or non-syndromic, associated MRI findings, and complications in the perioperative period with their incidence. We also tried to analyze the surgical outcome with the help of Sloan et al.’s classification system.

Materials and Methods
After obtaining ethical clearance from the Institutional Review Board, we conducted a cross-sectional study in our department. The study included all patients with craniosynostosis who were operated from 2008 to 2014 and who were on regular follow-up (minimum 2 years) with us. Patients who had already undergone a prior surgery outside and patients who were operated in our institution but lost to follow up were excluded from the study.

Methodology
In our study, 60 retrospective cases of craniosynostosis operated at our institute from 2008 to 2014 were included (with a minimum follow-up of 2 years). Data was collected including name, date of birth, gender, involved sutures, other medical conditions, whether syndromic craniosynostosis or not, whether symptoms and signs of intracranial hypertension were present or not, associated findings on MRI brain and cervico-medullary junction, type of surgery performed, age at which surgery was performed, perioperative complications (if any), and findings on follow-up. To be able to analyze the surgical results, we used the seven category classification system used by Sloan et al. in which Class 1 represented good to excellent correction and Class 7 represented compromised overall correction requiring re-operation.

Statistical evaluation
At the end of the study, data was collected and data analysis was done by using the Statistical Package for Social Sciences software, version 20.0 (International Business Machines Corporation, IBM, New York, USA). Qualitative data variables were expressed by using frequency and percentage (%). Quantitative data variables were expressed by using mean and standard deviation (SD). Chi-square test and Fisher’s exact test were used to find the association between diagnosis and various data variables associated with diagnosis. A value of $P < 0.05$ was considered statistically significant.

Results
Of the 60 cases of craniosynostosis, 43 were men (72%) and 17 were women (28%). 7 cases belonged to the syndromic craniosynostosis group (11.67%), 8 cases belonged to the oxycephaly group (13.33%), and the remaining 45 cases belonged to the “non-syndromic non-oxycephaly group” (75%). Of the seven syndromic patients, five were suffering from Crouzon’s syndrome, and one each was suffering from Apert’s syndrome and Pfeiffer’s syndrome. The bilateral coronal suture was the most common suture involved in syndromic craniosynostosis. Scaphocephaly and trigonocephaly groups had the maximum number of cases (11 each) [Figure 1]. All 11 cases of scaphocephaly, 7 of 11 cases of trigonocephaly, and 4 of 5 cases of Crouzon’s syndrome were men. Anterior plagiocephaly group showed female preponderance (three of four cases) [Figure 2]. Mean age at first surgery in the 60 cases was 3.85 years. Mean age at first surgery for men was 4.31 years and for women it was 2.71 years. Mean age at first surgery was earliest in the anterior plagiocephaly and trigonocephaly groups, that is, 1.67 years and 1.83 years, respectively [Figure 3].
Four of five cases of Crouzon’s syndrome (80%) and six of eight cases of oxycephaly (75%) had signs of raised intracranial pressure. In the non-syndromic and non-oxycephaly group, only 3 of 45 cases (6.67%) had signs of raised intracranial pressure [Figure 4]. By using Fisher’s exact test, a value of $P < 0.05$ showed a significant association between intracranial hypertension and syndromic craniosynostosis/ oxycephaly groups.

Chiari malformation was present in 80% of the cases of Crouzon’s syndrome, 62.5% of the cases of oxycephaly, and 4.44% of the cases belonging to the non-syndromic, non-oxycephaly group. Other MRI findings that were noted were corpus callosal agenesis, periventricular leukomalacia, and septum pellucidum cyst [Figure 5].

Perioperative complications were present in three of seven cases of syndromic craniosynostosis (42.86%), 4 of 8 cases of oxycephaly (50%), and 7 of 45 cases of non-syndromic, non-oxycephaly group (15.56%). Of the seven cases of intraoperative blood loss requiring more than one pediatric unit of whole blood, three cases belonged to the oxycephaly group, two were patients with Crouzon’s syndrome, and one each belonged to the scaphocephaly and brachycephaly groups. Two patients who developed intraoperative dural tear, which was repaired immediately belonged, one each, to the oxycephaly and Crouzon’s syndrome groups. Two patients developed cerebrospinal fluid (CSF) leak and pseudomeningocele formation in the postoperative period belonged, one each, to the scaphocephaly and two sutures involved groups. One patient with scaphocephaly and one patient with brachycephaly developed surgical site infection. One patient with “non-syndromic trigonocephaly with right posterior plagiocephaly” developed intraoperative cardiac arrest but was successfully revived [Figures 6 and 7].

Four of 7 cases of syndromic craniosynostosis, 3 of 8 cases of oxycephaly, and 2 of 45 cases of non-syndromic, non-oxycephaly group belonged to higher Sloan et al.’s class or compromised overall correction (Classes 5, 6, or 7). By using Fisher’s exact test, a value of $P < 0.05$ showed a significant association between syndromic craniosynostosis/oxycephaly groups and higher Sloan et al.’s class [Figure 8].

**Discussion**

Sloan et al.[8] in his paper observed that there were 157 men (62.8%) and 93 women (37.2%) in the study, with most of the male preponderance accounted for by the large sagittal synostosis group. Oliveira et al.[9] in his paper also observed that there was a male preponderance (71.3% men versus 28.7% women). The male preponderance in his study was mainly because of the trigonocephaly (86%) and scaphocephaly (84.5%) groups.[9] Zakhary et al.[10] in his paper observed that...
there were 73% men and 27% women. Bessenyei et al.\textsuperscript{[11]} in his paper observed that the sagittal suture was the most commonly involved, followed by the coronal, metopic, and lambdoid sutures. Kolar et al.\textsuperscript{[12]} in his paper noted a much higher incidence of metopic synostosis than has been reported in the traditional clinical literature. Like Kolar et al., we also obtained a higher incidence of trigonocephaly in our study. Even in our study, cases in the sagittal or metopic synostosis groups were overwhelmingly men (in fact, all 11 cases of sagittal synostosis were men), whereas those with unilateral coronal synostosis were predominantly women.
The incidence of syndromic craniosynostosis was 9.2% in Sloan et al.’s study, 20.5% in Oliveira et al.’s study, 6% in Zakhary et al.’s study, 12% in Bessenyei et al.’s study, and 11.67% in our study.

Mean age at first surgery in our study was 3.85 years. The ideal age for craniosynostosis surgery is around 6 months. Mean age at first surgery was on the higher side in our study due to late presentation of the cases.
Papilloedema was present in 9 of 60 cases (15%). Two of 5 cases of Crouzon’s syndrome (40%), 4 of 8 cases of oxycephaly (50%), 1 of 11 cases of scaphocephaly (9.1%), and 2 of 9 cases in the two sutures involved group (22.22%) had papilloedema on presentation.

Papilloedema regressed in all the nine cases postsurgery and there was improvement in vision in these patients. Four patients of 60 cases on presentation were blind (6.67%). On fundus examination, there was bilateral secondary optic atrophy. Two of five cases of Crouzon’s
syndrome and two of eight cases of oxycephaly had bilateral optic atrophy on presentation. Thus, signs of intracranial hypertension were seen in 13 of 60 cases enrolled in the study (21.67%). Four of five cases of Crouzon’s syndrome (80%) and six of eight cases of oxycephaly (75%) had signs of raised intracranial pressure.

Florisson et al.\textsuperscript{[14]} in his study concluded that the prevalence of papilledema in scaphocephaly was 9.7% and in trigonocephaly was 5.6%. Bannink et al.\textsuperscript{[15]} in his study observed that papilledema was present in 51% of the syndromic patients with craniosynostosis. Derderian et al.\textsuperscript{[16]} reported that patients with Crouzon’s syndrome had a 65% incidence of intracranial hypertension and patients with Apert syndrome had a 83% incidence of intracranial hypertension. Tim de Jong\textsuperscript{[17]} in his published thesis observed that the incidence of intracranial hypertension was 53% in Crouzon/ Pfeiffer syndrome, 33% in Apert syndrome, and 21% in Saethre Chotzen syndrome. Thus, we conclude that the incidence of intracranial hypertension is significantly higher in syndromic and complex craniosynostosis as compared to single-suture craniosynostosis.

Positive MRI findings were present in 15 of the 60 cases (25%), which included Chiari malformation in 12 cases and callosal agenesis, periventricular leukomalacia, and septum pellucidum cyst in 1 case each. Four of five cases of Crouzon’s syndrome (80%) and five of eight cases of oxycephaly (62.5%) had Chiari malformation. It was also present in one case each of lambdoid brachycephaly, posterior plagiocephaly, and Pfeiffer’s syndrome.

Cinalli et al.\textsuperscript{[18]} in his paper noted that Chiari malformation is a frequent finding in multisutural and syndromic craniosynostosis, occurring in 70% of patients with Crouzon’s syndrome, 75% with oxycephaly, 50% with Pfeiffer’s syndrome, and 100% with the Kleeblattschädel deformity. Leikola et al.\textsuperscript{[19]} in his paper observed that the incidence of Chiari malformation in non-syndromic single-suture craniosynostosis cases was 5.6%. Renier et al.\textsuperscript{[20]} in his study noted an incidence of 75% of Chiari malformation in cases of oxycephaly. Strahle et al.\textsuperscript{[21]} in his paper observed that Chiari malformation was more likely to be present in patients with isolated lambdoid synostosis (55%), multisuture synostosis (35%), and pansynostosis (80%) compared with patients with coronal synostosis (6%) or sagittal synostosis (3%). In our study, Chiari malformation was present in 80% of the cases of Crouzon’s syndrome and 62.5% of the cases of oxycephaly.

Perioperative complications were present in 14 of the 60 cases (23.33%). Seven of 60 cases had intraoperative
blood loss requiring more than one pediatric unit of whole blood transfusion (11.67%). Two patients developed surgical site infection which was managed conservatively with antibiotics (3.33%). Two patients had a dural tear while operating which was identified immediately and sutured (3.33%) and both had an uneventful postoperative period. Another two patients developed CSF leak and pseudomeningocele formation in the postoperative period. Both were initially managed conservatively. Of the two cases, one patient required reexploration and duraplasty. One patient developed intraoperative cardiac arrest due to sudden hypovolemia but was successfully resuscitated. Our study had a 0% mortality rate. Perioperative complications were present in 42.86% of the cases in the syndromic group, 50% of the cases in the oxycephaly group, and 15.56% of the cases in the “non-syndromic, non-oxycephaly” group.

Sloan et al.[8] in his study observed that there were two deaths (0.8%), both with Kleeblattschadel patients and morbidity/mortality were significantly associated with secondary versus primary operations and syndromic versus non-syndromic patients. Esparza et al.[22] also concluded that the best results were obtained in patients with isolated craniosynostosis and the worst in cases with syndromic and multisuture craniosynostosis. Breugem et al.[23] in his study observed that perioperative complications were minimal in non-syndromic craniosynostosis. Thus, it is safe to conclude that perioperative complications are more common in syndromic and complex craniosynostosis than in single-suture craniosynostosis.

In Sloan et al.’s[8] study, outcome analysis revealed the best surgical results with metopic synostosis and significantly worse results with the Kleeblattschadel deformity, multiple suture synostosis, and bilateral coronal synostosis. Even in our study, the best outcome and the least perioperative complications were seen in the trigonocephaly group. Four of seven cases of syndromic craniosynostosis and three of eight cases of oxycephaly belonged to higher Sloan et al.’s class or compromised overall correction (Classes 5, 6, or 7). By using Fisher’s exact test, a value of $P < 0.05$ showed a significant association between syndromic craniosynostosis/ oxycephaly and higher Sloan et al.’s class.

**Conclusion**

Only the light of knowledge and health education can dispel the darkness of ignorance. This study highlights the importance of educating the masses so that cases of craniosynostosis present early. The incidence of Chiari malformation, intracranial hypertension, and perioperative complications was significantly higher in the syndromic craniosynostosis and oxycephaly groups than in single-suture craniosynostosis. The best surgical outcome and the least perioperative complications in our study were seen in the trigonocephaly group. Compromised overall correction and reoperations were more common in the syndromic and complex craniosynostosis groups than in single-suture craniosynostosis.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Slater BJ, Lenton KA, Kwan MD, Gupta DM, Van DC, Longaker MT. Cranial sutures: a brief review. Plast Reconstr Surg 2008;121:170e-8e.
2. Cohen MM Jr. Craniosynostosis update 1987. Am J Med Genet Suppl 1988;4:99-148.
3. Murdoch-Kinch CA, Bixler D, Ward RE. Cephalometric analysis of families with dominantly inherited Crouzon syndrome: an aid to diagnosis in family studies. Am J Med Genet 1998;77:405-11.
4. Cohen MM Jr. Kreiborg S. Hands and feet in the Apert syndrome. Am J Med Genet 1995;57:82-96.
5. Kreiborg S, Cohen MM Jr. Characteristics of the infant Apert skull and its subsequent development. J Craniofac Genet Dev Biol 1990;10:399-410.
6. Vogels A, Fryns JP. Pfeiffer syndrome. Orphanet J Rare Dis 2006;1:19.
7. Goldstein SJ, Kidd RC. Value of computed tomography in the evaluation of craniosynostosis. Comput Radiol 1982;6:331-6.
8. Sloan GM, Wells KC, Raffel C, McComb JG. Surgical treatment of craniosynostosis: outcome analysis of 250 consecutive patients. Pediatrics 1997;100:E2.
9. Oliveira RS, Santos MV, Cruz AA, Andó A, Neto JM, Machado HR. Surgical treatment of craniosynostosis: a single institution’s outcome analysis of 303 consecutive patients. Rev Bras Cir Craniofac 2010;13:206-10.
10. Zakhary GM, Montes DM, Woerner JE, Notarianni C, Ghali GE. Surgical correction of craniosynostosis: a review of 100 cases. J Craniofac Surg 2014;42:1684-91.
11. Bessenyei B, Nagy A, Szakszon K, Mokánszki A, Balogh E, Ujfalusi A, et al. Clinical and genetic characteristics of craniosynostosis in Hungary. Am J Med Genet A 2015;167A:2985-91.
12. Kolar JC. An epidemiological study of nonsyndromal craniosynostoses. J Craniofac Surg 2011;22:47-9.
13. Panchar J, Uitchin V. Management of craniosynostosis. Plast Reconstr Surg 2003;111:2032-48; quiz 2049.
14. Florisson JM, van Veelen ML, Bannink N, van Adrichem LN, van der Meulen JJ, Bartels MC, et al. Papilledema in isolated single-suture craniosynostosis: prevalence and predictive factors. J Craniofac Surg 2010;21:20-4.
15. Bannink N, Joosten KF, van Veelen ML, Bartels MC, Tasker RC, van Adrichem LN, et al. Papilledema in patients with...
Apert, Crouzon, and Pfeiffer syndrome: prevalence, efficacy of treatment, and risk factors. J Craniofac Surg 2008;19:121-7.
16. Derderian C, Seaward J. Syndromic craniosynostosis. Semin Plast Surg 2012;26:64-75.
17. Tim de Jong. Long-term results in syndromic craniosynostosis. PhD thesis, Faculty of Plastic and Reconstructive Surgery, Erasmus University Rotterdam, Netherlands; 2012.
18. Cinalli G, Spennato P, Sainte-Rose C, Arnaud E, Aliberti F, Brunelle F, et al. Chiari malformation in craniosynostosis. Childs Nerv Syst 2005;21:889-901.
19. Leikola J, Koljonen V, Valanne L, Hukki J. The incidence of chiari malformation in nonsyndromic, single suture craniosynostosis. Childs Nerv Syst 2010;26:771-4.
20. Renier D, Cinalli G, Lajeunie E, Arnaud E, Marchac D. [Oxycephaly, a severe craniosynostosis. Apropos of a series of 129 cases]. Arch Pediatr 1997;4:722-9.
21. Strahle J, Muraszko KM, Buchman SR, Kapurch J, Garton HJ, Maher CO. Chiari malformation associated with craniosynostosis. Neurosurg Focus 2011;31:E2.
22. Esparza J, Hinojosa J. Complications in the surgical treatment of craniosynostosis and craniofacial syndromes: apropos of 306 transcranial procedures. Childs Nerv Syst 2008;24:1421-30.
23. Breugem CC, van R Zeeman BJ. Retrospective study of nonsyndromic craniosynostosis treated over a 10-year period. J Craniofac Surg 1999;10:140-3.