

## Ophthalmogenetic and Epidemiological Studies of Egyptian Children with Mental Retardation

<sup>1</sup>Amira A. Abdel Azeem; <sup>2</sup>Manal H. Abu EL Ela., <sup>1</sup>Fatma A Soliman and <sup>3</sup>Adel A. El-Din

<sup>1</sup>Ophthalmogenetics, <sup>2</sup>Public Health, <sup>3</sup>Pediatric Ophthalmology Departments, Research Institute of Ophthalmology.

---

**Abstract:** Background: Mental retardation (MR) is a congenital or early onset lifelong impairment of cognitive adaptive functioning or daily living skills. It is a serious and lifelong disability that places heavy demands on society and the health system. The prevalence of visual and ocular disorders in children with MR is high, and can influence sensory-motor development and learning ability. Purpose: Assessment of the genetic and epidemiologic aspects of mental retardation and clarifying the ocular and visual problems among mentally disabled children. Subjects and methods: A cross-sectional hospital based study was conducted, through a period of two years, included 190 children under 18 years of age with mild to profound intellectual disabilities who were diagnosed among 480 cases referred to the Genetic clinic, Research Institute of Ophthalmology for genetic diagnosis and counseling. The definition of MR and the criteria for diagnosis were adopted from the World Health Organization (WHO) classification. The etiology of MR was specified by obtaining information about the personal and family history that included a three generation pedigree analysis, with special attention to the presence of similar cases, thorough clinical examination including complete neurological evaluation, chromosomal and other investigative studies. Ophthalmologic examination included visual acuity testing, ocular motility, and examination of the external eye and anterior segment; cycloplegic refraction and fundus examination. Results: One hundred and ninety patients representing 39.6% of the total examined cases in two years were classified etiologically into 6 groups. Specific causes were found in 161 cases (84.7%) and the etiology was unknown in 15.3% of children. Metabolic and chromosomal disorders comprised the most common etiological problems of the examined mentally retarded children in this study. The percentage of mild, moderate, severe and profound MR was 67.5%, 26%, 5.8%, and 0.7%, respectively. Family history was positive in 34.7% of patients and autosomal recessive inheritance was the commonest mode of transmission (48.4%) that reflects the high percentage of consanguineous marriages among Egyptians. Microscopically visible chromosomal anomalies of intellectually disabled patients included 25 numerical and 11 structural aberrations. Errors of refraction and strabismus were the most common in children with chromosomal disorders (24.7%) and (28.1%) respectively. While the highest percentage of optic atrophy, retinal dystrophy, microphthalmia, cataract and corneal opacities were diagnosed in children with metabolic disorders representing 76.2%, 93.3%, 38.5%, 50% and 80% of cases diagnosed in all categories respectively. Conclusion: In this study, metabolic and chromosomal disorders represented the most common etiological problems among the examined mentally retarded children with the highest proportion of specific ocular and visual problems represented among them to the extent that the eye could be considered as a window for their diagnosis. In most cases, diagnosis will assist families in understanding the condition, its prognosis and recurrence risks; more epidemiological studies have to be undertaken to determine the magnitude of the problem and its pattern of distribution in our country. The results also emphasize the need for establishing an efficient system to provide regular ophthalmic care for children with mental retardation.

**Key words:** Mental retardation, Ocular disorders, Genetic studies, Epidemiology.

---

### INTRODUCTION

Mental retardation (MR) is a congenital or early onset lifelong impairment of cognitive adaptive functioning or daily living skills (Rehder and Fritz, 2005). It is a frequently occurring disorder with an

---

**Corresponding Author:** Amira A. Abdel Azeem, Ophthalmogenetics Department, Research Institute of Ophthalmology.

estimated incidence of 1-3% in developed countries (Rodriguez-Revinga Bodi L., *et al.*, 2006). Mental retardation is also, one of the most frequently encountered and distressing disabilities among children in developing countries (Ghising *et al.*, 2007). It constitutes a major problem in Egypt because it affects the quality of life of persons and the welfare of their families, as Tentamy *et al.*, 1994. found that the prevalence of mental retardation was 3.9% among an Egyptian population (Assuit Governorate).

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 (El-Hazmi *et al.*, 2003). The study of mental retardation is one of the most complex fields in human genetics, due to the fact that it presents a very high degree of clinical and genetic heterogeneity and at the present time, reported frequencies of diagnostic categories are remarkably variable (Mila-Racasens *et al.*, 2006).

The CNS lesions causing mental retardation can give rise to various clinical expressions such as seizures, cerebral palsy and hearing and vision impairment. The eye is embryologically very closely associated with cerebral development and the presence of structural eye abnormalities should always be noted (Raymond, 2007). The prevalence of visual and ocular disorders in children with MR can influence sensory-motor development and learning ability (Chang *et al.*, 2005; Karadag *et al.*, 2007). Moreover, visual disorders can cause restriction of mobility and patterns of movement that result in a greater dependency on formal and informal support systems (Isralowitz *et al.*, 2003 ).

The aim of this study was to clarify the genetic and epidemiologic aspects of MR with assessment of visual problems in these intellectually disabled children.

### **Subjects and methods:**

A cross-sectional hospital based study was carried out through a period of two years. The study included 190 children with mild to profound intellectual disabilities diagnosed from 480 cases referred to the Genetic clinic in Research Institute of Ophthalmology for genetic diagnosis and counseling. Patients were evaluated with obtaining information about the personal and family history that included all previous diagnostic investigations; a three generation pedigree, with special attention to the presence of similar cases or any cases with mental retardation or congenital anomalies. Thorough clinical examination including complete neurological evaluation and focused on the presence of any congenital anomalies with anthropometric studies were done to all patients. The patients had ophthalmologic examination including visual acuity testing, ocular motility, and examination of the external eye and anterior segment, cycloplegic refraction and fundus examination.

A suspected diagnosis was confirmed with appropriate laboratory techniques as chromosomal analysis by Giemsa Trypsin banding technique (Seabright, 1971). metabolic screening, and hormonal assay; and radio-imaging studies as computerized axial tomography (CAT), ultra sound (US), and magnetic resonance image (MRI). Intelligence Quotient (IQ) was estimated to determine the degree of MR. The severity of MR was categorized according to the World Health Organization (WHO) classification (1968). and the Diagnostic and Statistical Manual (4<sup>th</sup> Rev.)-DSM-IV (American Psychiatric Association, 2000).

Collected data were analyzed using SPSS database (version 10). Differences of qualitative data between groups were calculated using Chi-Square test, while Student t-test was used for quantitative data as a test of significance. A significance level of 0.05 was applied. Frequency distribution tables were used for data presentation.

## **RESULTS AND DISCUSSION**

One hundred and ninety mentally retarded patients representing 39.6% of the total examined cases in the Genetic clinic in two years were classified etiologically into 6 groups. Specific causes were found in 161 cases (84.7%) and 15.3% of children were unclassified, Table [1]. Table [2] showed the characteristics of the examined patients; males [102 (53.7%)] were more affected than females [88 (46.3%)] however there was no statistically significant difference between etiological groups as regard gender ( $X^2 = 10.53$  and  $P$  value = 0.1). Patients' ages ranged from 6 months to 18 years with mean age 4.3 years  $\pm$  4.0. Family history was positive in 34.7% of patients and the highest percentage was detected among patients with metabolic disorders (47%) and lowest among patients with perinatal insults (0.7%). Autosomal recessive inheritance was the most common mode of transmission (48.4%). Intelligence Quotient (IQ) was estimated for 154 patients; Mild mental retardation was the most common (67.5 %) and profound mental retardation was the least common (0.7% of patients). The difference of severity of mental retardation was statistically significant among different etiological groups ( $X^2 = 45.04$  and  $p$  value= 0.01). Although the mean parental age at time of conception was the highest among parents of children with chromosomal disorders (28.49 years old for mothers and 34.88 years old for fathers) compared to other groups, it was statistically not significant ( $P=0.49$ ) [Table 3]. Table [4] described the prenatal, postnatal and developmental abnormalities detected among children with intellectual disabilities. Microscopically visible chromosomal anomalies of intellectually disabled patients included 25 numerical and

11 structural aberrations Table [5].

**Table 1:** Etiologic classification of mentally retarded patients

Etiologic diagnosis	No	%
Developmental cranial& brain anomalies(DCBA)	30	15.8
Metabolic disorders (MD)	64	33.7
Chromosomal disorders	36	18.9
Recognizable genetic Syndromes(RGS)	16	8.4
perinatal insults (PI)	15	7.9
Unclassified group	29	15.3
Total	190	100.0

**Table 2:** Characteristics of the examined patients with mental retardation

Age at evaluation (years)	Mean ±SD	
Children	4.3 ± 4.0	
maternal age*	26.6 ± 6.7	
Paternal age *	32.6 ± 7.9	
Sex	No.	%
Males	102	53.7
Females	88	46.3
Birth order	No.	%
1 <sup>st</sup>	55	28.9
2 <sup>nd</sup>	55	28.9
3 <sup>rd</sup>	38	20.0
4 <sup>th</sup>	20	10.5
5 <sup>th</sup>	17	9
>5 <sup>th</sup>	5	2.6
Family history	No.	%
Positive	66	34.7
negative	124	65.3
Consanguinity	No.	%
positive	114	60.0
negative	76	40.0
Inheritance	No.	%
AR	92	48.4
X-linked	12	6.3
Chromosomal	36	19
Sporadic	50	26.3
IQ( 154 cases)	No.	%
Mild	104	67.5
Moderate	40	26
Severe	9	5.8
profound	1	0.7

\* = at time of conception

**Table 3:** The mean parental age at time of conception of patients with mental retardation

Etiologic group	Mean maternal age± SD	Mean paternal age± SD
Developmental cranial& brain anomalies(DCBA)	26 ±6.4	30.98±8.48
Metabolic disorders(MD)	25.55±6.45	31.57±8.25
Chromosomal disorders	28.49±7.27	34.88±9.1
Recognizable genetic Syndromes(RGS)	26.49±6.43	32.57±6.28
Perinatal insults(PI)	27.21±9	33.68±9.2
Unclassified group	27.3±5.2	34.37±5.38

t = 0.92 P = 0.49

Ocular and visual defects in children with intellectual disabilities were summarized in Table [6]. Table [7] showed ocular and visual defects among children with different etiological groups. Errors of refraction and strabismus were the most common in children with chromosomal disorders (24.7%) and (28.1%) respectively. While the highest percentage of optic atrophy, retinal dystrophy, microphthalmia, cataract and corneal opacities were diagnosed in children with metabolic disorders representing 76.2%, 93.3%, 38.5%, 50% and 80% of cases diagnosed in all categories respectively. The difference of ocular abnormalities among different groups was statistically significant ( $X^2 = 110.6$  and  $P=0.001$ ). Fig [1], [2], and [3] showed 3 karyotypes of different chromosomal aberrations in mentally retarded children. Fig [4], showed facial features of a child with trisomy 13 and Fig. [5], showed a mentally retarded child with a metabolic disorder (Hurler syndrome).

**Table 4:** Prenatal, postnatal and developmental abnormalities among children with intellectual disabilities

Abnormality	No.	%
<b>Prenatal abnormalities</b>		
Infections	4	2.1
Teratogens	14	7.4
Growth retardation	24	12.6
Prematurity	14	7.4
Others*	13	6.8
Delivery (induced)	35	
<b>Postnatal abnormalities</b>		
Infections	3	1.6
Growth retardation	35	18.4
Others**	39	20.5
<b>Developmental abnormalities</b>		
Obesity	8	4.2
Ocular and visual deficits	128	67.4
Hearing deficit	7	3.6
Convulsions	28	14.7
Combined	28	14.7

\*Sever vaginal bleeding, toxemia of pregnancy, decreased fetal movement, diabetic mother, hypertensive mother, surgical operation during pregnancy. \*\* Delayed first cry, cyanosis, neonatal jaundice necessitating therapy, small sized head (microcephaly), abnormal facial features, and deformity; and infections needed hospitalization.

**Table 5:** Chromosomal aberrations of mentally retarded children

Numerical aberrations	No of patients	Structural aberrations	No of patients
Trisomy 21	20	4p-	3
47, XX, +21	12	(46, XY, 4p-)	2
47, XY, +21	8	(46, XX, 4p-)	1
Trisomy 18	3	18q-	2
47, XX, +18	2	(46, XX, 18q-)	1
47,XY, +18	1	( 46, XY, 18q-)	1
Trisomy 13	2	1p- (46,XX/46, XX,1p-)	1
47, XX, +13	1	4q+ (46, XY, 4q+)	1
47, XY, +13	1	ring chromosome15	1
		46, XY, r(15)	
		16p- (46, XY, 16p-)	1
		16q- (46, XY,16q-)	1
		18p- (46, XY, 18p-)	1

**Table 6:** Ocular and visual defects among children with intellectual disability

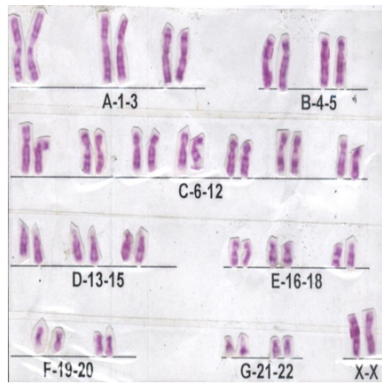
Ocular manifestations	No	%
Errors of refraction	73	38.4
Strabismus	32	16.8
Retinal dystrophy & subnormal retinal function	30	15.8
Optic atrophy & subnormal VEP	21	11.1
Microphthalmia	13	6.8
Cataract	6	3.2
Corneal opacities	5	2.6
Cerebral visual impairment	1	0.5

128 children had ocular or visual defects. Each affected child may have more than one ocular manifestation.

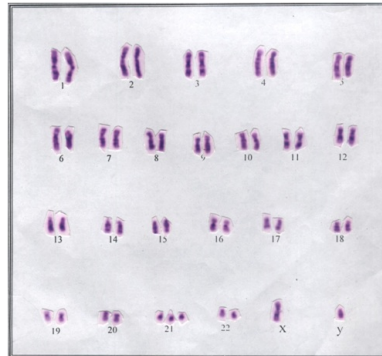
**Table (7):** Ocular and visual defects among different etiologial groups

Eye problems	Etiologic diagnosis												Total	
	DCBA		MD		Chromosomal disorders		RGS		PI		Unclassified group			
	No	%	No	%	No	%	No	%	No	%	No	%		
Errors of refraction	12	16.4	13	17.8	18	24.7	8	11.0	6	8.2	16	21.9	73	100.0
Strabismus	7	21.9	8	25.0	9	28.1	3	9.4		0.0	5	15.6	32	100.0
Optic atrophy and subnormal VEP	2	9.5	16	76.2		0.0	1	4.8	1	4.8	1	4.8	21	100.0
Retinal dystrophy and subnormal retinal function		0.0	28	93.3		0.0	2	6.7		0.0		0.0	30	100.0
Microphthalmia	2	15.4	5	38.5	2	15.4	2	15.4	1	7.7	1	7.7	13	100.0
Cataract	1	16.7	3	50.0		0.0	1	16.7		0.0	1	16.7	6	100.0
Corneal opacities		0.0	4	80.0		0.0		0.0	1	20.0		0.0	5	100.0
Cerebral visual impairment		0.0		0.0	1	100.0		0.0		0.0		0.0	1	100.0

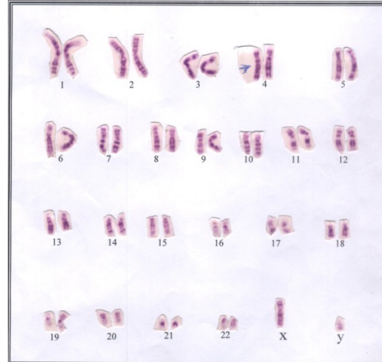
$X^2 = 110.6$  Df =35 P=0.001  
 DCBA= Developmental cranial& brain anomalies  
 MD= Metabolic disorders  
 RGS= Recognizable genetic Syndromes  
 PI= Perinatal insults



**Fig. 1:** Female karyotype showing 1p- (46, XX, 1p-)



**Fig. 2:** Male karyotype showing trisomy 21 (47, XY, +21)



**Fig. 3:** Male karyotype with 4q+ (46, XY, 4q+)



**Fig. 4:** Facial features of a child with trisomy 13



**Fig. 5:** A mentally retarded child with a metabolic disorder (Hurler syndrome).

### **Discussion:**

Diagnosis of mental retardation is made if an individual has an intellectual functioning level well below average with significant limitations in two or more adaptive skill areas (Mao and Pevsner, 2005). The etiology of mental retardation includes genetic, infectious, and perinatal events (Raymond, 2007). The genetic causes of mental retardation are highly heterogeneous and complex. Nowadays and thanks to the new techniques we are able to perform several studies, even though almost half of cases remain undiagnosed. (Rodriguez-Reventa Bodi *et al.*, 2006).

In this study mental retardation was classified etiologically into six main groups [table.1]. Taking etiological distinction into account would allow for more precise research and a better understanding of the condition. Metabolic causes comprised the most common etiological problem of the examined mentally retarded children (33.7%) in this study, followed by chromosomal disorders 18.9%, and the developmental cranial and brain anomalies 15.8%. The distribution among the different diagnostic categories varied considerably among studies. Besides differences in accepting a finding as diagnostic, also differences in the focus of the clinic may play a role (Battaglia *et al.*, 1999; Hunter, 2000; Shevell *et al.*, 2001). Although, we could not determine the direct etiology of mental retardation in 15.3% of cases in this study, but we studied the most appropriate pre and post natal abnormalities and associated developmental major signs in all cases for probable further evaluation [Table. 4].

The increased male to female ratio (1.2:1) is consistent with that reported in the earlier studies (Crow, Y., J. Tolmie, 1998). and this could be explained by cases with X-linked mental retardation (XLMR) which represented (6.3%) of patients of this study. It usually affects 1.8 per thousand male births and is categorized as "syndromic" or "non-specific" forms according to the presence or absence of specific signs in addition to the MR (Lisik and Sieroń, 2008). Patients with the first and the second birth orders were more common than others representing about 57.8% of all patients and this could be either explained by the medical care and prenatal diagnosis in the next pregnancies or the familial care of the mentally retarded child that consumes their time and money and also, the psychological effect on parents of mentally retarded children as they prefer having no more kids. Family history was positive in 34.7% of cases and positive parental consanguinity was detected in 60% of cases which is considered a high rate of consanguinity compared to the average consanguinity among the Egyptian population (about 31.79%) (Temtamy *et al.*, 1998). A previous epidemiological/ genetic study of mental retardation by (Temtamy *et al.*, 1994). showed parental consanguinity among 65% of Egyptian patients. Autosomal recessive mode of inheritance was reported in 48.4% of our cases which reflects the high percentage of consanguineous marriages among Egyptians.

The study also showed that the mean parental age at time of conception was the highest among parents of children with chromosomal disorders [Table. 3]. these results coincides with a recent study included three hundred ninety-four preimplantation genetic diagnosis for aneuploidy screening (PGD-AS) cycles after in vitro fertilization of females between 37 and 46 years of age, and the aneuploidy rate gradually increased with maternal age (Poll-The *et al.*, 2003).

Vision impairment can be a debilitating condition to mentally retarded individuals, affecting not only the social, emotional, mental and physical functioning of them, but also the individual's ability to perform basic and instrumental activities of daily living (Isralowitz *et al.*, 2005).

This study showed that the majority of individuals with mental retardation fell into the mild range [Table. 2] of mental retardation, and these individuals are usually dependable however visual problems would affect their ability to perform their activities. Ophthalmic examination revealed that 67.4% of the mentally retarded

patients had one or more ocular disorders [Tables 4, 6]. Medical eye screening by (Isralowitz *et al.*, 2003). of mentally retarded revealed that 79% had ocular problems. They recommended that people with intellectual disability should have an ophthalmologic and optometric screening to determine whether they can benefit from such interventions, including cataract removal and eyeglasses, to improve their quality of life.

In the present study, refractive errors were the most common types of ocular impairment (38.4%) among mentally retarded children which exceeds that detected by (El- Bayoumy *et al.*, 2007). (22.1%) among 5839 children of the general population in Cairo, Egypt. Similar to refractive errors, the prevalence of strabismus (16.8%) among individuals with MR was more than that of the various studies in different populations which have shown a prevalence of 1-5% for strabismus in the general population (Nair, 2006.).

Other ocular findings included retinal dystrophy (15.8%), followed by optic atrophy which represented 11.1% of cases and microphthalmia (6.8%). Cataract, corneal opacities and cerebral visual impairment represented 3.2%, 2.6% and 0.5% of cases respectively. Of all subjects 31.6% required corrective glasses, while 13.2% had corrective surgery for strabismus and all patients with cataract underwent cataract removal. (Ghising and his colleagues, 2007). had a cross sectional study of 134 mentally retarded students in Nepal and their examination revealed that more than half of the examined cases had one or more ocular disorders, and the most common type was also refractive errors (34.4%). In contrast, (Mwanza *et al.*, 2000). had a similar study in Kinshasa. They examined 73 mentally retarded subjects aged from 5 to 19 years. Ocular abnormalities were found in 60% of subjects however, Optic atrophy (16.4%) was the most common frequent disorder and refractive errors represented only 15% of cases.

The prevalence of visual and ocular defects varies with different etiologies as refractive errors and strabismus were more common among patients with chromosomal disorders [Table 7]. Chromosomal analysis of suspected cases of intellectually disabled patients revealed 25 numerical and 11 structural aberrations Table [5]. The most common chromosomal abnormalities associated with mental retardation were trisomy 21 representing 20/36 of the studied cases, followed by trisomy 18 (3/36), 4p- (3/36) and trisomy 13(2/36). Many recent studies concluded that there was relatively high frequency of major ocular anomalies associated with chromosomal syndromes (Lueder, 2006; Yurdakul *et al.*, 2006; Fimiani *et al.*, 2007; Mohd-Ali *et al.*, 2006) reported that children with Down syndrome have a high prevalence of ocular disorders with high percentage of refractive errors and strabismus. Haugen *et al* (2001). suggested that the mechanical factors in the cornea from the upward slanting of palpebral fissures may be major etiological factors in the astigmatism. Merrick and Koslowe (2001). stated that the majority of Down's syndrome children with strabismus have an acquired esotropia and they reported also that hypermetropia and accommodation weakness are probably important factors in esotropia in Down's syndrome patients. Lueder, 2006. documented that the presence of inferonasal iris colobomas and adjacent sectoral cataracts in patients with other dysmorphic findings should prompt chromosomal analysis for trisomy 13.

Ocular manifestations in inborn errors of metabolism occur in many diseases and may be associated with any part of all eye components. In a minority of diseases it is possible to attribute the eye symptoms to a single hereditary pathogenetic mechanism. More often the etiological relationship of the ocular defects to the metabolic disease is unknown. Diverse pathogenetic mechanisms may act via a common pathological pathway inducing ocular damage. The occurrence of eye abnormalities in metabolic disorders suggests that they are associated with direct toxic actions, errors of synthetic pathways or deficient energy metabolism (Platteau *et al.*, 2005).

In Conclusion: Metabolic and chromosomal disorders represented the most common etiological problems among the examined mentally retarded children in this study, with the highest proportion of specific ocular and visual problems represented among them to the extent that the eye could be considered as a window for their diagnosis. The genetic evaluation of the child with mental retardation continues to be an important challenge in genetic medicine. In most cases, diagnosis will assist families in understanding the condition, its prognosis and recurrence risks; and allows them access to prenatal diagnosis. In those undiagnosed cases with positive familial history a genetic counseling could be provided using empirical recurrence risks. More epidemiological studies have to be undertaken to determine the magnitude of the problem and its pattern of distribution in our country. The results also emphasize the need for establishing an efficient system to provide regular ophthalmic care for children with mental deficiency as these disorders could be detrimental for their education and daily activities.

## REFERENCES

- American Psychiatric Association 2000. Diagnostic and statistical manual of mental disorders (4<sup>th</sup> ed., Rev). Washington, DC: American Psychiatric Association.
- Battaglia, A., E. Bianchini, J. Carey, 1999. Diagnostic yield of the comprehensive assessment of developmental delay/ mental retardation in an institute of child neuropsychiatry. American J of Med. Gent., 82: 60-66.

- Chang, Y.S., M.H. Shih, H.C. Cheng, C.L. Teng, 2005. Ophthalmologic abnormalities in high school students with mental retardation in Taiwan. *J. Formos Med Assoc.*, 104 (8): 578-584.
- Crow, Y., J. Tolmie, 1998. Recurrence risks in mental retardation. *J. of Med. Genet.*, 35: 177-182.
- El-Bayoumy, B.M., A. Saad, A.H. Choudhury, 2007. Prevalence of refractive error and low vision among schoolchildren in Cairo. *East Mediterr Health J.*, 13(3): 575-9.
- El-Hazmi, M.A.F., A.A. Al-Swailem, N.A. Al-Mosa, A.A. Al-Jarallah, 2003. Prevalence of mental retardation among children in Saudi Arabia, *Eastern Mediterranean Health Journal*, 9: 1/2.
- Fimiani, F., A. Iovine, R. Carelli, M. Pansini, G. Sebastico, A. Magli, 2007. Incidence of ocular pathologies in Italian children with Down syndrome. *Eur. J. Ophthalmol.*, 17(5): 817-822.
- Ghising, R., S. Shakya, A. Rizyal, R. Shrestha, S. Shrestha, S. Wang-Harris, 2007. Prevalence of refractive errors in mentally retarded students of Kathmandu Vally. *Nepal Med. Coll. J.*, 9(4): 262-265.
- Haugen, O.H., G.A. Hovding, G.E. Eide, 2001. Biometric measurements of the eyes in teenagers and young adults with Down syndrome. *Acta. Ophthalmol. Scand.* 79(6): 616-625.
- Hunter, A., 2000. Outcome of the routine assessment of patients with mental retardation in genetics clinic. *American J. of Med. Genet.*, 90: 60-68.
- Isralowitz, R., M. Mada, A. Reznik, 2005. Vision needs of people with intellectual disability in residential facilities and community-based homes for independent living. *Disabil Rehabil.*, 15; 27(23): 1451-1453.
- Isralowitz, Richard, Madar, Michal, Lifshitz, Tova, Assa, Valentina, 2003. Visual problems among people with mental retardation. *International Journal of Rehabilitation Research.*, 26(2): 149-152.
- Karadag, R., R. Yagci, M. Erdurmus, U.C. Keskin, B. Aydin, M. Durmus, 2007. Ocular findings in individuals with intellectual disability. *Can. J. Ophthalmol.*, 42(5): 703-706.
- Lisik, M.Z., A.L. Sieroń, 2008. X-linked mental retardation-treatment scheme. *Wiad Lek.*, 61(4-6): 146-53.
- Lueder, G.T., 2006. Clinical ocular abnormalities in infants with trisomy, *Am. J. Ophthalmol.*, 141(6):1057-1060.
- Mao, R., J. Pevsner., 2005. The use of genomic microarrays to study chromosomal abnormalities in mental retardation. *Ment. Retard. Dev. Disabil. Res. Rev.*, 11(4): 279-285.
- Merrick, J., K. Koslowe, 2001. Refractive errors and visual anomalies in Down's syndrome. *Down syndr. Res. Pract.*, 6(3): 131-133.
- Mila-Racasens, M., L. Rodriguez-Revenga Bodi, I. Madrigal-Bajo, 2006. Diagnosis of genetic mental retardation. Protocol of study. *Rev Neurol.*, 7(42) 1: S103-7.
- Mohd- Ali, B., Z. Mohammed, M. Norlaila, N. Mohd-Fadzil, C.C. Rohani, N. Mohidin, 2006. Visual and binocular status of Down syndrome children in Malaysia. *Clinic Exp. Optom.*, 89(3): 150-154.
- Mwanza, J.C., C.M. Nkidiaka, D.L. Kayembe, C.Y. Maillet, E.J. Mukau, M.R. Tuela, 2000. Ophthalmologic abnormalities in mentally retarded. *Bull Soc Belge Ophtalmol.*, 277: 57-58.
- Nair, P., 2006. 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, p1,2, Copyright © Centre for Arab Genomic Studies.
- Poll-The, B.T., L.J. Maillette de Buy Wenniger-Prick, P.G. Barth, M. Duran, 2003. The eye as a window to inborn errors of metabolism. *J. Inherit Metab Dis.*, 26(2-3): 229-244.
- Platteau, P., C. Staessen, A. Michiels, A. Van Steirteghem, I. Liebaers, P. Devroey, 2005. Preimplantation genetic diagnosis for aneuploidy screening in women older than 37 years. *Fertil Steril.*, 84(2): 319-24.
- Raymond, G.V., 2007. Abnormal mental development. In, Principles and practice of medical genetics. 5<sup>th</sup> ed. Ed by D.L. Rimoin, J.M. Connor, R.E. Pyeritz, B.R. Korf 1(45).Churchill livingstone, Elsevier.
- Rehder, H., B. Fritz, 2005. Genetic causes of mental retardation. *Wien Med Wochenschr.*, 155(11-12): 258-267.
- Rodriguez-Revenga Bodi L., I. Madrigal-Bajo, M. Mila- Racasens, 2006. Genetic mental retardation. *Rev. Neurol.*, 10(43) 1: 181-186.
- Seabright, N.A., 1971. A rapid banding technique for human chromosomes. *Lancet*, 2: 971-972.
- Shevell, M., A. Majnemer, P. Rosenbaum, M. Abrahamowicz, 2001. Etiologic determination of childhood developmental delay. *Brain development*, 23: 228- 235.
- Temtamy, S.A., N. Abdel Maguid, I Mazen, S.R. Ismail, N.S. Kassem, R. Bassiouni, 1998. A Genetic epidemiological study of malformations at birth in Egypt. *EMHJ.*, 4: 2, 252-259.
- Temtamy, S.A., M.R. Kandil, A.M. Demerdash, W.A. Hassan, N.A. Meguid, H.H. Afifi, 1994. An epidemiological genetic study of mental subnormality in Assiut Governorate, Egypt. *Clinic. Genet.*, 46(5): 347-451.
- World Health Organization. 1968. Organization of services for mentally retarded. In Fifteenth report of the WHO Expert Committee on Mental Health. Geneva.
- Yurdakul, N.S., S Ugurlu, A. Maden, 2006. Strabismus in Down syndrome. *J. Pediatr. Ophthalmol. Strabismus.*, 43(1): 27-30.