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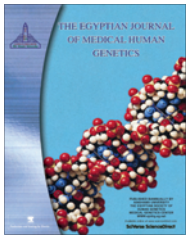

ORIGINAL ARTICLE

Ocular features in Egyptian genetically disabled children

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Abstract Ocular changes in genetically disabled children are great and of special importance. The aim of the present study was to delineate the nature and frequency of ocular defects in genetically disabled children. A cross sectional study was carried out. It included 95 genetically disabled children who were chosen from the medical genetics and ophthalmic departments, Ain-Shams University Hospitals, and examined for any associated ocular abnormalities. Studied patients were divided into six groups (Group I: Chromosomal disorders (Down syndrome), Group II: Genetic syndromes, Group III: Cranial anomalies, Group IV: Inborn errors of metabolism (IEM), Group V: Cerebral palsy, Group VI: Mental retardation). Anomalies of the eyelids were detected in 63.1% of our patients. They were significantly increased in group I [Chromosomal disorders (Down syndrome)], compared to other groups. Errors of refraction were detected in all Down syndrome patients.On the other hand some ocular findings were present in our Down syndrome patients and not reported in the literature before; these include, lacrimal fistula, lagophthalmos, heterochromia, macrocornea and ectropion in 3.3% of patients, tortous retinal vessels, entropion, and prominent upper punctum in 6.6%, ptosis in 10%, microcornea, absent foveal reflex, and blepharophimosis in 13.3% of our cases. Lacrimal apparatus abnormalities were detected in 11.5% of our patients, the highest frequency was detected among the chromosomal disorder group 27%. Conjunctival and scleral abnormalities were also detected in 10.5% of our patients, where the

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group of chromosomal disorders had the highest frequency (20%). Cornea and anterior chamber abnormalities were detected in 30.5%, these abnormalities had the same frequency (33%) in the groups of chromosomal disorders, genetic syndromes and inborn errors of metabolism. Iris and pupil abnormalities were detected in 15.7% of our patients. Lens abnormalities were detected in 10.5% of our patients, where the group of inborn errors of metabolism had the highest frequency (44%). Ocular muscles and mobility abnormalities were diagnosed in 47.3% of our patients. Fundus examination revealed abnormalities in 34.7% of patients,where the group of cerebral palsy had the highest frequency (50%).Our results emphasize that, the earlier and better the visual sense function, the greater the chance the child will achieve his potential.The ophthalmologist, paediatricians, geneticists must work hand in hand for detection of ocular disorders in genetically disabled children to initiate diagnostic and therapeutic measures to control the disease.

1. Introduction

Handicap and disability are used as synonym but they aren't [1]. The term ''disabled people'' as a political construction is widely used by international organisations of disabled people, such as Disabled Peoples' International (DPI) [2]. Disability, according to the World Health Organization [3], is defined as ''. . .an umbrella term, covering impairments, activity limitations, and participation restrictions''. According to the adopted UN Convention on the rights of persons with disabilities [4], persons with disabilities include those who have long-term physical, mental, intellectual or sensory impairments which, in interaction with various barriers, may hinder their full and effective participation in society on an equal basis with others [5].

Children may be considered to be handicapped, if, mentally or physically, they lag behind their contemporaries, or if they require special care, or if they have to make special adjustments in educational, emotional or social spheres. Whatever definition is used there will always be a number of borderline cases [6]. Some people with disabilities do not like the term ''handicap'' because of a belief that it originally meant someone who could not work and went begging with their cap in hand. This, appears to not be the true origin of the word. However, the term ''disabled people'' is generally preferred to ''people with disabilities'' [7].

In one survey, it was shown that 21.9% of cases of disability resulted from prenatal damage; 3.0% arose from perinatal factors; 29.0% were acquired during infancy and early childhood and 47.0% had no known cause [8].

The field of genetics has important implications for people with disability. Although only a limited number of national surveys have been conducted to identify the etiological factors in the development of disability, it is generally believed that 76% of disability is caused by genetic factors [9]. Genetic causes of disability may be due to chromosomal abnormalities which can involve the loss, gain, or exchange of genetic material from a chromosome pair. Such abnormalities often cause miscarriages, but may occasionally result in a baby with some kind of disability as Down syndrome. Also disabilities may be caused by specific genes that create damaging biomedical conditions [10]. There are over 3000 different genetic causes of disability. There are definite patterns of inheritance which govern whether or not various traits affect us. The most prevalent genetic conditions include Down syndrome, Klinefelter's syndrome, Fragile X syndrome, Neurofibromatosis, congenital hypothyroidism, Williams syndrome, Phenylketonuria (PKU), and Prader–Willi syndrome. Other genetic conditions include Phelan–McDermid syndrome (22q13del), Mowat–Wilson syndrome, genetic ciliopathy, and Siderius type X-linked mental retardation as caused by mutations in the PHF8 gene [11].

The number of children and adolescents with disability is significant. Two hundred million children, meaning 10% of the world's youth, are born with a disability or become disabled before the age of 18 [12]. The average percentage of people with disabilities in Egypt is 10%, that means we have around 7 million disabled people in Egypt, or 10% of the population. According to data available, more than 5% of children have significant disabilities. However accurate figures are hard to come because families are reluctant to disclose information about disabled members of their household. ''Many Egyptian families hide their disabled children so that even their neighbours are not aware of them'' [13].

Eyes are the most precious gift of God – they act as our window to the world. So it is important to take due care of eyes during the development of the child. A visual impairment occurs when any part of the optical system is defective, diseased, or malfunctions. If the visual impairment is the result of a defective part (or parts), it is usually present at birth (congenital). These include missing parts (e.g., absence of an iris; absence of the eyes themselves), defective systems (e.g., dislocation of the lens; holes in the retina; drainage systems that are stopped up), and hereditary conditions (e.g., refractive errors due to eyeballs that are too short or too long; improperly shaped corneas; albinism) [14]. Diseases can be pre-natal (e.g., insult to the fetus in utero), at birth or post natal (e.g., damage shortly thereafter), or adventitious (acquired later) (e.g., diseases that develop gradually such as diabetes and some types of retinal diseases). Malfunctions can be due to defective parts or, secondarily, to body diseases such as rubella. There are hundreds of eye problems (and combinations of problems) located in the optical system itself. The eye specialist (ophthalmologist/optometrist) is qualified to identify or diagnose these problems [15].

Ocular changes in genetically disabled children are great and of special importance for the clinician during the diagnostic process.

The objective of the present study is to delineate the nature and frequency of ocular defects in genetically disabled children.

2. Patients and methods

A cross sectional hospital based study was carried out through a period of 2 years. The study included 95 genetically disabled

children who were randomly chosen from the medical genetics and ophthalmic departments, Ain-Shams University Hospitals, and examined for any associated ocular abnormalities. The patients were 57 males and 38 females. Their age ranged from 2 to 13 years (mean age 6.75 ± 3.26 years). For all the patients, the following was done:

1. Detailed history including, age, sex, prenatal history: particulary in relation to maternal and paternal ages at time of conception, maternal health, exposure to infections, teratogenic drugs and radiation, complications of pregnancy as toxaemia and bleeding, pregnancy loss (abortion or still births), and neonatal death.
2. A three generation pedigree, with special attention to the presence of similar cases in the family, birth order and, consanguinity.
3. Thorough clinical examination including, complete examination of special organs of importance, detection of malformations and congenital anomalies anywhere in the body, in addition to anthropometric studies to all patients were done.
4. Ophthalmologic examination including, visual acuity testing, ocular motility and examination of the external eye and anterior segment, cycloplegic refraction and fundus examination to comment on. Iris was looked for colour, pattern defect, and adhesions to the position, mobility, swellings, lid margin, direction of palpebral fissure and width. Examination of the lacrimal system for lacrimal gland and drainage system. Examination of the conjunctiva for discharge, vascular engorgement, chemosis, mass, adhesions, dryness and change of colour, nodules and pigmentations. The cornea was examined by oblique illumination and by slit lamp in indicated cases when it is possible, for diameter, curvature, transparency, lustre, vascularity and irregularity of the surface. Anterior chamber was examined by oblique illumination and by slit lamp in indicated cases when it is possible, for depth, clarity and abnormal contents of anterior chamber. Lens was examined after dilatation of pupils by slit lamp for any opacity (cataract) and for position (sublaxation, dislocation). Measurement of I.O.P. under general anesthesia with Schiotz tonometer in suspected cases.
5. Radiological examination as plain X-ray of the skull, chest and heart, and skeletal survey. Echocardiography, Ultrasonography (abdominal and ocular), brain C.T.

Table 1 Etiological classification of genetically disabled children.

Aetiology	No.	%
Genetic diseases		
Group I: Chromosomal disorders (Down syndrome)	30	31.6
Group II: Genetic syndromes	21	22.1
Group III: Cranial anomalies	19	20.0
Group IV: Inborn errors of metabolism (IEM)	9	9.5
Group V: Cerebral palsy	10	10.5
Group VI: Mental retardation	6	6.3
Total	95	100

6. Biochemical tests: which include, aminogram and qualitative and quantitative detection of glycosaminoglycans.
7. Laboratory investigations: Complete blood picture, screening for STORCH infections and karyotype in suspected chromosomal disorders.
8. Instrumental investigations: Audiometry when deafness was expected. Electroencephalogram (E.E.G.) and Electroretinogram (E.R.G.).

3. Results

3.1. Studied patients were divided into six groups (Table 1 and Fig. 1)

The highest frequency was found among the chromosomal disorder group, followed in descending order by genetic syndromes, cranial anomalies, inborn errors of metabolism, cerebral palsy and mental retardation. There was no significant difference as regards age, sex and parental consanguinity between the studied groups ($P < 0.05$) (Table 2).

3.2. As regards the maternal age at birth in all groups

It was observed that the group of mental retardation (group VI) had the highest mean maternal age (42.83 ± 1.83 years), and the group of cerebral palsy (group V) had the lowest mean

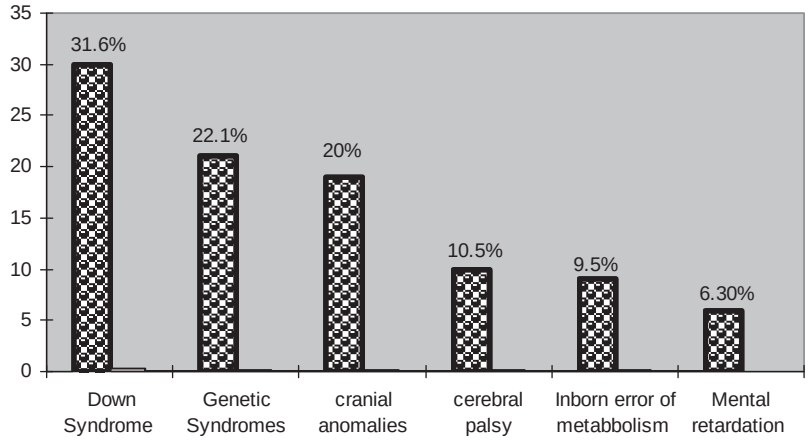

Figure 1 Etiological classification of handicapped children.

Table 2 Demographic characteristics of the examined patients, (95 patients).

Variable	Group I (30)		Group II (21)		Group III (19)		Group IV (9)		Group V (10)		Group VI (6)		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Sex: Males	20	67	11	52	11	58	6	67	6	60	3	50	57	60.0
Positive family history	3	10	6	29	5	26	4	44	0	0	2	33	20	21.0
Positive consanguinity	11	37	6	29	4	21	4	44	3	30	4	67	32	33.6
Positive complications during pregnancy[a]	7	23	3	14	1	5	1	11	6	60	2	33	20	21.0

[a] Hypertension, bleeding and trauma.

maternal age (28.90 ± 5.13). The highest mean paternal age was observed in the group of mental retardation (group VI) (42.83 ± 1.83 years), while the group of inborn errors of metabolism had the lowest mean paternal age (30.56 ± 7.49 years).

3.3. Ophthalmic examination of our patients (Tables 3–9)

3.3.1. Anomalies of the eyelids were detected in 60 of our patients (63.1%)

They were significantly increased ($P < 0.05$) in group I [chromosomal group (Down syndrome)] compared to other groups and 70% of Down patients had more than one eyelid anomaly.

3.3.2. As regards the lacrimal apparatus, 11 patients (11.5%) had lacrimal apparatus abnormalities

The highest frequency was detected among the chromosomal disorder group (8 patients, 27%), followed by the group of genetic syndromes ($P < 0.05$).

3.3.3. Conjunctival and scleral abnormalities were presented in 10 of our patients (10.5%)

The group of chromosomal disorders had the highest frequency (20%), followed by the group of genetic syndromes (10%) ($P < 0.05$).

3.3.4. Cornea and anterior chamber abnormalities were detected in 29 patients (30.5%)

The groups of chromosomal disorders, genetic syndromes and inborn error of metabolism had the same frequency (33%), followed by the group of cerebral palsy (30%). When each group is compared with the other as regards these anomalies, it was observed that the difference was statistically insignificant.

3.3.5. Iris and pupil abnormalities were found in 15 patients (15.7%)

The highest frequency was detected among the group of chromosomal disorders (8 patients, 27%) and the group of cranial anomalies (5 cases, 26%).The difference between our groups was statistically insignificant.

3.3.6. Lens abnormalities were noticed in 10 patients (10.5%)

Group IV of inborn error of metabolism had the highest frequency (44%), followed by the group of genetic syndromes (14%) and the difference between them was statistically significant ($P < 0.05$).

3.3.7. Ocular muscles and mobility abnormalities were diagnosed in 45 patients (47.3%)

The group of genetic syndromes and the group of cerebral palsy had the highest frequency (62% and 50%) respectively and the difference between the two groups was statistically insignificant.

3.3.8. Fundus examination revealed abnormalities in 33 patients (34.7%)

The group of cerebral palsy had the highest frequency (50%), followed by the group of cranial anomalies (42%) and the difference between the two groups was statistically insignificant.

3.3.9. Errors of refraction were detected in 42 patients (44.2%)

They were significantly increased in group I (chromosomal group, 63%) compared to other groups. Twenty percent of Down syndrome patients had more than one error of refraction.

4. Discussion

It can be difficult to assess visual fields in young children or in those whose development has been delayed, but this should be attempted [16]. The eyes can yield many clues for diagnosis of many genetic diseases, so as far as possible, every patient should do full ophthalmologic examination [17].

The most obvious ophthalmologic observation on first seeing the patient is that he or she is wearing thick spectacles. Deterioration in vision accompanied by personality change, intellectual deterioration or motor difficulties is very ominous and requires urgent further investigation. In these circumstances, fundal examination and examination of eye movements may reveal clues as to the aetiology of the disorder [18]. Our findings in this study focused on ocular features of genetically disabled children, they revealed that many genetic diseases are associated with ocular manifestations, some of them are obvious enough to be identified in any careful general examination, others may require consultation of an ophthalmologist. Many of these signs are not specifically pathognomonic, but, even so, they can often help to differentiate [19].

Ophthalmological anomalies are common in children with Down's syndrome. In the present study, Down syndrome represents 31.6% of our cases. In our patients ophthalmologic features were; upward slanting of palpebral fissure in 76.6% of cases, epicanthus of the eye lid in 26.6%, Brushfield's spots in 23.3%, nasolacrimal duct obstruction in 16.6%, microcornea, blepharophimosis and absent foveal reflex were detected in 13.3%, ptosis, chronic conjunctivitis and hypoplastic optic

Table 3 Ocular and visual defects among genetically disabled children.

Eye problems	Group I		Group II		Group III		Group IV		Group V		Group VI		Total %	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Eye lid abnormalities positive	28	93	11	52	7	37	4	44	6	60	4	67	60	63.1
Lacrimal apparatus abnormalities positive	8	27	3	14	0	0	0	0	0	0	0	0	11	11.5
Conjunctival and scleral abnormalities positive	6	20	2	10	1	5	0	0	0	0	1	17	10	10.5
Cornea and anterior chamber abnormalities positive	10	33	7	33	5	26	3	33	3	30	1	17	29	30.5
Iris and pupil abnormalities positive	8	27	1	5	5	26	1	11	0	0	0	0	15	15.7
Lens abnormalities positive	3	10	3	14	0	0	4	44	0	0	0	0	10	10.5
Ocular muscles and mobility abnormalities positive	13	43	13	62	9	47	4	44	5	50	1	17	45	47.3
Fundus abnormalities positive	10	33	7	33	8	42	2	22	5	50	1	17	33	34.7
Errors of refraction positive	19	63	10	48	7	37	2	22	3	30	1	17	42	44.2

disc were found in 10%, while entropion, congenital cataract, and hypopigmented fundus were detected in 6.6%, errors of refraction were detected in all of our patients (100%) as myopia in 36.7%, astigmatism in 33.3% and hypermetropia in 30% of cases. These findings were closely related to that reported previously in patients with Down syndrome [20–24]. Unlike previous reports [25–28] no congenital glaucoma, blepharitis, amblyopia, epiblepharon, keratoconus, and ganglionic neuroretinal hypoplasia were detected in Egyptian Down syndrome patients. On the other hand some ocular findings were present in our patients and to our knowledge not reported in the literature. These include, lacrimal fistula, lagophthalmos, heterochromia, macrocornea and ectropion in 3.3% of patients, tortous retinal vessels, entropion, and prominent upper punctum in 6.6%, ptosis in 10%, microcornea, absent foveal reflex, and blepharophimosis in 13.3% of cases. Creavin and Brown [29] performed a comprehensive review of the available literature to determine the common ophthalmic disorders in children aged 0–16 years with Down syndrome. They found that refractive errors was a common finding particulary hyperopia. Strabismus was also reported particulary esodeviation. Other frequent findings include poor visual acuity, nystagmus and blepharitis, whereas cataract and glaucoma were less common but had potentially serious implications for future vision. The UK Down's Syndrome Medical Interest group (DSMIG) guidelines for ophthalmic screening were locally implemented a protocol that include neonatal eye examination by an ophthalmologist and a comprehensive ophthalmological examination (cycloplegic refraction, ophthalmoscopy, and orthoptic assessment) by at least the age of 3 years. This will be anticipated to improve developmental and functional outcome in Down syndrome [30]. Some authors argue that the characteristic traits of Down's syndrome result from a combination of gene dosage effects as a result of extra copies of genes on chromosome 21 [31]. Variability in the ocular features of Down's syndrome could relate to polymorphism in these genes [32].

Others believe that the extra chromosomal material causes a generalized disruption in the genetic balance of cells. From this viewpoint non-specific developmental instability following aneuploidy accounts for ocular anomalies in Down's syndrome.

Rubinstein–Taybi syndrome represented 19% of patients of group II in our study. The most common ocular findings detected among these patients include, antimongoloid slant and hypertelorism in 75%, long eye lashes in 50%, epicanthus, astigmatism, macrocornea and glaucoma were observed in 25%, while more than one ocular anomaly was detected in 100% of cases. Our findings were nearly similar to what was previously reported that the main features that allow for diagnosis of Rubinstein–Taybi syndrome are congenital or juvenile glaucoma, ptosis of eyelids and refractive errors [33]. Unlike to what reported by van Genderen et al. [34], no nasolacrimal duct problems, cataract, coloboma, nystagmus, corneal and retinal abnormalities were detected in our patients. Quaranta and Quaranta [35], emphasized the importance of detailed, complete ocular examinations in patients with Rubinstein–Taybi syndrome, and also highlights that ocular abnormalities are rarely associated with this disease.

Crouzen syndrome is an autosomal dominant disorder with complete penetrance and variable expressivity. Gene locus has been mapped to chromosome 10q26 [36]. It is characterized by premature closure of calvarial and cranial base sutures as well as those of the orbit and maxillary complex (craniosynostosis) [37]. This disorder, accounts for approximately 4.5% of all cases of craniosynostosis [38]. In our study Crouzen syndrome represented 19% of patients of group II. The most common ocular findings in our cases were hypertelorism, which was present in all patients, followed by divergent squint and proptosis which were found in 50% of cases. Optic atrophy, papilloedema, antimongoloid slant were diagnosed in 25% of cases. These findings were similar to what reported by Ernest and Fernando [39]. Additionally, Hoefkens et al. [40] reported that, nystagmus, iris coloboma, aniridia, anisocoria, microcornea, megalocornea, cataract, ectopia lentis, blue sclera, glaucoma, luxation of the eye globes rarely occur among patients with Crouzen syndrome.

Hallermann–Streiff syndrome is a rare syndrome, which involves multiple congenital abnormalities affecting chiefly the

Table 4 Ocular signs detected among patients with Down syndromes (30/95 – 31.6%).

Variable	No.	%
Eye lid		
Upward slanting	23	76.6
Epicanthus	8	26.6
Blepharophimosis	4	13.3
Ectropion	1	3.3
Ptosis	3	10.0
Entropion	2	6.6
More than one anomaly	21	70.0
Lacrimal apparatus		
Lagophthalmos	1	3.3
N.L.D.[a] obstruction	5	16.6
Lacrimal fistula	1	3.3
Prominent upper punctum	2	6.6
Conjunctiva		
Chronic conjunctivitis	3	10.0
Cornea and anterior chamber		
Corneal opacity	2	6.6
Macrocornea	1	3.3
Microcornea	4	13.3
Iris		
Heterochromia	1	3.3
Brushfield's spot	7	23.3
Lens		
Congenital cataract	2	6.6
Ocular motility		
Nystagmus	9	30.0
Alt. convergent squint	1	3.3
Unilateral convergence	2	6.6
Fundus		
Absent foveal reflex	4	13.3
Hypoplastic optic disc	3	10.0
Tortous retinal vessels	2	6.6
Hypopigmented fundus	2	6.6
Errors of refraction		
Myopia	11	36.7
Hypermetropia	9	30.0
Astigmatism	10	33.3
More than one anomaly	6	20.0

[a] Naso lacrimal duct.

head and face. Virtually all cases are sporadic and thus there is no obvious pattern of inheritance. The most likely hypothesis is that of a single mutant gene (dominant) with most cases representing fresh mutations. A defect of elastin and abnormal glycoprotein metabolism has been reported [41]. This syndrome was found in two cases of our patients and it accounts for 9.5% of cases of group II, the most common ocular features detected were nystagmus, cataract and microphthalmia in all patients (100%), followed by antimongoloids slanting, blepharophimosis and divergent squint in 50% of cases. These findings come in agreement with other authors [42,43]. Myung et al. [44] experienced a case of Hallermann–Streiff syndrome in a 6 year old female with bilateral microphthalmia and congenital cataract. She also showed pinhole pupil, strabismus and aphakia, which is considered a rare ocular sign in Hallermann–Streiff syndrome. Other ocular findings that were reported [45] in Hallermann–Streiff syndrome but not found in our study include, blue sclera, posterior synechia, aphakia, and secondary glaucoma.

Bardet–Biedle syndrome is a multi-system autosomal recessive disorder [46]. In our study it represented 23.8% of patients of group II, retinitis pigmentosa was the commonest ocular sign detected among 80% of our patients. Other ocular findings detected in our patients include, nystagmus in 60%, pale optic disc and hypermetropia in 40%, bilateral persistent hyaloid system, attenuated retinal blood vessels and astigmatism in 20%. Nearly, similar findings were previously reported [47–49]. However unlike to what was previously reported by Hrynchak [50] glaucoma and cataract were not detected among our patients. On the other hand and to our knowledge, bilateral persistent hyaloids system which was found in one of our patients was not previously reported.

Noonan syndrome is a clinically heterogeneous condition. Genetic investigations have identified mutations in several genes. It is estimated that these mutations can explain approximately 60% of patients with Noonan syndrome [51]. In our study Noonan syndrome was detected in 4.7% of patients of group II. Ocular findings of our patient include, blepharophimosis, microphthalmia, alternating divergent squint and congenital cataract. Shaw et al. [52] reported that the characteristic facial features of Noonan syndrome include hypertelorism (74%), epicanthal folds (39%), down-slanting palpebral fissures (38%), ptosis (48%), strabismus (48%), refractive errors (61%), amblyopia (33%), nystagmus (9%), cataracts, uveitis and retinal findings (20%), as well as less common findings of optic disc hypoplasia, coloboma, and keratoconus. Ptosis associated with Noonan syndrome has been described by many authors [53,54]. Most of the previous findings were not reported in our patients.

Robinow syndrome is a severe skeletal malformation syndrome that also affects other organs and has characteristic facial features which, include macrocephaly, broad prominent forehead, ocular hypertelorism, prominent eyes and midface hypoplasia [55]. Robinow syndrome is rare syndrome [56]. It was described in 4.7% among our patients of group II. Ocular signs observed in our patient were, hypertelorism, antimongoloid slanting of palpebral fissure and macrocornea. Many authors described similar ocular findings [57–59].

Prader–Willi syndrome is the result of missing or abnormal genetic material on the paternally contributed chromosome 15 [60]. In people of all ethnic backgrounds Prader–Willi syndrome is usually diagnosed by the appearance and behaviors of a child, then confirmed by specialized genetic testing of a blood sample [61]. In our study Prader–Willi syndrome was diagnosed in one patient (4.7%), his ocular manifestations include upward slant, partial synophrys and alternating divergent squint. Libov and Maino [62] reported other ocular findings for patients with Prader–Willi syndrome which include iris hypopigmentation with depressed visual acuity, moderate to high refractive errors, strabismus, cataracts, congenital ocular fibrosis syndrome, diabetic retinopathy, and congenital ectropion uveal. The numerous ocular, systemic, and functional abnormalities of patients with Prader–Willi syndrome make it mandatory that all patients should routinely receive primary optometric vision care.

Neurofibromatosis (NF) is a collective name for a group of three genetically distinct but related disorders in which benign

Table 5 Ocular manifestations in the group of genetic syndromes (21/95 – 22.1%).

Syndrome	Eye problems	No.	%
Rubinstein–Taybi		4	19.0
	Antimongoloid slanting	3	75.0
	Hypertelorism	3	75.0
	Long eyelashes	2	50.0
	Epicanthus	1	25.0
	Hypermetropia	2	50.0
	Astigmatism	1	25.0
	Macrocornea	1	25.0
	Glaucoma	1	25.0
	More than one anomaly	4	100.0
Bardet–Biedle syndrome		5	23.8
	Retinitis pigmentosa	4	80.0
	Bilateral persistent hyaloids system	1	20.0
	Attenuated retinal B.V.	1	20.0
	Pale optic disc	2	40.0
	Nystagmus	3	60.0
	Divergent squint	1	20.0
	Hypermetropia	2	40.0
	Astigmatism	1	20.0
	More than one anomaly	5	100.0
Neurofibromatosis		1	4.7
	Lid neuroma	1	100.0
	Ptosis	1	100.0
	Proptosis	1	100.0
	More than one anomaly	1	100.0
Hallermann–Streiff		2	9.5
	Antimongoloid slanting	1	50.0
	Microphthalmia	2	100.0
	Nystagmus	2	100.0
	Cataract	2	100.0
	Blepharophimosis	1	50.0
	Divergent squint	1	50.0
Robinow syndrome		1	4.7
	Hypertelorism	1	100.0
	Antimongoloid slanting	1	100.0
	Macrocornea	1	100.0
	More than one anomaly	1	100.0
Prader–Willi syndrome		1	4.7
	Upward slant	1	100.0
	Partial synophrys	1	100.0
	Alternating divergent squint	1	100.0
Noonan syndrome		1	4.7
	Blepharophimosis	1	100.0
	Microphthalmia	1	100.0
	Alternating divergent squint	1	100.0
	Congenital cataract	1	100.0
	More than one anomaly	1	100.0
Crouzen syndrome		4	19.0
	Hypertelorism	4	100.0
	Proptosis	2	50.0
	Divergent squint	2	50.0
	Optic atrophy	1	25.0
	Papilloedema	1	25.0
	Antimongoloid slanting	1	25.0
	More than one anomaly	4	100.0
Sturge–Weber syndrome		2	9.5
	Lid-haemangioma	2	100.0
	Glaucoma	2	100.0
	Nystagmus	2	100.0
	More than one anomaly	2	100.0

Table 6 Ocular signs detected among patients with cranial anomalies (19/95 – 20%).

Aetiology	No.	%
Osteopetrosis	2	10.5
Macrocornea	1	5.2
Pin-pointed pupil	1	5.2
Nystagmus	2	10.5
Optic atrophy	1	5.2
Papilloedema	1	5.2
More than one anomaly	2	10.5
Microcephaly	5	26.3
Alternating divergent squint	2	10.5
Hypermetropia	1	5.2
Astigmatism	2	10.5
Myopia	2	10.5
More than one anomaly	3	15.7
Congenital hydrocephalus	10	52.6
Blepharophimosis	1	5.2
Microcornea	1	5.2
Antimongoloid slanting	1	5.2
Upward slanting	2	10.5
Sun set appearance	7	36.8
Papilloedema	4	21.0
Optic atrophy	6	31.5
More than one anomaly	8	42.1
Craniosynostosis	2	10.5
Macrocornea	1	5.2
Optic atrophy	2	10.5
Strabismus	1	5.2
More than one anomaly	2	10.5

Table 7 Ocular signs among patients with cerebral palsy (10/95 – 10.5%).

Anomaly	No.	%
Antimongoloid slanting	2	20.0
Epicanthus	2	20.0
Errors of refraction	2	20.0
Hypertelorism	1	10.0
Macrocornea	2	20.0
Nystagmus	1	10.0
Bilateral alternating convergent squint	2	20.0
Apparent convergent squint	2	20.0
Abnormal retinal pigmentation	2	20.0
Tortous retinal vessels	2	20.0
Wide optic pit	1	10.0
Absent foveal reflex	1	10.0
More than one anomaly	8	80.0

(non-cancerous) growths or tumours affect the nervous systems. They are neurofibromatosis 1 – or peripheral neurofibromatosis, neurofibromatosis 2 – or central neurofibromatosis and schwannomatosis which is a rare type that produces multiple benign tumors in the Schwann cells of peripheral nerves [63]. One case of neurofibromatosis (NF1) was included in our study representing 4.7% of patients of group II. Lid neuroma, ptosis and proptosis were observed in this patient. Many literature [64,65] reported similar ocular signs of NF1. Unlike to what was reported by Destro et al., [66] iris (Lisch) nodules, congenital glaucoma, plexiform neurofibromas of the eyelids, uveal hamartomas, and retinal lesions were not detected in our patient.

Table 8 Ocular signs detected among patients with inborn errors of metabolism (9/95 – 9.5%).

Aetiology	No.	%
Galactosemia	4	44.4
Cataract	4	44.4
Nystagmus	2	22.2
Blepharophimosis	1	11.1
Microphthalmia	1	11.1
More than one anomaly	3	33.3
Mucopolysaccharidosis	5	55.5
Puffiness of eyelids	3	33.3
Cloudy cornea	4	44.4
Nystagmus	1	11.1
Optic atrophy	1	11.1
More than one anomaly	4	44.4

Table 9 Ocular signs among the mental retardation group (6/95 – 6.3%).

Anomaly	No.	%
Antimongoloid slanting	1	16.6
Blepharophimosis	1	16.6
Greyish discolouration of eyelashes	1	16.6
Long eyelashes	1	16.6
Alternating convergent squint	2	33.3
Congenital tortous vessels	1	16.6
More than one anomaly	0	0

Sturge–Weber syndrome (SWS) belongs to a group of disorders collectively known as the phakomatoses (''mother-spot'' diseases). It consists of congenital hamartomatous malformations that may affect the eye, skin, and CNS at different times [67]. It was diagnosed in two cases of our patients (9.5%), ocular findings include lid-haemangioma, glaucoma and nystagmus. Cheng [68] reported closely similar findings.

Ocular signs detected among our patients with cranial anomalies differ according to the type of anomaly. Osteopetrosis has been diagnosed in 10.5% of our study group. They represented ophthalmologically with macrocornea in 5.2%, optic atrophy in 5.2%, papilloedema in 5.2%, nystagmus in 10.5%, pin pointed pupils in 5.2%. Many studies are in agreement with our findings [69,70]. On the other hand, exophthalmos and impaired extraocular muscle function which were, previously reported [71] as ocular signs of osteopetrosis were not observed in our patients.

Craniosynostosis was diagnosed in 10.5% of our patients. The ocular manifestation recorded were, macrocornea in 5.2%, optic atrophy in 10.5%, strabismus in 5.2%. Baranello et al. [72] reported similar ocular findings. However, in a retrospective review by Khan et al. [73] of 141 cases of syndromic craniosynostosis 40.3% of patients had astigmatism, anisometropia was detected in 18%, horizontal strabismus was found in 70% (38% exotropia, 32% esotropia), 39.8% of their patients had visual acuity of 6/12 or worse in their better eye, which means that refractive errors are common. On the other hand, macrocornea which was observed in our patients was not mentioned before. The ocular aspects of craniosynostosis

may be considered in terms of detection and prevention of visual loss, ocular motility problems, binocular vision, lacrimal duct problems and miscellaneous ocular problems [74].

Microcephaly is defined as a head circumference >3 standard deviations below mean for age and gender. It is a sign of a small brain (micrencephaly), and affected children usually have some degree of neurologic impairment [75]. It was diagnosed in 26.3% of our patients of group III, ocular manifestations include, alternating divergent squint in 10.5%, hypermetropia in 5.2%, astigmatism in 10.5%, myopia in10.5%, while more than one anomaly was detected in 15.7%. Similar findings were previously reported [76].

Congenital hydrocephalus is caused by a complex interaction of genetic and environment factors. Aqueductal stenosis (narrowing) is the most frequent cause. Blockage of fourth ventricle outlet (Dandy–Walker syndrome) or Chiari malformations (in association with Spina Bifida) are other common causes [77]. Congenital hydrocephalus was diagnosed in 10 cases (52.6%) of our patients of group III, ocular manifestation detected were blepharophimosis, microcornea and antimongoloid slant of palpebral fissure in 5.2% of patients, upward slant in 10.5%, sunset appearance in 36.8%, papilloedema in 21%, optic atrophy in 31.5% and more than one anomaly was detected in 42.1%. Some reports are in agreement to our results [78,79]. However, microcornea, antimongoloid slant and upward slant of palpebral fissure reported in our study were not mentioned before.

Cerebral palsy was diagnosed in 10.5% of our patients. In our study ocular signs include, antimongoloid slanting, epicanthus, errors of refraction, macrocornea, abnormal retinal pigmentation and tortous retinal vessels, each in 20% of cases. Nystagmus, foveal reflex, and wide optic pit in 10% of our patients, while strabismus was detected in 40%. A series of articles mentioned closely similar findings [80–84]. On the other hand, wide optic pit, which was detected in our patients, was not mentioned before.

Our study also comprised four cases of galactosemia, representing (44.5%) of patients in group IV. Cataract was noticed in 44.4% of patients, while nystagmus, blepharophimosis and microphthalmia were less frequent (22.2%). As regards cataract our results are nearly similar to what was reported previously [85,86]. Cuthbert et al. [87] mentioned that cataracts was reported in 30% of 314 individuals with galactosemia. On the other hand Hadeel et al. [88], reported a case of classic galactosemia that presented with a rare ocular finding, Peters' anomaly.

Hurler syndrome is a type of mucopolysaccharidosis called MPS I. It is the most severe type and it is categorized as MPS I H [89]. It has been diagnosed in five cases in our study, representing (55.5%) of group IV. Puffy eyelids was observed in 33.3% of cases, cloudy cornea in 44.4% of patients, while nystagmus and optic atrophy were noticed in 11.1% of the cases. In another Egyptian study, Shawky et al. [90] reported corneal clouding and early optic atrophy in 5.6% of patients with MPS type I. Other authors [91,92] reported that ocular manifestations of Hurler syndrome include, corneal clouding, pigmentary retinopathy, optic atrophy and glaucoma. In patients with MPS ophthalmological examination, including slit-lamp, fundus examination and regular measurement of the intraocular pressure, are necessary for the early detection and management of potential complications.

Mental retardation is a condition diagnosed before the age of 18 years that includes below-average general intellectual function, and a lack of the skills necessary for daily living. Mental retardation (MR) affects about 1–3% of the population [93]. Defects that may lead to mental retardation involve a lesion or lesions in the central nervous system (CNS) of diverse etiology, including genetic, nutritional, infectious, toxic and traumatic brain disorders [94]. The prevalence of visual and ocular disorders in children with MR is high, and can influence sensory-motor development and learning ability [95]. It constitutes a major problem in Egypt because it affects the quality of life of persons and the welfare of their families. Temtamy et al. [96] reported that the prevalence of mental retardation was 3.9% among an Egyptian population in Assuit Governorate. Although, we could not determine the direct etiology of mental retardation in 6.3% of cases in this study. We studied the most appropriate pre and post-natal abnormalities and associated developmental major signs in all cases for probable further evaluation. Ocular manifestation detected among them were, antimongoloid slanting, blepharophimosis, greyish discolouration of eye lashes, long eye lashes and congenital tortous retinal vessels in (16.6%) of cases, while alternating convergent squint was detected in 33.3% of the patients. The prevalence of strabismus among individuals with mental retardation was more than that reported in various studies in different populations which have shown a prevalence of 1–5% for strabismus in the general population [97].

5. Conclusion

On the whole, the most effective way to combat genetic disorders is through medical research. Currently, research in the molecular and cell biology of the eye holds promise for more effective management of heritable eye disorders and provides hope for therapy and, ultimately, cure for some genetic disorders.

As vision is the most important sense for general development and education. The earlier and better the visual sense function, the greater the chance the child has achieved his potential. The ophthalmologist, paediatricians, geneticists must work hand in hand for detection of ocular disorders in genetically disabled children to initiate diagnostic and therapeutic measures to control the disease. The results also emphasize the need for establishing an efficient system to provide regular ophthalmic care for genetically disable children.

References

[1] http://www.asphi.it – projects for handicap in relation to Information and Communication. Technologies. <http://www.tesionline.it/_>.
[2] Carmelo M, Donatella RP. From disablement to enablement: conceptual models of disability in the 20th century. Disabil Rehabil 2008;30(17):1233–44.
[3] World Health Organisation. Disabilities. <http://www.who.int/topics/disabilities/en/> [retrieved 2010].
[4] Australian Human Rights Commission. Who is protected by the DDA? <http://www.hreoc.gov.au/disability_rights/faq/Who_is_protected_/who_is_protected_.html> [retrieved 2010].
[5] http://www.iddc.org.uk/joomla/images/.../excom2010_ngo_lobby_doc_final.doc.

[6] Evans P. Aspects of the integration of handicapped and disadvantaged students into education. Evidence from quantitative and qualitative data. Paris: OECD/CERI; 2003. < http://www.snopes.com/ > .
[7] Virtanen M, Kivimaki M, Vahtera J, Elovainio M, Sund R, Virtanen P, et al. Sickness absence as a risk factor for job termination, unemployment, and disability pension among temporary and permanent employees. Occup Environ Med 2006;63(3):212–7.
[8] El-Hazmi MAF. Early recognition and intervention for prevention of disability and its complications. Eastern Med Health J 1997;3(1):154–61.
[9] El-Hazmi MAF. Genetic counselling theory and practice. In: Proceedings of the symposium on medical genetics in the setting of the Middle Eastern population. Riyadh: KACST Press; 1995. p. 243–8.
[10] Bennett JW. A primer in genetics. In: Abroms KI, Bennett JW, editors. Genetics and exceptional children. San Francisco: Jossey-Bass Inc.; 1981. p. 3–19.
[11] Laumonnier F, Holbert S, Ronce N, et al. Mutations in PHF8 are associated with X linked mental retardation and cleft lip/cleft palate. J Med Genet 2005(10):780–6.
[12] David J. An introduction to disability studies. 2nd ed.; 2001. ISBN: 1-85346-726-X.
[13] Gilbar R. Communicating genetic information in the family: the familial relationship as the forgotten factor. J Med Ethics 2007;33(7):390–3.
14 Holbrook C. Children with visual impairments: a parent's guide. Bethesda, MD: Woodbine House Inc.; 1996.
[15] Virginia EB. Preschool children with visual impairments. Written in collaboration with REGION XIII. EDUCATION SERVICE CENTER; 1991.
[16] Jugnoo SR. Examination of a child with visual loss. Community Eye Health 1998;11(27):36–8.
[17] Jones K. Smith's recognizable patterns of human malformation. 5th ed. Philadelphia, PA: WB Saunders; 1997.
[18] Dooley JM. The pediatric neurologic examination. In: Goldbloom RB, editor. Pediatric clinical skills. Philadelphia, PA: Churchill Livingstone; 1997. p. 223–44.
[19] Francois J. The significance of genetic research in ophthalmology. Birth Defects Orig Artic Ser 1982;18(6):3–25.
[20] Fimiani F, Iovine A, Carelli R, Pansini M, Sebastio G, Magli A. Incidence of ocular pathologies in Italian children with Down syndrome. Eur J Ophthalmol 2007;17(5):817–22.
[21] Haugen OH, Høvding G, Riise R. Ocular changes in Down syndrome. Tidsskr Nor Laegeforen 2004;124(2):186–8.
[22] Ebeigbe JA, Akpalaba R. Ocular health status of subjects with Down's syndrome in Benin City, Nigeria. Afr J Med Med Sci 2006;35(3):365–8.
[23] daChuna RP, Moreira JB. Ocular findings in Down's syndrome. Am J Ophthalmol 1996;122(2):236–44.
[24] Kim JH, Hwang JM, Kim HJ, Yu YS. Characteristic ocular findings in Asian children with Down syndrome. Eye (London) 2002;16(6):710–4.
[25] Awan KJ. Uncommon ocular changes in Down's syndrome (mongolism). J Pediatr Ophthalmol 1977;14(4):215–6.
[26] Akinci A, Oner O, Bozkurt OH, Guven A, Degerliyurt A, Munir K. Refractive errors and strabismus in children with Down syndrome: a controlled study. J Pediatr Ophthalmol Strabismus 2009;46(2):83–6.
[27] Wagner RS. Ocular genetics and Down syndrome. J Pediatr Ophthalmol Strabismus 2009;46(2):75.
[28] Rahi JS, Williams C, Bedford H, Elliman D. Screening and surveillance for ophthalmic disorders and visual deficits in children in the United Kingdom. Br J Ophthalmol 2001;85:257–9.
[29] Creavin AL, Brown RD. Ophthalmic abnormalities in children with Down syndrome. J Pediatr Ophthalmol Strabismus 2009; 46(2):76–82.
[30] Stephen E, Dickson J, Kindley AD, Scott CC, Charleton PM. Surveillance of vision and ocular disorders in children with Down syndrome. Dev Med Child Neurol 2007;49(7):513–5.
[31] Gardiner Katheleen. Gene-dosage effects in Down syndrome and trisomic mouse models. Genome Biol 2004;5:244.
[32] Bromham NR, Woodhouse JM, Cregg M, Webb E, Fraser WI. Heart defects and ocular anomalies in children with Down's syndrome. Br J Ophthalmol 2002;86:1367–8.
[33] Raoul CMH. Rubinstein–Taybi syndrome European. J Hum Genet 2006:981–5.
[34] van Genderen MM, Kinds GF, Riemslag FC, Hennekam RC. Ocular features in Rubinstein–Taybi syndrome: investigation of 24 patients and review of the literature. Br J Ophthalmol 2000;84:1177–84.
[35] Quaranta L, Quaranta CA. Congenital glaucoma associated with Rubinstein–Taybi syndrome. Acta Ophthalmol Scand 1998;76(1):112–3.
[36] Maeda T, Hatakenaka M, Muta H, Nakayama M, Nakazaki Y, Hiroyama T, et al. Clinically mild, atypical, and aged craniofacial syndrome is diagnosed as Crouzon syndrome by identification of a point mutation in the fibroblast growth factor receptor 2 gene (FGFR2). Intern Med 2004;43(5):432–5.
[37] Ahmed I, Afzal A. Diagnosis and evaluation of Crouzon syndrome. J Coll Physicians Surg Pak 2009;19(5):318–20.
[38] Bowling EL, Burstein FD. Crouzon syndrome. Optometry 2006;77:217–22.
[39] Ernest LB, Fernando DB. Crouzon syndrome. 2006;77(5):217–32.
[40] Hoefkens MF, Vermeij-Keers C, Vaandrager M. Crouzon syndrome: phenotypic signs and symptoms of the postnatally expressed subtype. J Craniofac Surg 2004;15:233–40.
[41] Albert J. Principles and practice of. Ophthalmology 2008;3(3):4213–5.
[42] Jones KL. Hallermann–Streiff syndrome. In: Jones KL, editor. Smith's recognizable patterns of human malformations. 6th ed. Philadelphia: WB Sanders; 2006. p. 110–1.
[43] Roulez FM, Schuil J, Mire PM. Corneal opacities in the Hallermann–Streiff syndrome. Ophthalmic Genet 2008;29(2):61–6. < http://www.faqs.org/periodicals/201007/2183193201.html#ixzz1D4JKYpy2 > .
[44] Myung EL, Im JC, Wha J. A case of Hallermann–Streiff syndrome with aphakia. Korean J Pediatr 2008(51):644–9.
[45] Miho S, Hiroko T, Emil A, Yoko O, Yozo M. Ultrasound biomicroscopic findings in Hallermann–Streiff syndrome. Jpn J Ophthalmol 2002;46:451–4.
[46] Beales PL, Warner AM, Hitman GA, Thakker R, Flinter FA. Bardet–Biedl syndrome: a molecular and phenotypic study of 18 families. J Med Genet 1997;34:92–8.
[47] http://www.en.wikipedia.org/wiki/Bardet-Biedl_syndrome.
[48] Ruth R, Sten A, Alan FW, Kristina T. Ocular findings in the Laurence–Moon–Bardet–Biedl syndrome. Acta Ophthalmol Scand 1996;74(6):612–7.
[49] Ruth R, Sten A, Margareta KB, Alan FW, Niels T, Thomas R, et al. Intrafamilial variation of the phenotype in Bardet–Biedl syndrome. Br J Ophthalmol 1997;81:378–85.
[50] Hrynchak PK. Bardet–Biedl syndrome. Optom Vis Sci 2000;77:236–43.
[51] Laurie B, Charles V. Noonan's syndrome guidelines cover clinical features, diagnosis, and management CME/CE. Medscape Education Clinical Briefs; 2010.
[52] Shaw AC, Kalidas K, Crosby AH, et al. Arch Dis Child 2007;92:128–32.
[53] Reynolds DJ, Rubin SE, Fox J, Kodsi SR. Ocular manifestations of Noonan syndrome in the pediatric patient. J AAPOS 2004;8(3):282–3.
[54] Zenker M. Genetic and pathogenetic aspects of Noonan syndrome and related disorders. Horm Res 2009;72(2):57–63.
[55] Afzal AR, Rajab A, Fenske CD, Oldridge M, Elanko N, Ternes-Pereira E, et al. Recessive Robinow syndrome, allelic to dominant

brachydactyly type B, is caused by mutation of ROR2. Nat Genet 2000;25(4):419–22.
[56] Patton MA, Afzal AR. Robinow syndrome. J Med Genet 2002;39(5):305–10.
[57] Kaissi AA, Bieganski T, Baranska D, Chehida FB, Gharbi H, Ghachem MB, et al. Robinow syndrome: report of two cases and review of the literature. Aust Radiol 2007;51:83–6.
[58] Suresh SS. Robinow syndrome. Indian J Orthop 2008;42(4):474–6.
[59] Patton MA, Afzal AR. Robinow syndrome. J Med Genet 2002;39:305–10.
[60] Butler MG, Travis T. Prader–Willi syndrome: clinical and genetic findings. Endocrinologist 2000:3S–16S.
[61] State MW, Elisabeth D. Genetics of childhood disorders: XV. Prader–Willi syndrome: genes, brain and behavior. J Am Acad Child Adolesc Psychiatry 2000;39(6):797–800.
[62] Libov AJ, Maino DM. Prader–Willi syndrome. J Am Optom Assoc 1994;65(5):355–9.
[63] Crawford AH, Schorry EK. Neurofibromatosis update. J Pediatr Orthop 2006;26(3):413–23.
[64] Viskochil D, Allanson JE, Cassidy SB. In: Allanson JE, Cassidy SB, editors. Management of genetic syndromes. New York: Wiley-Liss Inc.; 2001 [Chapter 14].
[65] Jacques C, Dietemann JL. Imaging features of neurofibromatosis type 1. J Neuroradiol 2005;32(3):180–97.
[66] Destro M, D'Amico DJ, Gragoudas ES, et al. Retinal manifestations of neurofibromatosis: diagnosis and management. Arch Ophthalmol 1991;109:662–6.
[67] Parsa CF. Sturge–Weber syndrome: a unified pathophysiologic mechanism. Curr Treat Options Neurol 2008;10:47–54.
[68] Cheng KP. Ophthalmological manifestations of Sturge–Weber syndrome. In: Brodensteiner JB, Roach ES, editors. Sturge–Weber syndrome; 1999.
[69] Venkateshwar V, Vaidya Ashima, Roy Partho, Sampat Sangeeta, De JK. Osteopetrosis. MJAFI 2003;59:344–6.
[70] Wilson CJ, Vellodi A. Autosomal recessive osteopetrosis: diagnosis, management and outcome. Arch Dis Child 2000;83:449–52.
[71] Bais AS, Sardana P, Arora M. Osteopetrosis – variable. Otorhinolaryngological manifestations. Indian J Otolaryngol Head Neck Surg 2003;55:113–6.
[72] Baranello G, Vasco G, Ricci D, Mercuri E. Visual function in nonsyndromic craniosynostosis: past, present, and future. Child's Nervous: ChNS Official J Int Soc Pediatr Neurosurg 2007;49(8):574–6.
[73] Khan SH, Nischal KK, Dean F, Hayward RD, Walker J. Visual outcomes and amblyogenic risk factors in craniosynostotic syndromes: a review of 141 cases. Br J Ophthalmol 2003;87:999–1003.
[74] Richard H, Barry J, David D, Robert E, Paul T. The clinical management of craniosynostosis. MacKeith Press. Britch Library Cataloguing; 2004 [in publication data].
[75] Fenichel GM. Clinical pediatric neurology: a signs and symptoms approach. 4th ed. Philadelphia: WB Saunders; 2001.
[76] DeMyer W. Microcephaly, micrencephaly, megalocephaly, and megalencephaly. In: Swaiman KF, Ashwal S, editors. Pediatric neurology: principles and practice. St. Louis: CV Mosby; 1999. p. 301–11.
[77] Toporek C, Kellie R. Hydrocephalus: a guide for patients, families and friends. Cambridge, MA: O'Reilly & Associates; 1999.
[78] Dubé P, Der Kaloustian VM, Demczuk S, Saabti H, Koenekoop RK. A new association of congenital hydrocephalus, albinism, megalocornea, and retinal coloboma in a syndromic child: a clinical and genetic study. Ophthalmic Genet 2000;21(4):211–6.
[79] Bayston R. Part two – the effects of hydrocephalus. Hydrocephalus Network News. <http://www.asbah.org/baystart2.html> [retrieved 2001].
[80] McClelland JF, Jackson AJ, Parkes J, Hill N, Saunders KJ. Visual acuity and disorders of ocular posture in children with cerebral palsy. Invest Ophthalmol Vis Sci 2005:46.
[81] Katoch S, Devi A, Kulkarni P. Ocular defects in cerebral palsy. Indian J Ophthalmol 2007;55(2):154–6.
[82] Katoch Sabita, Devi Anjana, Kulkarni Prajakta. Ocular defects in cerebral palsy. Indian J Ophthalmol 2007;55(5):397.
[83] Saunders KJ, Little JA, McClelland JF, Jackson AJ. Profile of refractive errors in cerebral palsy: impact of severity of motor impairment (GMFCS) and CP subtype on refractive outcome. Invest Ophthalmol Vis Sci 2010;51(6):2885–90.
[84] Arnoldi K, Jackson JH. Cerebral palsy for the pediatric eye care team: epidemiology, pathogenesis, and systemic findings. Am Orthopt J 2005;55:97–105.
[85] Jackson J, Castleberry C, Marlo G, Arnoldi KA. Diagnosis and treatment of ocular motor deficits. Am Orthopt J 2006;56(1): 86–96.
[86] Garcia ML, Ty EB, Taban M, David Rothner A, Rogers D, Traboulsi EI. Systemic and ocular findings in 100 patients with optic nerve hypoplasia. J Child Neurol 2006(11):949–56.
[87] Cuthbert C, Klapper H, Elsas L. Diagnosis of inherited disorders of galactose metabolism. Curr Protoc Hum Genet 2008 [Chapter 17, Unit 17.5, Case Report].
[88] Hadeel F, Fayka Al-Raqum, Dina R. Classic galactosemia presenting with unilateral Peters' anomaly. Med Princ Pract 2010;19:324–6.
[89] Wraith JE. Mucopolysaccharidoses and oligosaccharidoses. In: Fernandes J, Saudubray J-M, van den Berghe G, Walter JH, editors. Inborn metabolic diseases: diagnosis and treatment. 4th ed. New York, NY: Springer; 2006 [Chapter 39].
[90] Shawky RM, Abd El-Monim MT, El-Sebai AA, El-Sayed SM. Cardiac and ocular manifestations in Egyptian patients with mucopolysaccharidoses. Eastern Med Health J 2001;7(6):981–91.
[91] Scott HS, Ashton LJ, Eyre HY, et al. Chromosomal localization of the human alpha-L-iduronidase gene (IDUA) to 4p163. Am J Hum Genet 1990;47:802–7.
[92] Frangiegh GT, Traboulsi EI, Kenyon KR. Mucopolysaccharidoses. In: Gold DH, Weingest TA, editors. The eye in systemic disease. Philadelphia: JB Lippincott; 1990. p. 372–6.
[93] Rodriguez-Revenga Bodi L, Madrigal-Bajo I, Mila-Racasens M. Genetic mental retardation. Rev Neurol 2006;10(43):181–186.
[94] El-Hazmi MAF, Al-Swailem AA, Al-Mosa NA, Al-Jarallah AA. Prevalence of mental retardation among children in Saudi Arabia. Eastern Med Health J 2003;9:1–2.
[95] Chang YS, Shih MH, Cheng HC, Teng CL. Ophthalmologic abnormalities in high school students with mental retardation in Taiwan. J Formos Med Assoc 2005;104(8):578–84.
[96] Temtamy SA, Kandil MR, Demerdash AM, Hassan WA, Meguid NA, Afifi HH. An epidemiological genetic study of mental subnormality in Assiut Governorate, Egypt. Clin Genet 1994;46(5):347–451.
[97] Nair P. Strabismus, susceptibility to. Centre for Arab Genomic Studies. A Division of Sheikh. Hamdan Award for Medical Sciences. The Catalogue for Transmission Genetics in Arabs CTGA Database; 2006. p. 1, 2. Copyright © Centre for Arab Genomic Studies.