Ocular Findings of Down's Syndrome in Iraq

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Summary:

Background: *To identify and study the most common ocular findings in a pediatric age group of patients with Down's syndrome in Iraq.*
Methods: *A total number of 75 patients with Down's syndrome between 6 and 18 years of age prospectively underwent ocular examination, including visual acuity assessment, slit-lamp biomicroscopy, ocular motility, cycloplegic retinoscopy, and ophthalmoscopy.*
Results*: Ocular findings in decreasing prevalence were the following: upward slanting of the palpebral fissure with the outer canthus 2 mm or higher than the inner canthus (100%), epicanthal folds (60%), astigmatism (45%), strabismus (39%), myopia (30%), which was the most common refractive error, lacrimal system obstruction (29%), hyperopia (20%), blepharitis (10%), ambylopia (9%), iris abnormalities (6%), retinal abnormalities (5%), nystagmus (4%), and cataract (3%), and Visual acuity was assessed with Snellen chart and picture charts.*
Conclusion*: The early investigation and management of the ocular abnormalities in patients with Down's syndrome, by using Snellen chart and picture charts overcome the ocular difficulties concerning visual acuity, squint and other abnormalities, and minimize handicaps.*

Introduction:

The best known and most common chromosome related disease syndrome, formerly known as "mongolism", is now designated Down's syndrome after Langdon Down, who first described the clinical signs in 1866. The cost of training and maintaining Down's syndrome cases in the United States is estimated as $1 billion per year. Emotional stress in families with Down's syndrome children and adults is also a factor in their care. The need for effective counseling and prevention is readily apparent.[1]

Since trisomy-21 is an autosomal disorder it occurs often equally in both sexes. The average expectation of life is about 16.2 years[1], it has been lengthened with improved medical care, but relatively few individuals survive into their twenties[2].

Down's syndrome was the first human syndrome found to be due to a chromosomal disorder, discovered by Jerome Lejeune a physician in Paris who published his findings in 1959. An interesting aspect of this syndrome is the increased incidence among children of older mothers, a fact known more than twenty-five years before the discovery of the cause of the syndrome[3].

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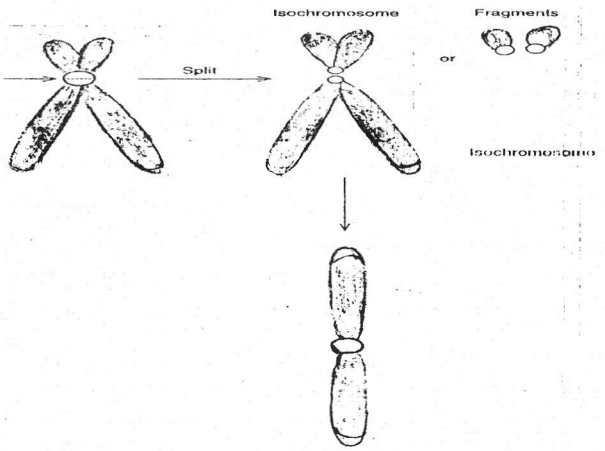
Genetics:

Down's syndrome (trisomy 21) was described earlier as the result of either a non-disjunction event during gametogensis or, rarely, a mitotic event. It is a function of maternal age and is not inherited. The probability of an unaffected relative of the trisomy 21 person having abnormal children is no greater than for a person of the same age chosen at random from the general population. However, about 4% of those with Down's syndrome have been found to have a translocation of chromosome 21, The translocational and non-translocational types of Down's syndrome have identical symptoms; however, a balanced translocation can be passed on to offspring. It is worth mentioning that aside from trisomy and translocation, Down's syndrome can come about through mosaicism, or a centromeric event. It is found that about 2% of individuals with Down's syndrome are mosaic for cells with both two and three copies of chromosome 21. There is some evidence that the original zygotes were trisomic but then a daughter cell lost one of the copies of chromosome 21. The severity of the symptoms of Down's syndrome in these individuals is related to the percentage of trisomic cells they posses. Mosaicism increases with maternal age, just as trisomy in general does. In extremely rare cases, Down's syndrome has been caused by the occurance of an abnormal chromosome 21 that has two identical long arms attached to the centromere, rather than a short and long arm. This type of chromosome is called an isochromosome and presumeably occurs by an odd centromeric fission

(fig.). Hence a person with a normal chromosome 21 and an isochromosome 21 has three copies of long arm of the chromosome 21 and shows Down's syndrome.[3]

Down's syndrome occurs once in about 700 live births among Europeans. Incidence at conception is estimated to be considerably higher (7.3 per 1000), the difference being reflected in fetal loss due to spontaneous abortion. About 1 in 6 children born alive with Down's syndrome die within the first year. Some patients with Down's syndrome have a total of only 46 instead of 47 chromosomes, but in such cases a translocation has joined the long arm of chromosome 21 with another chromosome in the same complement, most frequently number 14 [1] .



Division axis can from an isochromosome of the long arms & either an isochromosome of the short Fig:the break of the centromere of chromosome 21 perpendicular to the normal arms or two separate fragments .this can happen during anaphase of mitosis or meiosis II

Patients & Methods:

Children enrolled in this study were recruited from معهد هبة الله for special need children. Initially, 100 letters were sent to parents of children with Down's syndrome between the ages of 6 and 18 briefly discussing the intent, nature, and importance of this study. Parents who agreed to allow their child to participate in this investigation were taken to Al-Yarmouk Hospital ophthalmology out-patient department where they were examined.

Of the original 100 families contacted, 75 enrolled in the study .The remaining 25 families either had taken their children out of the institute or their children were severely mentally retarded and were unable to participate, or the parents simply refused to be a part of the study. With the parents' permission, information was obtained from previous ophthalmologic examinations. Parents were asked to complete a brief questionnaire pertaining to ocular disorders, previous ophthalmologic examinations, correction of refractive errors, and other visual concerns of their children. During the subsequent screening, the children's eyes were examined and their visual acuity was assessed by the participating technician who had special training in performing these procedures: Snellen letters, numbers, or picture charts were used to assess visual acuity. Although the refractive errors can be identified without the active co-operation of the subject, the above described method was chosen for this study, in order to be consistent. After screening, children were re-invited for a more thorough ophthalmologic examination. The examination included evaluation of ocular motility, strabismus, globe, ocular adnexa, and the fundus. Evaluation of the palpebral fissure was by placing a clear plastic straight-edge ruler across the bridge of the nose at the level of both inner canthi, and the vertical displacement of the outer canthi was measured. Upward slanting fissures were defined as 2mm or more above the horizontal line. In this study ambylopia was defined as having a significant visual loss not associated with fundoscopic abnormalities and not correlated with refraction, and when there was a difference of two Snellen acuity lines between the right and left eyes. All strabismus measurements were made with full refractive correction. The patients then underwent slit-lamp biomocroscopy examination of the eyelid margin, conjunctiva, corneal thinning or irregularities, iris abnormalities such as Brushfield's spots and stromal hypoplasia, and the lens. Cataracts were defined as any opacity of the lens. Indirect and direct ophthalmoscopy after mydriasis was used to examine the ratina, choroid and optic disc.

Results:

Data on age and gender for this study population included 6-18 years old males and females. Two examinations were required to collect all data for some study patients.

The results of ophthalmological screening are given in table 2. Slit-lamp examination was done and blepharitis discovered in 8 (10%) of patients, corneal abnormalities exclusively keratoconus being seen in only 2 patients (3%); whereas cataracts was seen in 9 patients (12%).

Patients with blue, green or light hazel irides were more likely to have identifiable Brushfield's spots or anterior stromal atrophy, 5 patients (6%), whereas patients with dark brown irides did not have such abnormality. Nystagmus was seen in only 3 patients, (4%).

Of the ocular findings given in table 3 and 4, upward slanting of palpebral fissure with the outer canthus 2mm or higher than the inner canthus was the must common finding in all age groups, both males and females, with no statistical difference among them. Whereas epicanthal folds were seen in

60% of patients equally distributed between both sexes in all age groups, lacrimal duct obstruction was seen in 29%.

Ambylopia was discovered in 6 patients (8%), no statistical difference being observed between males and females, in 2 patients (3%) of patients the ambylopia was due to strabismus, another 2 patients (3%) was due to cataract, in one patient (1.5%) myopia was the cause, and in another one (1.5%) hyperopia was the cause.

The fundal abnormalities seen were myopic changes and it were most common in individuals with myopia compared with those with emmetropia, hyperopia, or astigmatism (table 5).

Study patients had a higher prevalence of astigmatism (45%) compared with hyperopia (20%), myopia (30%), and emmetropia (5%) (table 5).

Strabismus was diagnosed in 29 patients (39%), and was statistically more frequent in patients between six and eleven years of age, compared with older population (table 3). Esotropia was the most common type 27 of the 75 children, which represent 36% of the study population, (table 6), and out of these 27 children, 12 were myopic with high accommodative convergence-to-accommodation ratio; and 10 were myopic with acquired non-accommodative esotropia. One patient had microtropia, one had exodeviation and another had hyperdeviation.

Statistical Methode:

Z test for difference in properties was used to explore significant difference between the groups.

P value of < o.o5 was considered significant.

Table 1 :Distribution of the study population by age and gender

sex / age	Male		Female		Total	
	No.	%	No.	%	No.	%
6-11 years	20	43.5	13	44.8	33	44
12-19 years	26	56.5	16	55.2	42	56
Total	46	100	29	100	75	100

Table 2 :Distribution of the study population by ophthalmologic abnormality detected by screening

	No.	%
Ptosis	1	1.5
Blepharitis	8	10
Strabismus= a. esotropia b. exotropia	28 26 2	37 35 3
Nystagmus	3	4
Corneal Abmormalities (keratoconus)	2	3
Iris Defects	5	6
Abnormal pupilary reaction to light	0	0
Cataract	9	12

Table 3 :Distribution of the study population By ocular features and age

	6-11 yr. (n = 33)		12-19 yr. (n = 42)		Total (n = 75)		Z value	P value
	No.	%	No.	%	No.	%		
Slanting Fissures	33	100	42	100	75	100	0	0.5
Epicanthal Folds	25	76	20	47	45	60	2.897	<0.01
Blepahritis	4	12	4	10	8	10	0.27	>0.05
Lacrimal Obstruction	12	36	10	24	22	29	1.12	>0.05
Strabismus	26	79	8	19	29	39	6.03	<0.001
Iris abnormalities	2	6	3	7	5	6	0.056	>0.05
Ambylopia:-								
1- Myopia	1	3	0	0	1	1.5	1	>0.05
2- Hyperopia	0	0	1	2	1	1.5	1	>0.05
3- Astigmatism	0	0	0	0	0	0		
4- Strabismus	0	0	2	5	2	3	1.5	>0.05
5- Cataract	1	3	1	2	2	3	0.1	>0.05
Nystagmus	1	3	2	5	3	4	0.4	>0.05
Retinal Abnormalities	1	3	3	7	4	5	0.8	>0.05

Table 4: Distribution of the gender of the study population by ocular features

	Male (n = 46)		Female (n = 29)		Total (n = 75)		Z value	P value
	No.	%	No.	%	No.	%		
Slanting fissures	46	100	29	100	75	100	0	>0.05
Epicanthal folds	30	65	15	52	45	60	1.3	>0.05
Blepharitis	15	33	8	28	23	31	0.46	>0.05
Lacrimal obstruction	15	33	7	24	22	29	1.05	>0.05
Iris abnormalities	4	9	1	3	5	7	1.13	>0.05
Ambylopic:	4	9	2	7	6	8	0.3	>0.05
1. Myopia	0	0	1	3	1	1.5	1	>0.05
2. Hyperopia	1	2	0	0	1	1.5	1	>0.05
3. Astigmatism	0	0	0	0	0	0		
4. Strabismus	2	4	0	0	2	3	1.4	>0.05
5. Cataract	1	2	1	3	2	3	0.27	>0.05
Nystagmus	3	7	0	0	3	4	0.27	>0.05
Retinal Abnormalities	3	7	1	3	4	5	1.3	>0.05

Table 5: Refractive error, fundal abnormalities of the study population

Refractive Error	Fundal Abnormalities				Total		Z value	P value
	Yes		No					
	No.	%	No.	%	No.	%		
Emmetropia	0	0	4	6	4	5	3	<0.01
Myopia	3	75	20	28	23	30	2.14	<0.05
Myopic Astigmatism	1	25	13	18	14	19	0.3	>0.05
Hyperopia	0	0	15	21	15	20	4.3	<0.001
Hyperopic Astigmatism	0	0	19	27	19	26	5.1	<0.001
Total	4	100	71	100	75	100		

Table 6: Strabismus characteristics in affected patients of the study population

	Patients	
	No.	%
Esodeviation:		
1. Congenital	4	14
2. Acquired:		
a. Refractive	12	41
b. Non refractive	10	34.5
3.Microtropic	1	3.5
4.Paralytic	0	0
Exodeviation	1	3.5
Hyperdeviation	1	3.5
Total	29	100

Table 7: Use of glasses in the study population

Type of Refractive Error	Using glasses		Total (n=75)	
	No.	%	No.	%
Myopic	8	35	23	30
Myopic astigmatism	2	14	14	19
Hyperopic	2	13	15	20
Hyperopic astigmatism	1	5	19	26

Discussion

Ocular abnormalities are common in Down's syndrome. Previous studies in affected children are few, presumably because of difficulties in obtaining an accurate visual acuity and in examining ocular structures.

Among the 75 cases represented the study population, 46 were males (61.3%). The male to female ratio is 1.6: 1. No statistical difference was found between male and female patients concerning any of the ocular features ($p > 0.05$).

Higher number of the studied cases were in the age group of 12 – 19 years 42 patints (56.5%)(Table 1). No statistical difference was found between patients in the two age groups concerning ocular findings except for epicanthal folds and strabismus (see below).

Upward slanting of palpebral fissures, the most frequent ocular finding, was present in 75 patients (100%). This is higher than the 82% found in a study of 182 patients in Brazil reported by Cunha and Moriera [4], and the same as a study done in Asia reported by Wagner [5]. This variation is presumably related to age, racial factors, measurement techniques, or to a combination of these.

We found epicanthal folds to be the second most prevalent feature (60%). This prevalence has been reported as low as 9% [4] and as high as 100%[6]. This large variation may be related to age and racial factors. Several authors have reported a decreasing prevalence with older age and a slower regression of the epicanthal folds in children with Down's syndrome compared with normal subjects[4]. However, we did find a statistical difference among patients in the two age groups being higher in patients 6-11 years old (76 %) (P < 0.03).

Blepharitis was noted in 10% of the patients in this study and was evenly distributed in all age groups. A higher percentage has been reported in Brazilian patients (30%) [4]. Catalano postulated that the high frequency of blepharitis is related to an impaired immune response [7], and Millis believed it is because of the abnormal skin of Down's syndrome individuals, which is more susceptible to infections [8].

Total or partial lacrimal drainage obstruction was observed in 22 patients (29%). Similar findings have been reported by Cunha and Moriera [4].

The occurrence of keratoconus and acute hydrops, in this disease has received little attention from ophthalmologists. Cullen and Butler reported 8 patients (5.5%) of the Down's syndrome patients examined; three of them showed the simple form of the disease, one developed acute keratoconus while under observation, and four others were thought to show the end result of such occurrence in the past (hydrops) [6]. In our study we found two patients (3%) with the simple form of the disease, (table 2). This ocular problem, although rare, constitute a chronic threat to vision in mentally retarded group already suffering from visual handicap and general sensory deprivation.

Brushfield's spots are prevalent in Down's syndrome and vary between 13% and 52% [4] of patients. With our patients Brushfield's spots and hypoplasia of the iris were observed in 5 patients (6%). Despite the use of slit-lamp biomicroscopy in 95% of patients, the prevalence of this study is lower than that in previous reports, all of which described Brushfield's spots in greater than 13% of patients. The lower prevalence in our study may be related to the higher incidence of dark irides in the Iraqi population. Cunha and Moreira found that these iris anomalies were statistically more frequent in lightly colored irides [4].

The reported prevalence of cataracts in patients with Down's syndrome (12% [9,10] to 54% [11]) varies because some investigators have included only those cataracts which would seem dense enough to cause visual difficulty, and the use of slit-lamp biomicroscopy was uncommon. Cunha and Moriera found cataract in 13% in Brazil [4]. In the present study, cataract occurred in 9 patients (12%).

Cunha and Moriera described a markedly higher number of retinal vessels crossing the margin of the optic nerve head and reported this finding in association with an unusual, spoke like appearance of the vasculature of nearly 21% of patients with Down's syndrome [4]. We found this pattern of fundal abnormality, and myopic degeneration in 4 patients (5%). Patients with fundal abnormalities had significantly higher proportion of myopia ($p < 0.05$) than patients without.

Patients without fundal abnormality had significantly higher proportion of emmetropia ($p< 0.01$), hyperopia ($p < 0.001$) and hyperopic astigmatism ($p < 0.001$). No significant difference was found between the age groups ($p > 0005$).

Marked ametropia has been associated with Down's syndrome; however, previous studies used different criteria for the definition of a refractive error. Cunha and Moriera examined 152 children with Down's syndrome between 6 and 19 years of age and found myopia in 12%. Astigmatism was the most common ametropia in their study, and was evident in 60% [4]. Gardiner examined 22 patients and found that 50% of the patients were myopic and 15% were hyperopic[12]. In our sample myopia was the most common ametropia observed (30%). Twenty percent were hyperopic and 35% of the examined patients had astigmatism; 19% myopic astigmatism, and 26% hyperopic astigmatism. Thus, compared with previous studies, we found similar prevalence of ametropia.

Strabismus has been reported to occur in 17% to 44% of patients with Down's syndrome, with most authors identifying esodeviations[4,13].In this study, the prevalence of strabismus was similar to that in previous studies (39%) of patients. Most of our patients with strabismus had an esodeviation (table 6) and of these 27 (93%) patients, 4 (14%) patients were having congenital esotropia, 12 (41%) had refractive esotropia, 10 (34.5%) had non refractive esotropia, where as microtropia observed in only one patient (1.5%). Exotropia was found in one patient (1.5%) in this study, it has been reported 1% in the study of Cunha and Castro Moreira in Brazil. Hyperdeviations have been uncommon (only 3% in their study) [4]. In this study, we observed one patient with hyperdeviation (1.5%). There was a statistical difference between patients in the two age groups being higher among age group 6-11 years (79%, $p<0.001$), the cause may be due to early detection and management attained by the parents of our sample of patients.

Nystagmus has been reported in 18% of individuals with Down's syndrome [4], where as we identified 3 patients (4%) with nystagmus (table 2), this difference may be due to the fact that the

patients examined are enrolled in a school which implies that they have relatively good vision.

Ambylopia has been seldom evaluated in Down's syndrome, despite the high prevalence of strabismus. Jaeger observed ambylopia, in 13% of children with Down's syndrome who have been examined[11]. In the present study, ambylopia was diagnosed in 6 patients (8%) of the 75 patients examined, this difference may be due to the fact that our study cases gain special care from their parents, as they attain school their vision has becoming important to them.

8 of the 23 myopic patients are using glasses, (35%), while only 2 of the 14 myopic astigmatism patients are using the glasses (14%), we have 15 hyperopic patients, only 13% are using glasses, and 19 of our patients have hyperopic astigmatism, only one of them (5%) is using the glasses. No such comparison was found in the previous studies to compare it with.

Conclusion

In conclusion, the effectiveness of the visual acuity testing methodology varied for each age group, and we concluded that the Snellen and picture Charts are useful in testing affected children. Upward slanting of the palpebral fissures and epicanthal folds were the most prevalent ocular features in Down's syndrome. We found a higher frequency of upward slanting of palpebral fissures compared with previous reports

The results of this study suggest that children with Down's syndrome may be at greater risk for visual impairment, and that they may present with ambylopia. Therefore, it is important that these children be followed and treated appropriately to minimize that risk. Also, early treatment of strabismus and high refractive errors should reduce the level of ambylopia. Because of the increased prevalence of ambylopia, frequently observed refractive errors, and other ocular disorders in youngsters with Down's syndrome it is paramount that these children undergo ophthalmologic examination early in life and be followed and treated appropriately. Normal visual acuity is important for any child. However, if the child is mentally retarded, as most individuals with Down's syndrome are, an additional handicap or sensory impairment may further limit the child's overall functioning and may prevent the child from participating in significant learning processes.

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