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Prevalence of nystagmus among pediatric cases presented to Mansoura Ophthalmic Center; one year study

Mohamed M. bellah[1], Manal A. Kasem[2], Wessam I. Elshawaf[3], Rasha M. Elzeini[4]

[1] Resident of ophthalmology, Mansoura Ophthalmic Hospital, Egypt

[2] Professor of Ophthalmology-Faculty of medicine – Mansoura University

[3]lecturer of Audiology - Faculty of medicine – Mansoura University

[4] lecturer of Ophthalmology - Faculty of medicine – Mansoura University

Corresponding author: Mohammed M. bellah, Resident of ophthalmology, Mansoura Ophthalmic Hospital, Egypt, Mansoura city, Daqahlia governorate, Egypt. Postal code:35522, Tel: +201067076651, E mail: momoatz1990@gmail.com

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Running Title: Prevalence of nystagmus among pediatric cases.

Abstract

Purpose: Study epidemiological characteristics and Prevalence of nystagmus among pediatric cases presented to Mansoura Ophthalmic Center through one year.

Method: a prospective cross-sectional study included all nystagmus cases in children aged (0-18) years attending outpatient clinics of Mansoura Ophthalmic Center in the period between April 2018 and April 2019. Complete ocular examination and nystagmus assessment were done.

Results: Number of children presented to outpatient clinics in Mansoura Ophthalmic Center was 24154, 13230 were males and 10924 were females. The prevalence of nystagmus among these cases was 72 (0.3%), 42 were males and 30 were females. Median age among nystagmus cases was 5.5 years (0.33-17). Median BCVA was 0.77800 logMAR (0.00 - 2.400). Abnormal head posture (AHP) was detected in 24 cases (33.3%). Strabismus was present in 47.2 % of cases. Abnormal findings in the children referred for investigations were 71.4 % in ERG, 43% in VEP, 24.5% in MRI brain. Etiological types of nystagmus of studied cases were sensory nystagmus in 36 cases (50 %), neurological cause in 13 cases (18.1%), infantile idiopathic nystagmus in 8 cases (11.1%), fusional maldevelopment syndrome in 6 cases (8.9%), spasmus nutans in 4 cases (5.6%), gaze evoked nystagmus & combined sensory and neurological nystagmus both were 2 cases (2.8%), one case (1.4%) of mono ocular nystagmus of childhood.

Conclusion: The most common etiological types; were sensory nystagmus followed by neurological, infantile idiopathic, fusional maldevelopment syndrome in the same order. Strabismus and abnormal head posture (AHP) are common in nystagmus.

Key words: Nystagmus, abnormal, prevalence, etiological types

Introduction:

Nystagmus is a condition in which one or both eyes make uncontrollable oscillating movements. Infantile nystagmus (IN) is a condition that occurs in children between the ages of 3 and 6 months, while the foveation reflex is still maturing[1].

Acquired nystagmus is the term for nystagmus that develops later in life. Infantile nystagmus is generally thought to be a rare condition. Infantile nystagmus can be caused by a variety of visual and brain system abnormalities[2].

When no cause can be found, the condition is known as idiopathic infantile nystagmus (IIN). Patients with IIN typically have better vision than patients with ocular disease. Because of the numerous possible causes, the presence of IN frequently necessitates extensive investigation[3].

Despite extensive research into nystagmus over many years, many questions about diagnosis, treatment, and overall

management remain unanswered. It is estimated that up to 50% of infantile strabismus patients will have either infantile nystagmus syndrome (INS) or fusion maldevelopment nystagmus syndrome (FMNS)[4].

The prevalence of any form of nystagmus (not only IN) is estimated at 0.17% in people under the age of 18 years old. In contrast, the prevalence is much higher in the adult population (0.27%). This increase is related to cases of acquired nystagmus.[5]

Patients and methods:

A prospective cross-sectional study.

Inclusion criteria:

- All nystagmus cases in children aged (0-18) years attending outpatient clinics of Mansoura Ophthalmic Center in the period between April 2018 and April 2019 either discovered during examination or previously diagnosed**.**

Exclusion criteria:

- Other involuntary eye movements as ocular flutter, ocular opsoclonus, ocular bobbing, superior oblique myokymia.

Methods:

All patients were subjected to a thorough history taking, full ophthalmic examination and work up according to each case needs.

❖ Recording of patients, data included:

History taking, measurement of best corrected visual acuity [BCVA] was recorded then transformed to logMAR notation for statistical purposes, Children under 2 years old were tested using central steady maintained (CSM) method or optokinetic drum, children (2 _ 4) years old were tested using LEA chart, children above 4 years old were tested using landolt chart. Cycloplegic refraction using cyclopentolate 1% eye drops instilled 3 times within 1 hour then refraction was obtained using autorefractometer or retinoscopy. Anterior segment examination using slit lamp biomicroscopy.

Fundus examination using direct and indirect ophthalmoscopes. Ocular motility assessment. Check for associated strabismus by hirschberg test, cover –uncover test, alternate cover test, prism cover test. Abnormal head posture. Stereopsis using Lang test. Color vision using ishihara test. Nystagmus examination which includes laterality, direction, null zone, conjugacy and dissociation, behavior in convergence, behavior in all directions, latent nystagmus by Cover one eye then the reverse, observation for several minutes to exclude periodic alternating nystagmus. Optokinetic nystagmus was used to help in diagnosis as following[6].

- Normal: a smooth pursuit movement followed by contraversive saccade back to primary gaze or direction of visual interest.
- Reversed: saccade followed by smooth pursuit as in congenital nystagmus
- Asymmetry: in latent nystagmus, unilateral parieto occiptal lesion, unilateral vestibular lesion
- Symmetrically reduced: progressive supranuclear palsy

Investigations as ERG (Flash ERG or Multifocal ERG)**,** Pattern reversal Visual evoked potentials (VEP) or Pattern onset/offset VEPs in children older than 6 years old or flash VEPs in infants or children were uncooperative or younger than 6 years old, ERG and VEP were done in any case with no evidence of neurological problems and ocular examination couldn't reveal obvious cause for nystagmus, brain MRI to detect any neurological diseases causing nystagmus if there was any evidence in clinical examination that there was neurological problem or if there were signs of acquired nystagmus and before diagnosing case as Infantile idiopathic nystagmus to detect any hidden brain abnormalities.

Videonystgmography (VNG**)** was used to test ocular motor system to detect any neurological problem or possibly a problem in the pathway connecting the vestibular system to the brain. It was used also to document and confirm nystagmus direction that have been examined clinically, it was done in cooperative children whom age between (6_18) years old.

Statistical analysis of the data:

- Data were fed to the computer and analyzed using IBM SPSS Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. Qualitative data were described using number and

percent. Quantitative data were described using median (minimum and maximum) for non-parametric data and mean, standard deviation for parametric data after testing normality using Kolmogrov-Smirnov test. Significance of the obtained results was judged at the (0.05) level.

Ethics approval and consent to participate:

This prospective cohort study was approved by Mansoura Medical Research Ethics Committee, Faculty of Medicine, Mansoura University. Patients legal guardians were considered, informed consent prior to study participation was obtained from parents of each participant in the study assuring confidentiality.

RESULTS

Number of children presented to outpatient clinics in Mansoura Ophthalmic Center from April 2018 to April 2019 was 24154, 13230 were males and 10924 were females. The prevalence of nystagmus among these cases was 72 (0.3%).

Median age for studied cases of nystagmus was 5.5 years (0.33-17). Sex was 42 males and 30 females. Median age of onset of the nystagmus was 6.5 months according to history taking, children less than 6 months old at onset were 37 cases and more than 6 months old were 19 cases while couldn't be remembered by parents in 16 cases as shown in table (1).

Table (1): Analysis of Demographic data in the cases of the study

	N=72	%
Age/years		
Median (range)	5.5 (0.33-17)	
Sex		
Male	42	58.3
Female	30	41.7
Age of onset /months		
Can't remember	16	22.2
<6 months (infantile)	37	51.4
≥6 months (acquired)	19	26.4

Family history of nystagmus was positive in (18) 25%, Sister (9) was the most common followed by brother (7) and only one case for mother and grandfather as shown in table (2)

Table (2): Analysis of Family history of nystagmus in the studied cases.

Family history	**n=72**	**%**
• Negative	54	75
• Positive	18	25
• Sister	9	12.5
• Brother	7	9.7
• Mother	1	1.4
• Grandfather	1	1.4

About BCVA, median BCVA was 0.77800 with minimum 0.00 and maximum 2.400. 12 children couldn't be assessed (24eyes), 6 eyes were excluded as exact value of VA couldn't be determined but visual acuity was impaired by OKN test or CSM method, 2 eyes visual acuity were HM and 4 eyes visual acuity were CF; those 6 eyes were converted to numerical values for statistical purposes (2.1 logMAR for CF and 2.4 logMAR for HM). [7]

About cycloplegic refraction, after excluding 6 eyes couldn't be refracted and 5 sound eyes in 5 unilateral nystagmus cases, The Cycloplegic refraction of 133 eyes of studied cases was sphere only in 8 eyes (7 hyperopia and 1 myopia), astigmatism in 122 eyes (7 eyes simple astigmatism, 102 eyes compound astigmatism, 13 eyes mixed astigmatism) and 3 eyes was emmetropia. Cut off values were hyperopia if > + 0.5 sphere, myopia if < -0.5, astigmatism if more than 0.5, emmetropia (- 0.5 - + 0.5) as shown in table (3)

Table (3): Analysis of cycloplegic refraction of eye among studied cases

Refraction		**N=133**	**%**
Sphere only		**8**	**6**
	Myopic	1	0.7
	Hyperopic	7	5.3
Astigmatism		**122**	**92**
Simple	**Myopic**	4	3
	Hyperopic	3	2.2
Compound	**Myopic**	48	36
	Hyperopic	54	41
Mixed		13	9.8
Emmetropia		**3**	**2**

Abnormal head posture was positive in 24 cases (33.3%) in the form of 8 cases head tilt (11.1%), face turn in 16 cases (22.2%), no cases of chin elevation or depression, 5 cases of head nodding (7%), one of them was during reading only as shown in table (4)

Table (4): Analysis of AHP in the studied cases

	n=72	**%**
AHP		
Positive	24	33.3
Head tilt	8	11.1
Face turn	16	22.2
Head nodding		
yes	4	5.6
During reading only	1	1.4

Strabismus among cases of nystagmus was common (54.2%). 33 cases were orthotropia, 23 cases were exotropia (32%), 9 cases were esotropia (12.5%), 6 cases were combined (8.3%) strabismus (horizontal and vertical deviation), one case was vertical strabismus (SOP + secondary SOOA). Among cases of strabismus, 5 cases underwent strabismus surgery and they become ortho (3 cases of XT, 1 esotropia, 1 combined)

Table (5): Analysis of prevalence of strabismus among the studied cases**.**

Strabismus	**n=72**	**%**
Orthotropia	33	45.8
Exotropia	23	32
Esotropia	9	12.5
Combined	6	8.3
Vertical squint	1	1.4

Diagnostic work up was done in patients with no obvious cause (ERG, VEP, MRI). ERG and VEP were done in 14 cases (19.4 %) with abnormal finding in 71.4 % in ERG (myopia and retinal dystrophy were the most common findings), 43% in VEP. MRI was done in 73.6% of nystagmus cases with abnormal findings in 24.5% (leukomalacia was the most common finding).

Etiological types of nystagmus of studied cases were sensory nystagmus in 36 cases (50 %), neurological cause in 13 cases (18.1%), infantile idiopathic nystagmus in 8 cases (11.1%), fusional mal development syndrome in 6 cases (8.3 %), spasmus nutans in 4 cases (5.6%), gaze evoked nystagmus and combined sensory and neurological both were 2 cases (2.8%), one case (1.4%) of mono ocular nystagmus of childhood.

Causes of sensory nystagmus in descending order; albinism and congenital cataract each of them 10 cases (27.8%), retinal dystrophy was found in 5 cases (13.8%), high myopia in 4 cases (11.1%), chorioretinal coloboma in 2 cases (5.55%). Neurological nystagmus causes were leukomalacia in 3 cases (23.1%), encephalomalacia in 2 cases (15.4%), epilepsy in 2 cases (15.4%) as shown in the table (5)

Table (6): Analysis of etiological types of nystagmus in the studied cases

	n=72	%
Sensory nystagmus	**36**	**50**
• Albinism	**10**	27.8
• congenital cataract	**10**	**27.8**
• Retinal dystrophy	**5**	13.9
• high myopia	**4**	**11**
• chorioretinal coloboma	**2**	**5.5**
• Leber congenital amaurosis	**1**	**2.8**
• Optic disc hypoplasia + nanopthalmos	**1**	**2.8**
• Aniridia + congenital cataract	**1**	**2.8**
• ROP	**1**	**2.8**
• congenital Cataract + congenital glaucoma	**1**	**2.8**
Neurological nystagmus	**13**	**18.1**
• Leukomalacia	**3**	**23.1**
• Encephalomalacia	**2**	**15.4**
• Epileptogenic	**2**	**15.4**
• Unknown	**1**	**7.7**
• Down + Hypothyroidism	**1**	**7.7**
• Down only	1	7.7
• Corpus callosum dysgliosis and lissencephaly	**1**	**7.7**
• Traumatic cerebral malacia	**1**	**7.7**
• Hypothyroidism	**1**	**7.7**
Infantile idiopathic nystagmus	**8**	**11.1**
Fusional maldevelopment nystagmus	**6**	**8.3**
Spasmus nutans	**4**	**5.6**
Combined sensory and neurologic nystagmus	**2**	**2.8**
Retinal dystrophy + leukomalacia	1	50
Retinal dystrophy + neurological insult	1	50
Gaze evoked nystagmus (not neurological cause)	**2**	**2.8**
Monocular nystagmus of childhood	**1**	**1.4**

DISCUSSION

The prevalence of nystagmus in pediatrics has previously been reported, and results vary from one study to another. This difference in prevalence could be due to differences in study design, genetics, parents awareness, pre and postnatal care.

Most studies estimate the prevalence of nystagmus as part of larger epidemiological studies of children with poor vision without differentiate between infantile and acquired nystagmus[8].

In our study, prevalence of nystagmus in cases presented to outpatient clinics in Mansoura ophthalmic center through one year was 0.3%. There were 72 cases; 42 were males (58%) and 30 were females (42%)

Similar to our study prevalence, Iranian study Hashemi *et al* to determine the prevalence Of ptosis and nystagmus in the general rural population, The prevalence of nystagmus in this study was 0.39%[9].

In Repka *et al* study that include only preschool-aged children ,in Baltimore, Maryland, United States, nystagmus prevalence was 0.35 % which is almost same as our study[10].

Also in Olmsted County, Minnesota study, birth prevalence was 1 in 821 (0.12%). Similar to our study gender percentage, 42 children (59.2%) were male, 29 were female (40.8%)[2].

In Leicestershire and Rutland, United Kingdom, Sarvananthan et al conducted nystagmus study included all nystagmus forms, they found the prevalence of nystagmus in general population was 24.0 per 10,000 population (0.24%). In the 18 years or younger age group, the prevalence was 16.6 per 10,000 (0.17 %) population [11]. Another study in capital region of Denmark about children with infantile nystagmus and diagnosed during 7-years period (2010- 2017), 50.5% were males and 49.5% were females. The overall prevalence of infantile nystagmus was 6.1 per 10 000 live births (0.061%)[8]. This difference in prevalence in Sarvananthan et al study or the study in denmark in comparsion to our study may be due to conducting these studies among general population in city not medical center as in our study.

Different study in south korea conducted by Lee *et al* about the prevalence of strabismus and nystagmus over 3 years from 2008 to 2011, The prevalence of nystagmus was 0.1%[12].

Median Age of children of the nystagmus in our study was 5.5 years, in contrast to Nash, David L, Diehl, N. N. and Mohney study which was 12.7 months[2].

A family history of nystagmus in close relatives of our cases was reported in 25%. Most common causes of nystagmus in their relatives in descending order were ocular pathology, albinism and congenital idiopathic nystagmus.

Similar to our study family history percentage, nystagmus was present in the families of 25.26% cases in the study conducted by Inal *et al*[13]. In contrast, family history of nystagmus in close relatives conducted by Hvid *et al* reported in 6 %[8].

In our study, median BCVA was 0.77800 with minimum 0.00 and maximum 2.400. In Healey *et al* study about infantile nystagmus syndrome, Visual acuity ranged from 0.06 to 1.60 log MAR[14].

cycloplegic refraction in our study was 42.8% hyperopic astigmatism as the most common refraction then 39% myopic astigmatism followed by 9.7% mixed astigmatism, 5.3% hyperopia, 2.2% emmetropia, 0.7% myopia.

In contrast to our study, Perveen *et al* study showed that (42%) had myopic astigmatism as the most common refractive error then (30%) eyes had hyperopic astigmatism, 20 (18%) eyes had hyperopia and 11 (10%) eyes had myopia[15].

Also Mazhar and Shakeel study showed that myopic astigmatism was the most common error (57.14%) followed by mixed astigmatism (25.71%) then hyperopic astigmatism (17.14%) patients[16].

In our study, AHP was present in 33.3 % of cases which is similar to Guenena *et al* study percentage 36 % [17]. Our finding was lower than Hertle *et al* study which was 54 % [18] and higher than David L. Nash, Diehl and Mohney study which was (21.1%)[2].

Strabismus among cases of nystagmus in our study was 54.2%, which was similar to Hvid *et al* study (58%)[8], strabismus prevalence was higher in Noval *et al* study which showed that up to 64% of all patients had strabismus [19] and in Hertle *et al* study which showed that 81% had strabismus[18], strabismus was lower in David L Nash, Diehl and Mohney study which revealed that Exotropia or esotropia was present in (40.3%) patients[2].

In our study, exotropia was (32%) and esotropia was (12.5%), but in contrast, Hvid *et al* study showed that esotropia was 35% and exotropia was reported in 6% [8], Noval *et al* study showed an equal distribution between eso and exo deviations[19].

Diagnostic work up was done in patients with no obvious cause (ERG, VEP, MRI). ERG and VEP were done in 19.4 % of cases with abnormal finding in 71.4 % in ERG, 43% in VEP. In MRI, it was done in 73.6% with abnormal findings in 24.5%

In Batmanabane *et al* study about children with isolated nystagmus who underwent MRI between (2008 – 2014), 15.5% had abnormalities on MRI brain[20].

In contrast, children with early onset nystagmus and normal ocular examination in Gaber *et al* study underwent ERG and flash VEP, ERG were abnormal in (37.5%) patients, Flash VEP was abnormal in (81.3%) patients[21].

In our study, the causes of nystagmus were sensory nystagmus in 36 cases (50 %), neurological cause in 13 cases (18.1%), infantile idiopathic nystagmus in 8 cases (11.1%), fusional mal development syndrome in 6 cases (8.3 %), spasmus nutans in 4 cases (5.6%), gaze evoked nystagmus and combined sensory and neurological both were 2 cases (2.8%), one case (1.4%) of mono ocular nystagmus. Most common Causes of sensory nystagmus in descending order; albinism and congenital cataract both 10 cases (27.8%), retinal dystrophy was 5 cases (13.8%), high myopia in 4 cases (11.1%), chorioretinal coloboma in 2 cases (5.55%)

In Olmsted County, Minnesota study conducted by David L. Nash, Diehl and Mohney, The most common types of nystagmus in declining order; nystagmus associated with retinal and optic nerve disease (sensory nystagmus) 32.4% as the most common type which is similar to our study , infantile idiopathic or congenital motor nystagmus (31.0%), fusional

mal development syndrome (24.0%). Causes of sensory nystagmus; Albinism 30.4% was the most common same as our study followed by, Optic Nerve Hypoplasia 13.0%, Leber Congenital Amaurosis 8.7%, Congenital Cataracts 8.7%, Foveal Hypoplasia 8.7%[2].

The study in capital region of Denmark (Danish cohort study) which focused on infantile nystagmus, the most common causes of infantile nystagmus were in descending order: sensory ocular nystagmus (44% of cases) as the most common cause as in our study, idiopathic infantile nystagmus (32% of cases), neurological disease and syndromes (20% of cases) The most common ocular cause of nystagmus was albinism in 20% followed by ocular pathology which is similar to our study[8].

So all studies agreed that sensory nystagmus was the most common cause but the 2nd most common cause was different in our study than others because Danish cohort study and minnesota study focused on infantile nystagmus with age of onset 6 months or younger unlike our study which included early and late onset nystagmus (age of onset before or after 6 months) in pediatric cases.

Conclusion

Sensory ocular nystagmus is the most common type followed by neurological and infantile idiopathic nystagmus. Albinism and congenital cataract are the most common causes of sensory nystagmus. Strabismus and AHP are common association with nystagmus.

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DATA AVAILABILITY

All data are included in this article.

Corresponding author

Correspondence to: Mohammed Moatz bellah

Email: momoatz1990@gmail.com

Affiliations

Mohammed M. Bellah, Mansoura Ophthalmic Center, Faculty of Medicine, Mansoura University, Mansoura, Egypt.

Ethics declarations

Conflict of interest

Mohamed M. bellah, Manal A. Kasem, Wessam I. Elshawaf, Rasha M. Elzeini. all authors have no conflicts of interest that are directly relevant to the content of this review.

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