Epidemiological profile of childhood esotropia in a tertiary eye hospital in Dakahlia governorate, Egypt

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Short title: Childhood esotropia in lower Egypt

Abstract

Purpose: To study epidemiology of different subtypes of childhood esotropia among children in dakahlia governorate, Egypt.

Design: Prospective observational clinical cross-sectional study.

Participants: Esotropic children (less than 18 years old) attending strabismus clinic in Mansoura ophthalmic center in the period from from July 2021 to July 2022.

Methods: Socio-demographic data were obtained from participants. History including family history, consanguinity, delivery history and systemic diseases were obtained as well. Examination included best corrected visual acuity, cycloplegic refraction, fixation preference, significant A or V pattern, motility assessment, angle of deviation, fusion, stereopsis and associated strabismus.

Results: Six hundred twenty-six (626) esotropic children were included. 287 children (45.8%) were diagnosed as accommodative esotropia (ET). Infantile ET was defined in 122 children (19.5%), non-accommodative ET in 49 children (7.8%), restrictive ET in 31 children (5%), sensory ET in 14 children (2.2%), convergence excess ET in 5 children (0.8%), residual ET in 77 children (12.3%) and consecutive ET in 35 children (5.6%) of cases. Family history of strabismus was present in 22.5% of patients. 250 esotropic children from our cohort (39.9%) had amblyopia. Defective binocular vision and stereopsis was found in 72.5% of cooperative patients.

Conclusion: Accommodative esotropia was the most common form of esotropia in our study cohort. Infantile esotropia came in the 2^{nd} place then non accommodative ET. Restrictive esotropia and sensory esotropia were less common. Amblyopia and decreased binocular vision pose a great challenge in childhood ET, even in the accommodative group. Good screening program, early referral and proper management are mandatory to prevent irreversible visual and binocular vision problems in pediatric age group.

Keywords: Epidemiological profile, childhood esotropia, childhood.

INTRODUCTION:

Esotropia is a type of eye misalignment in which one or both eyes turn inward. Esotropia is the most common form of childhood strabismus especially in the 1st decade of life. It affects approximately 3% to 4% of the pediatric population. ET is less common than exotropia (XT) in Asians, but it's much more common in western populations¹². Akowuah et al.'s meta-analysis in Africa³ revealed higher prevalence of esotropia (0.5%) compared to exotropia (0.2%). However, they stated that ET prevalence in Africa is lower than its worldwide prevalence due to extremely low survival rate of preterm in Africa and their population-based studies.. Elmoddather, M.⁴ has found esotropia to be the most common

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form of strabismus (54.3%) in pediatric population in Assiut city, upper Egypt.

Untreated esotropia leads to amblyopia and decreased binocularity. Strabismus may lead to psychological problem to the child, decreased communication skills, bullying, low selfesteem and low employability chances in adulthood⁵.

Accurate data on epidemiology of esotropia and its subtypes can help us planning an effective screening program for early detection, referral and proper management of this deviation for better motor and sensory outcomes.

Unfortunately, there is a lack of epidemiologic studies in developing countries studying prevalence of esotropia, its subtypes and related visual burdens. Studies by Mohney et al.⁶, Greenberg, et al.¹ and Khorrami-Nejad et al.⁷ contribute data from the United States, and Iran, respectively.

The aim of this work is to study the epidemiology of various forms of childhood esotropia in an otherwise neurologically free children attending pediatric ophthalmology and strabismus clinic at Mansoura Ophthalmic center.

PATIENTS AND METHODS

This was a prospective observational clinical crosssectional study held in ophthalmic center, Mansoura University, Egypt in the period from July 2021 to July 2022. This study included esotropic children and adolescents less than 18 years old. Patients with neurological insult, ocular or head trauma were excluded from our study.

Full history was obtained (name, age, sex, systemic diseases), perinatal and developmental history, age of onset of strabismus, family history of strabismus and the consanguinity.

Type of Esotropia was checked for every patient. Full ophthalmic examination included cycloplegic refraction and best-corrected visual acuity (BCVA) using Landolt's broken ring chart then transformed to LogMAR for statistical purpose.

Patients were subjected to alternate prism cover test or krimisky test. Fixation preference was documented. Duction and version movements of both eyes were assessed. Significant A or V patterns and any associated strabismus were documented. Bagolini test was used to assess fusion, Lang test was used for quantitative assessment of near stereopsis.

A slit lamp examination was performed for anterior and posterior segments to exclude any pathology.

The study design was submitted for approval by Institutional review board (IRB), Faculty of Medicine, Mansoura University under protocol no. MS.21.08.1618.

Statistical Analysis:

Data were entered into Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences statistical analysis (SPSS 24.0, IBM/SPSS Inc., Chicago, IL) software for analysis. Baseline characteristics of the study population were presented as frequencies and percentages (%) or mean values \pm standard deviations (SD) and median (Range).

For comparison of data, Chi-Square test was used to compare two or more independent groups of qualitative data. The comparison between more than two independent groups with quantitative non-parametric data was conducted using Kruskal-Wallis test. Probability (p value) ≤ 0.05 was considered to be statistically significant.

RESULTS

This study included 626 patients. The median age of the patients at presentation was 5.50 years, with a range (0.50 -18 years). The distribution across age groups is illustrated in figure 1.

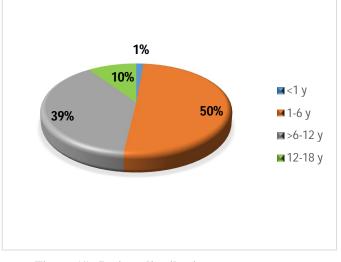


Figure (1): Patient distribution across age groups

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Among the participants, 327 individuals (52.2%) were male, while the remaining 299 (47.8%) were female.

Positive family history was detected in 141 patients (23%). Siblings accounted for 58 cases (41.1%), parents for 21 cases (14.9%).

Positive consanguinity was documented in 134 patients (21.4%). 31 patients had a history of preterm delivery (5%).

Regarding subtypes of ET; 227 patients were diagnosed as Partially Accommodative esotropia (PAET) (36.3%), 60 had Fully Accommodative esotropia (FAET) (9.6%), 122 had infantile ET (19.5%), 49 had non-accommodative ET (7.8%), 31 had restrictive ET (5%), 14 had sensory ET (2.2%), 5 had intermittent ET (0.8%), 5 had convergence excess ET (0.8%), 35 had consecutive ET (5.6%), 77 had residual ET (12.3%) and 1 had recurrent ET (0.2%).

Figure (2) illustrates subtypes of esotropia among the 626 participants.

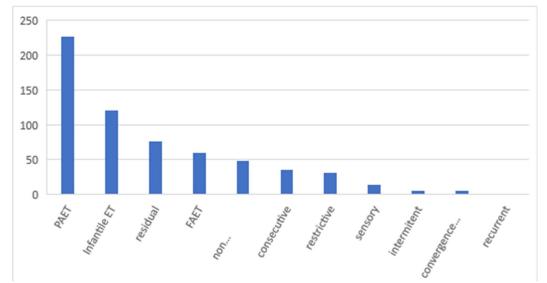


Fig. 2: Types of Esotropia among the studied group

Causes of sensory esotropia in our study were anisometropic amblyopia in 6 cases (42.8%), congenital cataract in 2 cases (14.3%), combined congenital cataract and congenital glaucoma 1 case (7.1%), unilateral ptosis in 2 cases (14.3%), retinopathy of prematurity (ROP) in 2 cases (14.3%) and a corneal opacity in 1 case (7.1%)(figure 3).

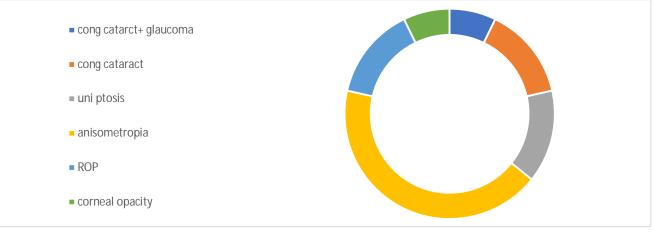


Fig. 3: causes of sensory ET.

Cycloplegic refraction in different types of esotropia are refraction were found between the different subtypes of esotropia.

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Table 1: Cycloplegic refraction in different esotropia subtypes (spherical equivelan)		· · · ·	1.00	• • • •	/ 1 · 1 · 1 ·)	
	Table I. ('vclopie	anc retraction ir	n ditterent ecotro	mig subtypes (spherical equivelant)	
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	PAET	FAET	Infantile ET	non- accomm odative	Restrict ive ET	Sensory	Intermit tent ET	Conver gence excess	Consecu tive ET	Residua l ET	Recurre nt ET	P value
				ЕТ				ЕТ				
Cyclop												
legic	+3.50	+3.50	+0.75	-3.00	+1.17	+0.04	+2.72	+0.42	+0.41	+1.31	+0.50	
	(+9.75	(+8.75 -	(+2.75	(-18.50	(-17.00	(+9.00	(+4.25	(+1.75	(+6.00	(+5.25	(+0.50	≤0.001*
refracti	+0.50)	0.50)	-2.25)	+2.00)	+3.75)	-15.00)	+0.50)	-1.25)	-7.75)	-8.75)	+0.50)	
on	,	,	,	,	,	,	,	,	,	,	,	

Visual acuity couldn't be assessed in 37.86% of children. In cooperative children, a mean BCVA in the dominant eyes was 0.32 (SD \pm 0.22), and in non-dominant eyes was 0.4 (SD \pm 0.25).

Amblyopia was found in 39.9% of cases. 93% of sensory ET cases, 47% of accommodative ET cases and 45% of nonaccommodative ET cases had amblyopia.

Table 2: Angle of deviation in different types of esotropia.

Angle of deviation after correction with full hypermetropic glasses in near (NCC) and far (DCC) are illustrated in table 2. A statistically significant difference was observed in the angle of deviation among the different types of ET (p-value ≤ 0.001).

	PAET	FAET	Infantile ET	non- accomm odative ET	Restricti ve ET	Sensory ET	Intermit tent ET	Conver- gence excess ET	Consecu tive ET	Residua l ET	Recurre nt ET	P value
NCC	18 (8-30)	Ortho	38 (20-50)	33 (12-65)	14 (12-15)	30 (15-40)	8 (6- 10)	15 (20-10)	17 (8- 25)	16 (10- 40)	8	≤0.001*
DCC	14 (4-30)	Ortho	39 (15-50)	32 (12-65)	13 (10-15)	28 (15-40)	8 (6- 10)	ortho	14 (8- 25)	16 (8- 35)	8	≤0.001*

* NCC; near co-corrected angle * DCC; distant co-corrected angle

Significant patterns were observed in 26 cases (4.1%). Apattern was identified in 7 cases, V-pattern was identified in 19 cases. 293 cases had associated strabismus (46.8%). Inferior Oblique overaction (IOOA) was the most common in 250 cases (40.3%) (table 3). Table 3: Associated strabismus among ET patients.

Associated strabismus	The studied group (n=626)				
IOOA	250 (40.3%)				
SOOA	6 (1.0%)				
DVD	2 (0.3%)				
Nystagmus	3 (0.5%)				
IOOA & DVD	2 (0.3%)				
Combined	30 (4.8%)				

Dissociated vertical deviation

Bagolini test was done in 402 cases, 328 of them are fusing (52.4%). Lang test was done in 385 cases, positive

stereoacuity was seen in 104 of cases (16.6%). Detailed results for fusion and stereopsis in the most common subtype of ET

(accommodative ET) are illustrated in table 4.

Table 4: fusion and stereopsis in PAET and FAET.

Types of		Bagolini				Lang			
	Total	Fusing	Non- fusing	Not done	P value	Positive	Negative	Not done	P value
PAET	227	147	26	54		42	125	60	
PALI 221	221	(64.7%)	(11.5%)	(23.8%)	≤0.001*	(18.1%)	(55.3%)	(26.5%)	
	C 0	47 (700/)	0 (00/)	12 (000/)	≤0.001*	24 (200()	10 (20 50/)	18	≤0.001*
FAET	60	47 (78%)	0 (0%)	13 (22%)		24 (39%)	18 (30.5%)	(30.5%)	

DISCUSSION

Our study included 626 esotropic children and adolescents. The median age of presentation was 5.50 years with a peak prevalence between 1 and 6 years suggesting a potential developmental susceptibility to esotropia during this period. Greenberg et al.¹ reported an esotropia prevalence in Minnesota, US was 2% in patients younger than 19 years with highest incidence in the first 5 years agreeing with our study. Elmoddather, M.⁴ also found that 66% of cases with ET were presented from 3-6 years agreeing with our study peak prevalence.

Median age of presentation of infantile ET was 2.25 years old, which is considered a late presentation. Most patients were told by the pediatrician that it may resolve by time.

Some surgeons recommend very early surgery <u>for</u> <u>infantile esotropia</u> (within 6 months of onset). Reduced DVD severity, and minimizing delay in sensorimotor and gross motor development are great advantages of early intervention⁸.

Male: female ratio was 1.09:1 indicating a slightly higher prevalence in boys. Greenberg et al.'s¹ study had nearly the same finding. Some studies reported a higher prevalence in girls^{5,9} others found no significant inter-gender differences^{10,11,12}.

In our study, 21.4% of patients had a positive consanguinity. Accommodative ET and infantile ET cases had

a 23% and a 13% positive family history respectively in our study. This was similar to Zaikas et al.¹⁴. Çorak Eroğlu F et al.¹⁵ had a significantly higher rate of positive family history in both accommodative and infantile esotropia cases 55.5% and 38.1% respectively. Multifactorial pattern of inheritance was suggested in accomodative ET.

Preterm infant has a higher risk for ET. Our study identified 5% of cases had preterm birth. Yetkin et al.¹³ noted a history of preterm birth in 12.5% of ET cases. Zhang et al.¹⁶ found preterm birth was associated with 4.5% of strabismus cases.

Accommodative ET was the commonest subtype in our study along with Mohney et al.⁶, Greenberg et al.¹, Torp-Pedersen et al.¹⁷ and Khorrami-Nejad et al.⁷

In our accommodative ET cases, The PAET cases are 4 times the FAET cases. This was the reverse of what occurs in Greenberg, et al.¹ This may be true due to incompliance with glasses wearing and amblyopia therapy.

This was different from Major A et al.'s¹⁸ findings considering infantile esotropia as the commonest type of strabismus, accounting for 28-54% of all esotropias.

Infantile ET accounted for 19.5% of the ET cases in our study. It comes in the 2nd place of the most common ET forms in our cohort. This was similar to Torp-Pedersen et al.'s¹⁷ finding in Danish population but was markedly higher than what was found in Mohney⁶, Greenberg et al.¹ and Khorrami-

Nejad's⁷ studies which was 5.4%, 8.1%, 9.7% of all cases of ET respectively.

This occurred despite the fact that patients with neurological diseases were excluded from our study to overcome the conflict of diagnosing them as infantile ET¹⁹. The higher prevalence of infantile esotropia may be partly due to its apparent presence in the outpatient clinic. Amblyopia, inferior oblique dysfunction, dissociated vertical deviations and nystagmus, invariably lead to more frequent visits compared with other forms of childhood esotropia²⁰. This elevated prevalence may be true due to ethnic variation, so a population-based study is recommended.

Acquired non accommodative ET in our study was 7.8%, lower than other studies which reported it to be 16.6%, 10.4% and 17.83% in Greenberg et al.¹, Mohney⁶ and Khorrami-Nejad et al.⁷ studies respectively. It maybe underreported in our cohort as parents reported that deviation started since birth, therefore it might have been mistaken for infantile ET.

Restrictive ET in our study was 5% also similar to Mohney⁶ who reported it to be 3.2 % and Greenberg et al.¹ who reported it 6.5%.

Our study reported sensory ET to be 2.2% which is a slightly lower rate compared to Greenberg et al.¹ and Mohney⁶ studies who reported it to be 6.5% and 6.8% respectively. This may be due to excluding trauma from our study. Anisometropic amblyopia was the most common cause of sensory ET in our study (42.8%) similar to Greenberg et al. study¹ (37%).

Paralytic ET was not reported in our study as well due to the exclusion of trauma, which is the most common cause of abducent nerve palsy²¹.

In the current study, 39.9% of ET cases had amblyopia, similar to results by Robaei, D. et al.²² who reported amblyopia in 48.2% of esotropic cases.

Our study revealed a median cycloplegic refraction of +1.87 with a wide range from -18.50 to +9.75. Mohney's study⁶ had a mean cycloplegic refraction +3.59 with a range from -13.25 to +8.88. This aligns with Faghihi and Chia's observations of a correlation between esotropia and hyperopia^{9,23}.

Aligning with Hiles et al.²⁴ findings, a significant difference in the angle of deviation was found among esotropia subtypes, IOOA was also the most common associated strabismus in both studies.

In this study, 52.4% of ET cases were fusing by Bagolini test. 16.6% had positive stereopsis by Lang test. Good stereoacuity was found in 23% of accommodative ET cases in our study, similar to Demirayak study¹⁹. Also, Lee et al.²⁵ reported that 37% of accommodative ET had good stereopsis.

Most studies agree that stereopsis has an abrupt onset at 3-4 months of age and the rate of stereoacuity maturation is rapid during the first year of life¹⁹. Accommodative esotropia usually presents in children between 2 and 3 years of age. Therefore, patients with refractive accommodative esotropia are expected to have fair stereoacuity if they have orthotropia after correction of hyperopia¹⁹.

However, studies reported that the functional organization of the maturing visual system seems to be sensitive to disruption by an abnormal visual experience up to 4 years of age, which could lead to an unfavorable prognosis for restoration of normal stereopsis, even if orthotropia is achieved¹⁹.

This explains why patients with FAET in our study had defective stereoacuity in 30.5% of examined cases despite achieved orthotropia after spectacle correction.Birch et al.²⁶ recommended that patients should use correcting glasses at an early stage during intermittent ET or within a max of 3 months after the onset of constant deviation to prevent irreversible defect of stereopsis.

This study has strength points as there was no studies focussing on the prevalence of different esotropia subtypes in our country. Our study was a prospective one, all cases were examined by an experienced ophthalmologist. A large sample size (626 cases) gave our study more strength.

However, the limitations of our study is that neurological diseases, trauma cases were excluded and the study included only one center. Multicenter study and a population based one is recommended in future research work.

CONCLUSIONS

This study concluded that:

Accommodative esotropia is the most common type of childhood ET. Unlike other studies in USA and Iran, Infantile ET is the 2nd most common form of childhood ET. Non accommodative ET is the 3rd common form of childhood esotropia. It is more common than restrictive and sensory ET.

Most common cause of sensory ET is anisometropic amblyopia. Amblyopia and decreased binocular vision pose a great challenge in childhood ET, even in the accommodative group.

Early screening of infants with high risk factors: preterm, +ve family history, consanguinity is beneficial..Early referral of esotropic children to experienced ophthalmologists for better evaluation and proper timely management is recommended for better motor and sensory outcome.

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Conflict of interest

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REFERENCES

- Greenberg AE, Mohney BG, Diehl NN, Burke JP. Incidence and types of childhood esotropia: a population-based study. Ophthalmology, 2007;114(1): 170-174.
- Mohney BG. Common forms of childhood strabismus in an incidence cohort. American journal of ophthalmology, 2007;144(3): 465-467.
- Akowuah PK, Adade S, Nartey A, Owusu E, Donkor R, Ankamah-Lomotey S, Frimpong AA, Adjei-Anang J & Kobia-Acquah E. Strabismus and amblyopia in Africa – a systematic review and meta-analysis, Strabismus, 2023;31:1, 31-44.
- Elmoddather M. Prevalence of Strabismus and Its Types in Pediatric Population and The Outcomes of Different Treatment Modalities: A 3-Year Prospective Study in A Referral Eye Center in Upper Egypt. The Egyptian Journal of Hospital Medicine, 2022;86; 826-830.
- Thakre SR, Poptani SM, Jyotika Prasanna Mishrikotkar. Clinical profile of esotropia patients in a tertiary care center with application of the CEMAS classification. The Pan-American Journal of Ophthalmology, 2024;6(3):79.
- Mohney BG. Common forms of childhood esotropia. Ophthalmology, 2001;108(4):805-809.
- Khorrami-Nejad M, Akbari MR, Khosravi B. The prevalence of strabismus types in strabismic Iranian patients. Clinical optometry, 2018;19-24.
- Bhate M, Flaherty M, Martin FJ. Timing of surgery in essential infantile esotropia - What more do we know since the turn of the century? Indian J Ophthalmol, 2022;70(2):386-395.

- Faghihi M, Ostadimoghaddam H, Yekta AA. Amblyopia and strabismus in Iranian schoolchildren, Mashhad. Strabismus, 2011;19(4): 147-152.
- Qanat AS, Alsuheili A, Alzahrani AM, Faydhi AA, Albadri A, Alhibshi N, et al. Assessment of different types of strabismus among pediatric patients in a tertiary hospital in Jeddah. Cureus, 2020;12(12).
- Chen X, Fu Z, Yu J, Ding H, Bai J, Chen J, et al. Prevalence of amblyopia and strabismus in Eastern China: results from screening of preschool children aged 36–72 months. British Journal of Ophthalmology, 2016;100(4): 515-9.
- Hashemi H, Pakzad R, Heydarian S, Yekta A, Aghamirsalim M, Shokrollahzadeh F, Khoshhal F, Pakbin M, Ramin S, Khabazkhoob M. Global and regional prevalence of strabismus: a comprehensive systematic review and meta-analysis. Strabismus, 2019;27(2):54-65.
- Yetkin AA, Turkman IH. Evaluation of clinical characteristics and risk factors of strabismus cases. Northern Clinics of Istanbul, 2023;10(2), 157.
- Ziakas NG, Woodruff G, Smith LK, Thompson JR. A study of heredity as a risk factor in strabismus. Eye (Lond), 2002;16(5):519-21.
- 15. Çorak Eroğlu F, Oto S, Şahin Fİ, Terzi Y, Özer Kaya Ö, Tekindal MA. The Role of Heredity and the Prevalence of Strabismus in Families with Accommodative, Partial Accommodative, and Infantile Esotropia. Turk J Ophthalmol; 2020;50(3):143-150.
- 16. Zhang XJ, Lau YH, Wang YM, Kam KW, Ip P, Yip WW, et al. Prevalence of strabismus and its risk factors among school aged children: The Hong Kong Children Eye Study. Scientific Reports, 2021;11(1): 13820.
- Torp-Pederson T, Boyd HA, Skotte L, Haargaard B, Wohlfahrt J, Holmes JM, Melbye M. Strabismus Incidence in a Danish Population Based Cohort of

children. JAMA Ophthalmol, 2017;135(10): 1047-1053.

- Major A, Maples WC, Toomey S, DeRosier W, Gahn D. Variables associated with the incidence of infantile esotropia. Optometry;2007;78(10):534-41.
- Demirayak. Evaluation of stereopsis level and its associated factors in patients with refractive accommodative esotropia. Arch Clin Exp Med, 2021;6(3):92-5.
- Louwagie CR, Diehl NN, Greenberg AE, Mohney BG. Is the incidence of infantile esotropia declining?: a population-based study from Olmsted County, Minnesota, 1965 to 1994. Arch Ophthalmol 2009;127(2):200-3.
- Srimanan W. Outcomes and Factors Associated with Successful Strabismus Surgery for Abducens Nerve Palsies: A Retrospective Study and Literature Review. Clinical Ophthalmology, 2024;18: 1945-1958.
- 22. Robaei D, Rose KA, Ojaimi E, Kifley A, Martin FJ, Mitchell P. Causes and associations of amblyopia in a population-based sample of 6-year-old Australian children. Arch Ophthalmol, 2006;124(6):878-84.
- 23. Chia A, Dirani M, Chan Y-H, Gazzard G, Eong K-GA, Selvaraj P, et al. Prevalence of amblyopia and strabismus in young Singaporean Chinese children. Investigative ophthalmology & visual science, 2010;51(7):3411-3417.
- Hiles DA, Watson BA, Biglan AW. Characteristics of infantile esotropia following bimedial rectus recession. Arch Ophthalmol, 1980;98(4), 697-703.
- Lee HJ, Kim SJ, Yu YS. Stereopsis in patients with refractive accommodative esotropia. J AAPOS, 2017;21(3):190-195.