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Ocular Manifestations in Various Syndromes in Children

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ABSTRACT

Purpose: This study aimed to determine the prevalence of different genetic syndromes associated with ocular manifestations in an Indian pediatric population, identify and characterize the most common ocular abnormalities observed across these genetic syndromes, and provide insights to inform targeted screening protocols and management strategies for ocular health in patients with genetic syndromes.

Methods: An observational study was conducted at Jaslok Hospital and Research Center in Mumbai, India. The study included 100 children below 16 years of age with established diagnoses of various syndromes. Comprehensive ocular examinations were performed, including visual acuity assessment, slit lamp examination, cycloplegic refraction, fundoscopy, and other relevant tests.

Results: The study encompassed eight genetic syndromes, with Down's syndrome being the most prevalent (50% of cases). Refractive errors were the most common ocular manifestation, affecting 97% of patients across all syndromes. Strabismus was the second most prevalent ocular issue, observed in 39% of patients. Syndrome-specific ocular features were also identified, such as upward slanting palpebral fissures in Down's syndrome, limbal dermoids in Goldenhar syndrome, and Lisch nodules in Neurofibromatosis-1.

Conclusion: This study highlights the high prevalence and diverse nature of ocular manifestations in children with genetic syndromes. The findings underscore the importance of early and regular ophthalmological screenings in these patients to ensure timely detection and management of ocular abnormalities, potentially improving overall quality of life and visual outcomes.

Keywords: Genetic syndromes, ocular manifestations, pediatric ophthalmology, Down's syndrome, Neurofibromatosis, refractive errors, strabismus, congenital anomalies

I. INTRODUCTION

Syndromes are defined as a group of symptoms which can be congenital or acquired which involve many systems of the body, including eyes, or it may be attached to an assortment of signs and symptoms for which the etiology is known (eg. Down's syndrome, Marfan syndrome, Trisomy 13).

Ocular involvement gives rise to various ocular manifestations [1]. Some ocular manifestations are specific for a particular syndrome, like Lisch nodules seen in Neurofibromatosis [2].

Ophthalmologists play a very important role in helping pediatricians to arrive at a diagnosis and treat these ocular manifestations while preserving the vision [1]. Management of number of diseases/syndromes requires team work between different branches of medicine. Ophthalmologist is an indispensable member of such team.

Hence a study of these ocular manifestations is of paramount importance.

There are various syndromes with ocular manifestations like Down syndrome, Neurofibromatosis, Sturge Weber Syndrome, Marfan's Syndrome, Mucopolysaccharidosis, and Albinism various syndromes associated with Retinitis Pigmentosa etc. [1].

Mostly, all syndromes involve various systemic manifestations. Ocular manifestations are also one of them. Most of the literature on ocular manifestations in various syndromes is available in western population. We therefore selected this topic for our study to determine prevalence of ocular manifestations in commonly seen syndromes in Indian pediatric population.

Our research objectives include:

1. Determining the prevalence of different genetic syndromes associated with ocular manifestations in our study population.
2. Identifying and characterizing the most common ocular abnormalities observed across these genetic syndromes,

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3. Providing insights to inform targeted screening protocols and management strategies for ocular health in patients with genetic syndromes.

II. METHODS

Study Procedure:

The study was conducted at Jaslok Hospital and Research Center, located on Dr. G Deshmukh Marg in Mumbai-India. The study duration was from April 2022 to March 2024, following an observational design. The study population consisted of 100 children diagnosed with known syndromes visited to pediatric OPD. The sample size of 100 patients was determined through power calculations, (Confidence interval-95%, SD-0.5, α-0.05, β-0.2).

Inclusion criteria for the study were children below 16 years of age with an established diagnosis of an existing syndrome, confirmed either by genetic testing or by meeting the diagnostic criteria for the disease. Exclusion criteria included patients who had undergone surgical treatment for ocular manifestations, highly uncooperative children, cases where preliminary clinical examination did not fulfill criteria for the described syndrome, and children above 16 years of age.

Ethical and scientific committee approval was obtained before initiating the study, and written informed consent was acquired from all patients after explaining the protocol. The study employed various tests, including visual acuity assessment, torch light examination, slit lamp examination, ocular movement evaluation, cycloplegic refraction with retinoscopy, fundoscopy, OCT when necessary, fundus photography when applicable, intraocular pressure measurement(air puff or Applanation tonometry), and perimetry where applicable.

Statistical Analysis:

Data analysis was performed using the professional statistics package EPI Info 7.0 version for Windows. Descriptive data was represented as mean ± standard deviation for numeric variables, and percentages and proportions for categorical variables. Appropriate tests of significance, such as Chi-square test and Fisher's exact test, were employed depending on the nature and distribution of variables. A p-value of less than 0.05 was considered statistically significant.

III. RESULTS

The study encompassed a total of 100 patients with various genetic syndromes, with a significant majority (73%) being under 8 years of age (Table-1).

Down's syndrome was the most prevalent condition, accounting for 50% of the cases, followed by Neurofibromatosis-1 (NF-1) at 14%, Tuberous Sclerosis at 10%, and smaller proportions of Goldenhar Syndrome, Neurofibromatosis-2 (NF-2), Sturge Weber Syndrome (each at 6%), Moebius Syndrome (5%), and Albinism (3%). Notably, 21% of the patients reported a significant family history of genetic disorders(Table-2, graph 1).

Among all the patients visited consequently in the OPD, 85% had symptoms, however 15% had no ocular symptoms at all. Sturge weber syndromes patients were mostly asymptomatic (Table-3).

Across all syndromes, refractive errors emerged as the most common ocular manifestation, affecting 97% of patients. The distribution of refractive errors varied, with myopic astigmatism being the most frequent (30%), followed closely by hyperopic astigmatism (29%), myopia (23%), and hyperopia (15%). Strabismus was the second most prevalent ocular issue, observed in 39% of patients, with esotropia (29%) being more common than exotropia (10%) (Table-4).

Strabismus (squint) was the second most prevalent ocular issue, observed in 39% of patients. A detailed analysis of squint prevalence across different syndromes revealed interesting patterns. Down's Syndrome demonstrated the highest prevalence of squint, accounting for 48% of esotropia cases and 50% of exotropia cases. Sturge Weber Syndrome contributed to 26% of esotropia cases. Tuberous Sclerosis presented a mixed picture, with 13% of esotropia cases and 37.5% of exotropia cases. Moebius Syndrome was associated with 13% of esotropia cases, while Albinism accounted for 12.5% of exotropia cases. Interestingly, Goldenhar Syndrome, Neurofibromatosis-1, and Neurofibromatosis-2 did not present any cases ofstrabismus in this study.

Notably, orthophoria (absence of squint) was most common in Down's Syndrome patients (51% of orthophoria cases), followed by Goldenhar Syndrome and Neurofibromatosis-2 (10% each)(Table-5)

In patients with Down's syndrome, all individuals presented with upward slanting of palpebral fissures and refractive errors. Other common features included epicanthal folds (60%), strabismus (38%), and less frequently, blepharitis and nystagmus (10% each), keratoconus (6%), and lens opacities (5%).

Goldenhar syndrome patients predominantly exhibited limbal dermoid (67%),

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eyelid coloboma (50%), and various refractive errors. Moebius syndrome was characterized by universal presentation of facial nerve palsy with lateral rectus paralysis, while 60% had refractive errors and 40% presented with iris coloboma along with uveal coloboma.

All patients with Albinism demonstrated nystagmus, with a high prevalence of exotropia (67%) and varying types of astigmatism. Neurofibromatosis-1 patients universally presented with café-au-lait spots, axillary freckling, Lisch nodules, and refractive errors, while also showing a range of other ocular manifestations including glaucoma (35%) and optic nerve glioma (15%).

In Neurofibromatosis-2, all patients had lens opacities and refractive errors, with a high proportion (67%) also presenting with optic nerve gliomas. Sturge Weber syndrome was characterized by universal presentation of port wine stain and refractive errors, with some patients also exhibiting glaucoma with choroidal haemangioma and iris heterochromia (33%).

Tuberous sclerosis patients uniformly presented with adenoma sebaceum, ash leaf spots, Shah greens patch, subungual hamartoma, retinal hamartomas, angiofibroma of the lid, and refractive errors. Additionally, a high proportion (90%) exhibited non-paralytic strabismus, while half of the patients had subependymal nodules.

These comprehensive findings underscore the diverse and complex nature of ocular manifestations associated with various genetic syndromes, emphasizing the critical importance of thorough ophthalmological examinations in affected individuals for proper diagnosis and management.

Table No.1 Age wise distribution

Genetic Syndromes	Age category	
	0-8 years	>8-16 years
	Count %	Count %
Down's Syndrome	28 38.4%	22 81.5%
GoldenharSyndrome	4 5.5%	2 7.4%
MoebiusSyndrome	5 6.8%	0 .0%
Albinism	2 2.7%	1 3.7%
Neurofibromatosis -1	12 16.4%	2 7.4%
Neurofibromatosis -2	6 8.2%	0 .0%
Sturge Weber Syndrome	6 8.2%	0 .0%
Tuberous Sclerosis	10 13.7%	0 .0%
Total	73 100.0%	27 100.0%

Table no.2: Syndrome wise distribution with Significant family history

Genetic Syndromes	Family history		Total
	Yes	No	
	Count (%)	Count (%)	
Down's Syndrome	8 (33.3%)	42 (55.0%)	50 (50%)

GoldenharSyndrome	0 (0%)	6 (7.9%)	6 (6%)
MoebiusSyndrome	0 (0%)	5 (6.6%)	5 (5%)
Albinism	3 (12.5%)	0 (0.0%)	3 (3%)
Neurofibromatosis -1	6 (25%)	8 (10.5%)	14 (14%)
Neurofibromatosis -2	3 (12.5%)	3 (4.0%)	6 (6%)
Sturge Weber Syndrome	0 (0%)	6 (7.9%)	6 (6%)
Tuberous Sclerosis	4 (16.7%)	6 (7.9%)	10 (10%)
Total	24 (100%)	76 (100%)	100

Table No.3- Patients with Ocular Complaints

Genetic Syndromes	Ocular complaints	
	Yes	No
	Count %	Count %
Down's Syndrome	40 80%	10 20.0%
GoldenharSyndrome	6 100%	0 0%
MoebiusSyndrome	5 100%	0 0%
Albinism	3 100%	0 0%
Neurofibromatosis -1	14 100%	0 0%
Neurofibromatosis -2	6 100%	0 0%
Sturge Weber Syndrome	1 17%	5 10%
Tuberous Sclerosis	10 100%	0 0%
Total	85 (85%)	15 (15%)

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Table No. 4: Comparison of refractive errors among all syndromes:

Genetic Syndromes	**Refractive Error**				
	Myopia	**Myopic Astigmatism**	**Hyperopia**	**Hyperopic Astigmatism**	**Emmetropia (Normal)**
Down's Syndrome	**16**	**14**	**9**	**11**	**0**
Goldenhar Syndrome	**0**	**1**	**2**	**3**	**0**
Moebius Syndrome	**0**	**0**	**0**	**3**	**2**
Albinism	**0**	**1**	**0**	**1**	**1**
Neurofibromatosis -1	**3**	**4**	**3**	**4**	**0**
Neurofibromatosis -2	**2**	**2**	**1**	**1**	**0**
Sturge Weber Syndrome	**2**	**1**	**0**	**3**	**0**
Tuberous Sclerosis	**0**	**7**	**0**	**3**	**0**
Total	**23 (23%)**	**30 (30%)**	**15 (15%)**	**29 (29%)**	**3 (3%)**

Table No-5: Comparison of strabismus among all syndromes:

Genetic Syndrome	SQUINT		
	Yes		No
	Esotropia Count, %	Exotropia Count, %	Orthophoria Count, %
Down's Syndrome	11 (48%)	8 (50%)	31 (51%)
Goldenhar Syndrome	0 (0%)	0 (0%)	6 (10%)
Moebius Syndrome	3 (13%)	0 (0%)	2 (6.4%)
Albinism	0 (0%)	2 (12.5%)	1 (1.6%)
Neurofibromatosis -1	0 (0%)	0 (0%)	14 (2.3%)
Neurofibromatosis -2	0 (0%)	0 (0%)	6 (10%)
Sturge Weber Syndrome	6 (26%)	0 (0%)	0 (0%)
Tuberous Sclerosis	3 (13%)	6 (37.5%)	1 (1.6%)
Total	23 (100%)	16 (100%)	61 (100%)

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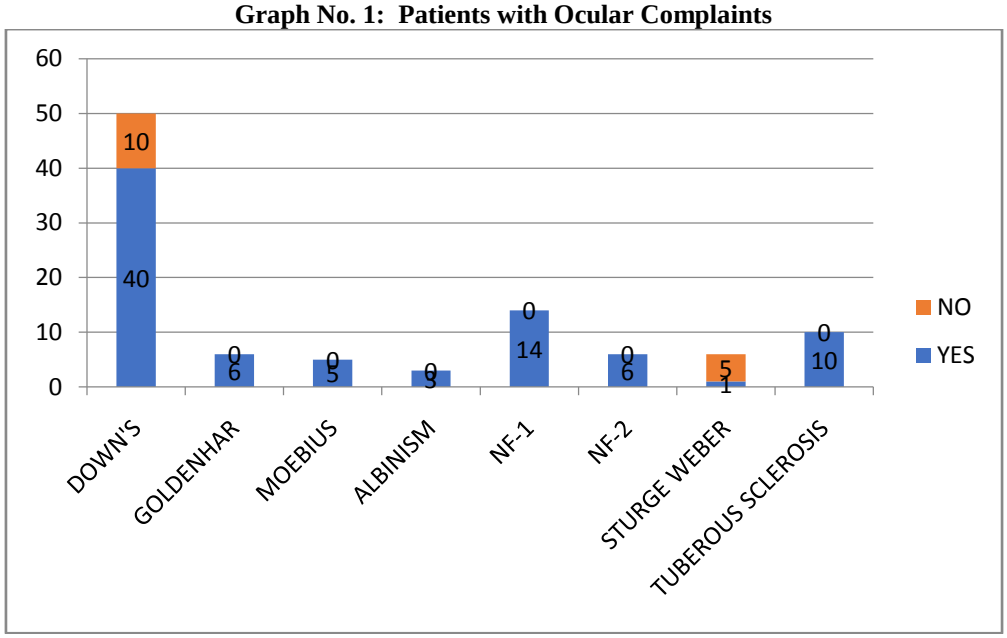
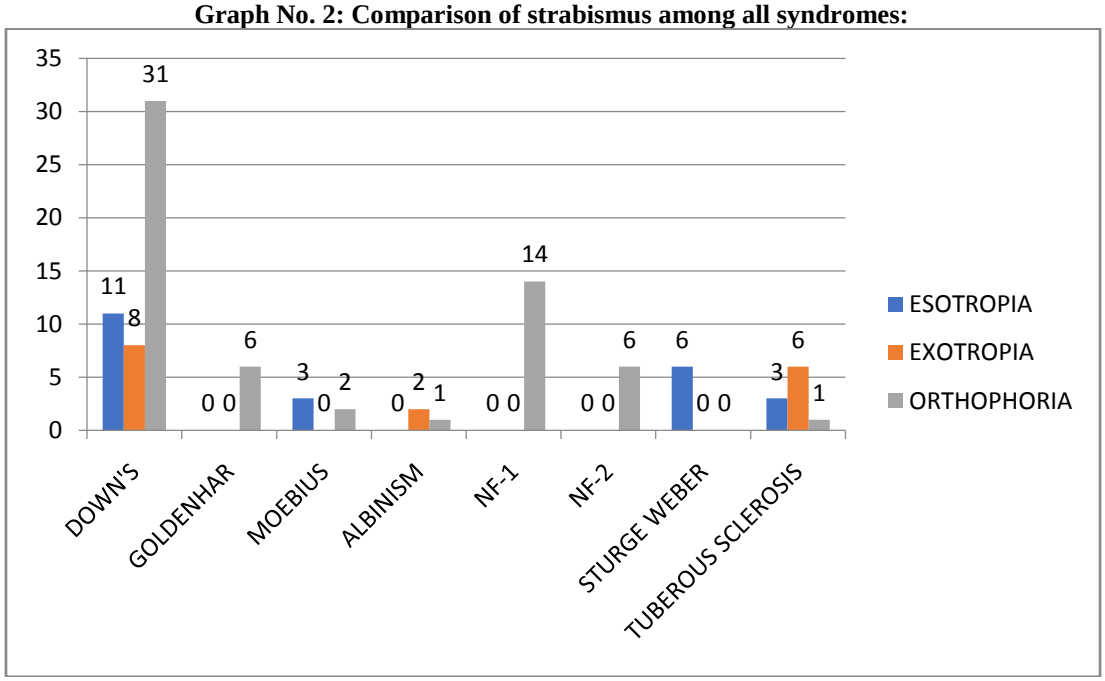
Graph No. 1: Patients with Ocular Complaints



X axis- Various syndromes.
Y axis- No. of patients in each syndrome

Graph No. 2: Comparison of strabismus among all syndromes:



IV. DISCUSSION

This study examined ocular manifestations in 100 patients with various syndromes, including Down's syndrome, Goldenhar syndrome, Moebius syndrome, Albinism, Neurofibromatosis type 1 and 2, Sturge-Weber syndrome, and Tuberous sclerosis.

Down's Syndrome:

Down's syndrome was the most prevalent, found in 50% of the study population. Most patients were in the 0-8 years age group, likely due to more noticeable developmental delays in this age range. Ocular manifestations included upward slanting palpebral fissures (100%), epicanthal folds (60%), and strabismus (38%). Refractive errors were present in all patients, with astigmatism being

the most common (50%). These findings largely align with previous studies, though some variations were noted, possibly due to age, racial factors, measurement technique, or to a combination of these. For instance, our prevalence of upward slanting palpebral fissures (100%) was higher than the 63% reported by Kim et al. [3].

Goldenhar Syndrome:

Six patients were diagnosed with Goldenhar syndrome. Ocular manifestations included limbal dermoid (67%), iris coloboma (33%), and eyelid coloboma (50%). These findings were generally consistent with previous studies, though the prevalence of limbal dermoid was higher in our study compared to the 30-60% reported in literature [4, 5].

Moebius Syndrome:

Five patients were identified with Moebius syndrome, all male and under 8 years of age. All patients exhibited facial nerve palsy with lateral rectus palsy, consistent with the typical phenotype described in previous studies [6, 7, 8, 9]. Iris coloboma and uveal coloboma were found in two patients, which is not commonly reported in literature.

Albinism:

Three patients with albinism were studied, all male. Due to the small sample size, our findings may not be representative of the broader albinism population.

Neurofibromatosis:

Fourteen patients had NF-1 and six had NF-2. In NF-1, café-au-lait spots and axillary freckling were found in 100% of patients, consistent with literature [10, 11, 12, 13]. Lisch nodules were present in all NF-1 patients, higher than some previous reports [14].

For NF-2, all patients had lens opacities, and 67% had optic nerve gliomas, which is higher than the 38-81% typically reported for cataracts [15, 16].

Sturge-Weber Syndrome:

Six patients were diagnosed with Sturge-Weber syndrome. All patients presented with port-wine stains, and 33% had glaucoma associated with choroidal hemangiomas, which aligns with previous studies [17, 18].

Tuberous Sclerosis:

Ten patients had tuberous sclerosis. Retinal hamartomas were found in 100% of patients, which is at the upper end of prevalence reported in previous studies [19]. Non-paralytic strabismus was observed in 90% of patients, which is higher than typically reported.

Overall, while many findings were consistent with existing literature, some variations were observed. These differences could be attributed to factors such as sample size, age distribution, racial factors, or the specialized nature of our tertiary care center. As noted in the text, the prevalence of all syndromes in our study was found to be higher than previous studies, likely because our hospital is a tertiary care center where only selected cases are referred. Further studies with larger sample sizes may be needed to confirm these findings and explore potential explanations for the variations observed.

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