Profile of infantile strabismus at a tertiary eye care center in India

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Purpose: To study the profile, risk factors, and management outcomes of infantile strabismus at a tertiary eye care center. Methods: We prospectively analyzed the data of infants (children less than 1 year of age) who presented at our institute from August 2018 to December 2019. We excluded infants who did not complete a minimum follow-up of 6 months. Detailed meticulous history based on a set of standardized questionnaires was obtained and a comprehensive ophthalmological examination of the child was performed. Data were collected regarding refractive error (astigmatism; myopia; hyperopia; anisometropia [<1.0 DS or >1.0 DS]; astigmatism [<1.0 DS or >1.0 DS]) and the type of strabismus. Results: During this period, we saw 4,773 infants, out of which 123 infants were diagnosed to have infantile-onset strabismus (hospital prevalence of 2.6%). Boys and girls were equally affected. Sixty-two patients had esotropia, 37 had exotropia, 2 had hypotropia, and 22 had pseudo strabismus. Prematurity, hypermetropia, and anisometropia had increased odds of developing esotropia, whereas delivery by cesarean section, delayed cry at birth, infantile seizures, parental consanguinity, delayed development of milestones, and myopia had increased odds of developing exotropia. Twenty-nine patients underwent a surgical correction. The mean deviation at the first visit was 42.59 ± 15.40 PD and 8.25 ± 12.70 PD at the last visit. For all patients who underwent a squint surgery, the change in ocular deviation was clinically and statistically significant (P-value <0.0001, paired t-test).

Conclusion: The hospital prevalence of infantile strabismus in our cohort was found to be 2.6%. Our study suggests that esotropia is two-fold more common in our cohort as compared to exotropia. Further, our study highlights risk factors for the development of strabismus in infancy, which must be kept in mind and awareness must be created among pediatricians. Surgical correction should be considered early during the infantile period, because it may lead to promote the development of good binocular vision.

Key words: Infantile, pediatric ophthalmology, strabismus, surgery

Strabismus is a common presentation in pediatric ophthalmology clinics. Esotropia is the most common type of strabismus, having a worldwide prevalence of 1–2% in all age groups[1,2] and accounts for 50% of the total strabismus patients.[3] On contrary, exotropia is more frequent in Asians presumably due to the high prevalence of myopia in the latter group.[4,5] However, it is well known that the prevalence of strabismus in infancy is detrimental to the development of binocular vision, and if left untreated, it can lead to suppression and amblyopia. Because this age group falls during the critical age for the development of normal cortical visual centers, prompt diagnosis and treatment early in life play a crucial role in preventing visual impairment. To the best of our knowledge, there is limited literature on the prevalence of strabismus in infants, especially from India. We, therefore, performed this study to understand the pattern of infantile strabismus presenting to a tertiary care center.

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Methods

The study was a prospective observational study conducted at a tertiary eye care center (L V Prasad Eye Institute) in South India from August 1, 2018, to December 31, 2019. We analyzed records of consecutive infants (children under the age of 1 year) seen during this period across various ophthalmology subspecialties. However, children who did not complete a minimum follow-up of 6 months were excluded. Written informed consent was obtained from the parents. A detailed and meticulous history based on a set of standardized questionnaires was noted from the parents. A comprehensive ocular examination of the child was performed including assessment of facial dysmorphism, visual acuity assessment using fixation behavior or Teller acuity cards, cycloplegic refraction, Hirschberg test, Krimsky, and Modified Krimsky test whenever possible, followed by anterior and posterior segment evaluation. Refractive errors were classified using the spherical equivalents (SE). Emmetropia was defined as -0.5 to + 0.5 diopter sphere (DS); myopia was defined as > -0.5 DS.

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and hyperopia was defined as $>0.50$ DS. If anisometropia was present, the refractive error was defined as SE of the less hyperopic eye because accommodative convergence is potentially driven by accommodation of the less hyperopic eye. Astigmatism was defined as a cylindrical error $>1.0$ DS. If astigmatism was present in both eyes, the more astigmatic eye was used to classify refractive error. Clinical variables included the following variables: refractive error (emmetropia, myopia, and hyperopia), anisometropia ($<1.0$ DS or $>1.0$ DS), and astigmatism ($<1.0$ DS or $>1.0$ DS). Data were also collected regarding factors that can influence the risk of strabismus in infancy, that is, prematurity, low birth weight infantile seizures, parental consanguinity, and delayed milestone development.

**Statistical analysis**

Data were collected and summarized using Microsoft Excel (Microsoft Inc, Richmond, USA). Statistical analysis was performed using the SPSS software.

Appropriate measures for central tendency, proportions, standard deviations (SD), and confidence interval (CI) were used to summarize categorical and continuous variables. Normative data were compared using paired $t$-test and non-normative data were compared using the Mann–Whitney $U$ test. Categorical data were analyzed using the Chi-square test. Univariate and multivariate logistic regression analysis was used to analyze the effect of various factors on association with esotropia and exotropia in infancy. A $P$ value of $<0.05$ was considered statistically significant.

**Results**

During our study period, 4,773 infants presented to our center, whose indications ranged from retinopathy of prematurity, congenital nasolacrimal duct obstruction (CNLDO), developmental delay with visual impairment, congenital cataract, squint, congenital glaucoma, nystagmus, ptosis, retinoblastoma, capillary hemangioma, corneal opacities, infections, ocular trauma, and anophthalmic socket. Out of these, 209 had manifest strabismus giving a prevalence of 4.3%; and 123 patients completed a minimum follow-up of 6 months who were included in our study. The total numbers of male patients were 61 (49.59%), whereas the number of female patients was 62 (50.41%). Esotropia was the most common subtype and was seen in 62 patients (50.4%), whereas exotropia was seen in 37 patients (30.1%). The remaining patients had pseudo strabismus (17.9%), and hypotropia (1.6%). Sixty-eight patients (55.3%) presented directly to our institute, whereas 55 patients (44.7%) were referred to our institute (44 by an ophthalmologist, 11 by a pediatrician).

The mean age at presentation was $9.1 \pm 2.7$ months [Fig. 1]. The most common age at presentation was $>6$ months (86.18%). In children with esotropia, the mean age at presentation was $9.4 \pm 2.6$ months and boys were more commonly affected than girls (34 boys and 28 girls); whereas in the exotropia group, the mean age at presentation was $8.7 \pm 2.9$ months in the exotropia group and girls were more commonly affected (16 boys, 21 girls).

Thirty-six patients had an onset of deviation since birth. Among these, 21 patients (58.33%) had esotropia and 14 patients (38.89%) had exotropia. Fifteen patients (12.2%) had a positive family history of squint. Infants born via cesarean section had two times higher odds of developing exotropia than those born by normal delivery (Odds ratio [OR]: 1.5, 95% confidence interval [CI]: 0.6 to 3.4). The risks of developing exotropia were found to be higher (OR: 1.6, 95% CI: 0.4 to 6.1) in children having delayed cry as compared to immediate cry after birth.
Esotropia was commonly seen in both term and pre-term infants. The occurrence of esotropia in pre-term children was two times higher than in term children (OR: 2.1; 95% CI: 0.1 to 4.3). We found no significant association between family history, delayed or immediate cry at birth, gestational age, or birth weight with ocular deviation. History of seizure at birth was found to be significantly associated with ocular deviation and had a 3.6 times higher likelihood to develop exotropia (OR: 3.6, 95% CI; P=0.02 chi-square test). Twenty patients (16.3%) had a history of parental consanguinity and were associated significantly with the development of strabismus (P = 0.002, Chi-square test). The odds of developing exotropia were higher (OR: 2.2, 95% CI: 0.8 to 5.9) in patients having parental consanguinity as compared to patients without parental consanguinity.

The overall distributions of the refractive error have been provided in Fig. 2. Sixty-three patients had anisometropia with 31 (49.2%) belonging to the esotropia group. Thirty-one patients had astigmatism, with 16 patients belonging to the esotropia group.

Overall, we found prematurity, hypermetropia, and anisometropia have increased odds of developing esotropia, whereas delivery by cesarean section, delayed cry at birth, infantile seizures, parental consanguinity, delayed development of milestones, phototherapy for jaundice, and myopia having increased odds for developing exotropia.

Distribution of deviation
Esotropia was found in 62 patients. The mean deviation in the esotropia group was 36.8 ± 13.1 PD at the initial visit. 22 patients underwent extraocular muscle surgery, 27 patients were treated with glasses and patching alone, 3 patients were referred to the visual rehabilitation department for vision stimulation exercises, while 1 patient was observed. At the last visit, the mean deviation in the esotropia group was found to be 18.7 ± 18.8 PD. The change in ocular deviation was found to be significant (P ≤ 0.0001, paired t-test).

Exotropia was diagnosed in 37 patients (31%). Overall, the mean deviation in the exotropia group was 37.1 ± 14.8 PD at the initial visit. Five patients were planned for surgical intervention, 15 patients were referred to the vision rehabilitation department for vision stimulation exercises, 10 patients were prescribed glasses or monocular patching, whereas 4 patients with good control of intermittent exotropia were observed. The mean deviation was 30.8 ± 17.1 PD at the last visit. The change in ocular deviation was statistically significant (P = 0.016, paired t-test). However, this was not clinically significant, because this would mean persistence of large-angle deviation even after treatment, necessitating the need for surgery.

Pseudostrabismus was diagnosed in 22 patients. At the last visit, three patients had persistence of pseudo squint, one of whom had a positive family history along with hypermetropia.

Twenty-nine patients underwent squint surgery [Fig. 3], among whom 22 patients had esotropia, 5 patients had exotropia, whereas 2 patients had hypotropia. The mean deviation at the first visit was 42.6 ± 15.4 PD and 8.25 ± 12.70 PD at the last visit. For all the patients who underwent a squint surgery, the change in ocular deviation was clinically and statistically significant (P-value <0.0001, paired t-test).

Discussion
As stated earlier, very few studies have looked into the clinical profile of infantile strabismus in India. In our study, we found...
esotropia as the most common deviation, which was similar to published literature from around the world.\textsuperscript{[1,6]} However, this is in contrast to the finding in other Asian countries such as Singapore and Korea where the exodeviations are more common due to the high prevalence of myopia in their population.\textsuperscript{[4,5]} We found no gender predilection, which possibly reflects that an equal number of boys and girls received timely medical attention. This is similar to the prior report by Chew et al.\textsuperscript{[2]} It also suggests that the disease can affect both boys and girls equally.

Exotropia was more commonly associated with a positive family history of squint, which is similar to prior reported literature.\textsuperscript{[3,4,7]} We also found parental consanguinity to be significantly associated with the development of strabismus similar to previously published literature.\textsuperscript{[6]} Consanguinity could increase the risk of strabismus due to the increase in the number of mutations in a homo-allele for recessive diseases.\textsuperscript{[6]} This is especially helpful to know in a country such as India where there is still a high prevalence of consanguineous marriage and hence an early screening and counseling in a couple of consanguineous marriages would help in the early identification of strabismus in the offspring. For infants with a birth weight of less than 2,500 gm, there was an equal risk for the development of esotropia and exotropia. This is similar to a previous study by Chew et al.\textsuperscript{[3]} However, we found no significant association between low birth weight and strabismus, which was in contrast to the published literature.\textsuperscript{[6,9]} This could be due to the limited referrals of low-birth weight infants to squint clinic. We found esotropia to be 2.5 times more common than exotropia in prematurely born infants. Our results were similar to published literature previously.\textsuperscript{[6,10]} It is hypothesized that prematurity hampers the development of the oculomotor control centrally because they are at a higher risk of brain injury, which eventually leads to the early development of strabismus in these patients. However, there seems to be no definite answer to why esotropia is more common in these infants. In our study, infants born by C-section had a higher risk for the development of strabismus, particularly exotropia, which was similar to the published literature previously.\textsuperscript{[6]} This could be due to the fact that usually a cesarean section is performed when there is an associated complication or risk to the fetus or the mother. Seizure was found to have a statistically significant ($P = 0.021$, Chi-square test) association with strabismus. Patients with seizure and delayed development had a higher risk for exotropia, which is similar to the literature because their normal cortical development is altered, which causes impairment in ocular fusion.\textsuperscript{[11]}

In our cohort, patients with myopia had a higher likelihood of developing exotropia, whereas hyperopia was commonly seen in patients with esotropia, which also is similar to prior published data.\textsuperscript{[6,12,13,14]} It is postulated that the fusional control at distance is weakened in myopes due to blurred distant vision. For near vision, a less accommodative effort is required for a clear image, which resulted in less accommodative convergence. This prolonged suboptimal convergence may lead to the breakdown of the fusional control and may predispose to exotropia development.\textsuperscript{[12]} We found astigmatism to be commonly associated with the development of esotropia. Our results were contradictory to previously published literature where astigmatism of $>1$D was associated with at least a 2-fold increased risk for exotropia.\textsuperscript{[6,14]} This difference could be present since astigmatism was noted to be less in our cohort, that is seen in 25% cases, as compared to other studies having 34-50% cases. It could also be since our study included only infants in contrast to other studies where there was a wide range of age groups being evaluated.

We found a significant reduction in the mean deviation for both the esotropia and exotropia groups. Twenty-two patients with esotropia and 5 patients with exotropia underwent squint surgery. The change in ocular deviation was significant in these infants ($P < 0.0001$). Hence an early surgery does improve the ocular alignment. Our results were similar to previously published literature.\textsuperscript{[13-19]} however, a longer follow-up would be needed to assess the number of re-surgeries further required and the improvement in stereopsis in these infants in the long run.

Although identifying whether a child has an exotropia or esotropia was relatively easy, performing accurate orthoptic measurements in such young or uncooperative children was difficult. Another limitation of our study was that we looked at only a finite number of potential risk factors. Few of the tests were not possible in all infants due to a lack of necessary
cooperation. Also, we were only able to assess the hospital prevalence, which cannot be generalized to the population as a whole. In general, hospital-based prevalence is likely to be higher than the general population due to referral bias.

The strength of our study strength is that all children received comprehensive eye examinations by a well-trained pediatric ophthalmologist and a standardized protocol was followed in determining refractive error by cycloplegic refraction and strabismus by cover testing and Krimsky tests. A further long-term longitudinal study of these infants would be needed to observe the change in visual acuity and stereopsis.

Conclusion
The current study suggests that overall the incidence of strabismus in infancy is low. However, a history of seizures at birth, parental consanguinity, delayed cry at birth, and delayed development were associated with a higher risk of developing exotropia. Pre-term infants had higher risks of developing esotropia. These factors must be kept in mind and awareness must be created among pediatricians for close observation of children with these risk factors for the development of squint and the importance of early referral and treatment. Because uncorrected refractive errors especially hyperopia is commonly seen in these patients, hence comprehensive ophthalmologists should be educated about the correct method of prescription of glasses for infants with a squint and advise mono-ocular occlusion whenever indicated. We also found infants who underwent squint surgery had a significant improvement in ocular alignment.

We recommend early screening and referral for strabismus especially in patients with family history, developmental delay, refractive errors, and other risk factors, for timely referral and appropriate management.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

References
1. Engle EC. Genetic basis of congenital strabismus. Arch Ophthalmol 2007;125:189-95.
2. Chew E, Remaley NA, Tamboli A, Zhao J, Podgor MJ, Klebanoff M. Risk factors for esotropia and exotropia. Arch Ophthalmol 1994;112:1349-55.
3. Cotter SA, Varma R, Tarcezy-Hornick K, McKean-Cowdin R, Lin J, Wen G, et al. Risk factors associated with childhood strabismus: the multi-ethnic pediatric eye disease and Baltimore pediatric eye disease studies. Ophthalmology 2011;118:2251-61.
4. Han KE, Baek SH, Kim SH, Lim KH. Epidemiologic Survey Committee of the Korean Ophthalmological Society. Prevalence and risk factors of strabismus in children and adolescents in South Korea: Korea National Health and Nutrition Examination Survey, 2008–2011. PLoS One. 2018;13:e0191857.
5. Chia A, Roy L, Seeney L. Comitant horizontal strabismus: an Asian perspective. Br J Ophthalmol 2007;91:1337-40.
6. Torp-Pedersen T, Boyd HA, Poulsen G, Haargaard B, Wohlfahrt J, Holmes JM, et al. Perinatal risk factors for strabismus. Int J Epidemiol 2010;39:1229-39.
7. Lee HJ, Kim SJ, Yu YS. Clinical characteristics of sibling patients with comitant strabismus. Int J Ophthalmol 2017;10:772.
8. Bagheri M, Farvardin M, Saadat M. A study of consanguineous marriage as a risk factor for developing comitant strabismus. J Community Genet 2015;6:177-80.
9. Pott JW, Sprunger DT, Helveston EM. Infantile esotropia in very low birth weight (VLBW) children. Strabismus 1999;7:97-102.
10. Pennefather PM, Clarke MP, Strong NP, Cottrill DG, Dutton J, Tin W. Risk factors for strabismus in children born after 32 weeks' gestation. Br J Ophthalmol 1999;83:514-8.
11. Das VE. Strabismus and the oculomotor system: insights from macaque models. Ann Rev Vis Sci 2016;2:37.
12. Tang SM, Chan RY, Bin Lin S, Rong SS, Lau HH, Lau WW, et al. Refractive errors and concomitant strabismus: a systematic review and meta-analysis. Sci Rep 2016;6:1-9.
13. Eustace P. Myopia and divergent squint in West Indian children. Br J Ophthalmol 1972;56:559.
14. Yahya AN, Sharanjeet-Kaur S, Akhir SM. Distribution of Refractive Errors among Healthy Infants and Young Children between the Age of 6 to 36 Months in Kuala Lumpur, Malaysia — A Pilot Study. Int J Environ Res Public Health 2019; 16:4730.
15. Yoo EJ, Kim SH. Optimal surgical timing in infantile exotropia. Can J Ophthalmol 2014;49:358-62.
16. Gerth C, Mirabella G, Li X, Wright T, Westall C, Colpa L, et al. Timing of surgery for infantile esotropia in humans: effects on cortical motion visual evoked responses. Invest Ophthalmol Vis Sci 2008;49:3432-7.
17. Bang SP, Lee DC, Lee SY. Surgical outcome of intermittent exotropia with improvement in control grade subsequent to part-time preoperative occlusion therapy. J Pediatr Ophthalmol Strabismus 2018;55:59-64.
18. Simonsz HJ, Kolling GH, Unnebrink K. Final report of the early vs. late infantile strabismus surgery study (ELISSS), a controlled, prospective, multicenter study. Strabismus 2005;13:169-99.
19. Bagheri M, Farvardin M. The clinical effect of surgical timing in infantile exotropia. Journal of American Association for Pediatric Ophthalmology and Strabismus 2018;22:167-9.