ABSTRACT

Purpose: To review the clinically significant ophthalmologic manifestations in individuals with Down’s syndrome.

Material and Methods: Classic review of the literature in different scientific databases, using the MeSH words "Down's syndrome", "Down syndrome", "ocular manifestations", "ophthalmic manifestations", "trisomy 21". The articles were selected in the English and Portuguese languages, published since the year 2000.

Results: Ophthalmic disorders are extraordinarily prevalent in individuals with Down’s syndrome. The most consistent ocular finding is the presence of a prominent epicanthic fold. In children, the prevailing ocular findings are refractive errors, hyperopia and astigmatism being the most common ones; and strabismus, mainly in the form of esotropias. For the adults, cataracts are the leading cause of ophthalmologic disorders. Blepharitis and conjunctivitis are also a very common condition in these patients. Keratoconus and Brushfield spots were described as being frequent in this population; however they do not seem to be as common as related in older studies.

Conclusions: Individuals with Down’s syndrome are at a greater risk of visual impairment; hence, ophthalmologic evaluation must be included in their routine medical care. A delay in the diagnosis and treatment of these disorders can lead to visual impairment and adversely affect their quality of life. Therefore, early detection should be emphasized near family physicians and pediatricians, to improve developmental and functional outcomes for children and adults with Down’s syndrome.

Keywords: Down’s syndrome, ophthalmic disorders, quality of life, early detection

RESUMO

Objetivos: Rever as manifestações oftalmológicas clinicamente significativas nos indivíduos com Síndrome de Down.

Resultados: As patologias oftalmológicas são extraordinariamente prevalentes nos indivíduos com Síndrome de Down. A característica ocular mais consistente é a presença de uma dobra epicântica proeminente. Nas crianças, os achados oculares predominantes são os erros de refração, sendo a hipermetropia e o astigmatismo os mais comuns; e o estrabismo, principalmente na forma de endotropias. Nos adultos, as cataratas são a principal causa de patologia oftalmológica. A blefarite e a conjuntivite são também condições muito comuns nestes pacientes. Queratocone e Manchas de Brushfield foram descritas como frequentes, no entanto não parecem ser tão comuns quanto relatados em estudos mais antigos.

Conclusões: Indivíduos com Síndrome de Down têm maior risco de deficiência visual, portanto a avaliação oftalmológica deve ser incluída na sua avaliação médica de rotina. Um atraso no diagnóstico e tratamento destas patologias pode levar à deficiência visual e afetar adversamente a sua qualidade de vida. Assim sendo, a deteção precoce deve ser enfatizada junto dos Médicos de Família e dos Peditras, para melhorar os resultados do desenvolvimento e funcionais das crianças e adultos com Síndrome de Down.

Palavras-chave: Síndrome de Down, patologia oftalmológica, qualidade de vida, deteção precoce

INTRODUCTION

Down’s syndrome (DS) is the one of the most common human chromosomal anomalies. It is a genetic disorder caused by the presence of a third copy of chromosome 21, typically associated with characteristic facial features, delay in physical growth and intellectual disability.

A myriad of opthalmic disorders is associated with DS including refractive errors, strabismus and cataracts. Earlier studies have shown risk for abnormalities in virtually all structures of the eye, including the lid, iris, cornea, lens, and retina, and no specific opthalmic disorder seems to be pathognomonic of this syndrome.

Visual impairment, whose prevalence is estimated at 77% in DS, significantly decreases independent living skills, communication and language skills, social skills, and initiative and persistence among these patients. Therefore, if not identified and treated, vision impairment constitutes an additional burden to anyone with DS, being a significant cause of preventable secondary handicap at all ages.

The treating physician, whether the Family Physician, the Pediatrician or the Ophthalmologist, should be aware of the most common opthalmic manifestations in patients with Down’s syndrome because if overlooked, they may lead to permanent visual impairment owing to the development of amblyopia.

The aim of this study is to review the clinically significant opthalmologic manifestations in individuals with Down’s syndrome.

MATERIAL AND METHODS

A classic review was conducted by reviewing the literature in different scientific databases, using the MeSH words “Down’s syndrome”, “Down syndrome”, “ocular manifestations”, “ophthalmic manifestations”, “trisomy 21”. There were selected the articles in the English and Portuguese languages, published since the year 2000.

An Overview of Down’s Syndrome

Down’s syndrome is a genetic disorder due to the presence of 47 chromosomes instead of 46, with an extra copy of chromosome 21 which may be either full or partial. DS is the most commonly diagnosed chromosomal abnormality in live-born infants, occurring approximately in 1 in 600–1000 live births worldwide, in all races and socio-economic levels. Although its
incidence seems stable, the life expectancy and quality of life have increased remarkably due to improved medical care.\textsuperscript{8}

Three variants of DS are known;\textsuperscript{8} trisomy 21, translocation and mosaic. Trisomy 21 is the most common type comprising 95\% of all cases, hence trisomy 21 is used synonymously as DS. There are various risk factors for trisomy 21, but only advanced maternal age and altered or aberrant recombination are well-documented.\textsuperscript{8}

Down syndrome is associated with a characteristic phenotypic which define the syndrome, including distinctive facial and physical features, intellectual disability, health disorders and shortened life expectancy.\textsuperscript{6} The physical features include brachycephaly, unusually round face, short neck, small ears, flat nasal bridge, microgenia, macroglossia due to a small oral cavity and short height.\textsuperscript{2,8} Other features are shorter limbs, a single transverse palmar crease, brachydactyly, lax ligaments, xerotic skin, muscle hypotonia and protuberant abdomen.\textsuperscript{2,8} Medical conditions such as cardiac malformations, skeletal abnormalities, obesity and several degrees of intellectual impairment are frequent.\textsuperscript{2,3,8}

The most common ocular features are small and almond shaped eyes caused by a prominent epicanthic fold of the eyelid, obliquely positioned and narrow palpebral fissures, upward slanting eyes, and increased interinternal canthal distances.\textsuperscript{2,8,10} Ocular and visual disorders include high refractive errors, strabismus and amblyopia, ptosis, blepharitis, nasolacrimal duct obstruction, nystagmus, keratoconus, speckling of the iris (Brushfield’s spots), cataracts, glaucoma and retinovascular anomalies.\textsuperscript{4,8}

The effects of DS differ among individuals depending on the extent of the mutation; therefore, physical development, mental abilities, personality and abilities vary considerably.\textsuperscript{8}

\textbf{RESULTS}

It is exceedingly common for individuals with Down’s syndrome to have an ophthalmic disorder. The most consistent ocular finding is the presence of a prominent epicanthic fold, occurring in about 96.7\%.\textsuperscript{11} The most frequent ocular findings in children are refractive errors, strabismus, nystagmus, and nasolacrimal duct obstruction.\textsuperscript{10,12} Cataracts are the ophthalmic disease with the highest prevalence in adults, followed by severe refractive errors, strabismus, and conjunctivitis.\textsuperscript{7}

\textbf{1. Refractive Errors}

Clinically significant refractive errors are more prevalent than in the general population and vary with age. Six years and younger children have a higher prevalence of hyperopia; patients between 6 and 10 years old have a higher prevalence of astigmatism (oblique astigmatism has been found to be the most prevalent type); patients older than 10 years have more cataracts, strabismus, and iris abnormalities. Therefore, hyperopia and astigmatism are the most common refractive errors in DS.\textsuperscript{10} These children develop amblyopia due to strabismus and refractive errors.\textsuperscript{2} These children can also present with anisometropia.

Myopia seems to be correlated with cardiac abnormalities, as found in several studies, although the basis for this association are not clear yet.\textsuperscript{2,10} Refractive errors are the second most frequent disorder in adults, cataracts being the leading cause.\textsuperscript{4}

\textbf{2. Accommodation}

Patients with DS have a reduced accommodation, especially at near, and poorer fixation and visual attention.\textsuperscript{9,13} Glasses to correct hyperopia have not been shown to improve accommodation.

\textbf{3. Strabismus}

Strabismus is present in 30-45\% of cases\textsuperscript{1,2,7} and esotropias are widely the most common.\textsuperscript{7,10} Asians seem to have a higher prevalence of exotropia as compared to Caucasians and racial factors may play a role.\textsuperscript{2}

\textbf{4. Cataracts}

Compared to the general population, there is a tenfold increase in congenital cataract in children with Down syndrome.\textsuperscript{5,9} In adults they are four times more common than in the general population, making them the most frequent ophthalmic disorder in adults with DS (42\%).\textsuperscript{4,9} Cataracts in DS are age related, and its risk increases rapidly at 40 years of age, significantly younger than the
general population; this seems to be in accordance to be accelerated biological aging characteristic of DS.\textsuperscript{4}

5. **Nystagmus**

Nystagmus is present in 10-30\% of patients, with fine, rapid horizontal movements, and does not require specific investigation or intervention.\textsuperscript{9-12}

6. **Keratoconus**

Keratoconus was reported in older studies as a condition frequently causing visual impairment, but recent studies have shown its prevalence isn’t as high as initially thought. The latest reviews report this disorder in 3-8\% of patients. Nonetheless, they should be closely monitored since they may require corneal transplant surgery.\textsuperscript{4,7}

7. **Iris Anomalies**

Iris anomalies in DS include anterior stromal hypoplasia and Brushfield spots and do not change with age.\textsuperscript{10} Brushfield spots are detected more frequently in light-coloured irides.\textsuperscript{11} In recent studies, Brushfield spots do not seem to be as prevalent as in older studies,\textsuperscript{10} being found in 52\% of children and are not of clinical significance.

8. **Eyelids and eyelashes**

Eyelid abnormalities including upward slanting palpebral fissures, prominent epicanthal folds, blepharitis and congenital ectropion are often seen in DS.

Blepharitis occurs in 10-30\% of individuals with DS and may be related to their narrow palpebral fissures or an increased susceptibility to infection associated with the impact of trisomy 21 on the immune system.\textsuperscript{4,9,11} Conjunctivitis is also very common, occurring in 10-20\% of individuals.\textsuperscript{1,3-5} Both may be treated in the usual way, requiring no specialized treatment.\textsuperscript{4}

9. **Lacrimal disease**

There is a high prevalence of epiphora (35\%), due to nasolacrimal duct obstruction (12-30\%) and anomalies,\textsuperscript{2,12} the later including punctal agenesis, canalicular atresia, canalicular and canal stenosis.

10. **Fundus examination**

Fundus examination shows retinal dystrophy with numerous vessels (over 18) crossing the optic disc margin and extending into retinal periphery, and optic hypoplasia.\textsuperscript{2,10,12} In a minority, focal hyperplasia of the retinal pigment epithelium is present.\textsuperscript{10} Optic disc pallor has been reported in 1-5\%.

11. **Visual cortex**

DS children have reduced visual acuity and contrast sensitivity that cannot be fully corrected with glasses.\textsuperscript{13} The basic vision capacities affected in DS are the sensitivity to contrast variation in spatial patterns, depth perception, and colour vision.

11.1. **Sensitivity to contrast variation**

Individuals with DS have decreased sensitivity at all spatio-temporal frequency combinations,\textsuperscript{6} whereby fine details and discrimination cannot be detected unless the objects are very close. Thus, reduced spatial vision affects the ability to read signs and watch television (high spatial frequency deficits) and to recognize objects and faces (low spatial frequency deficits).

Researchers such as *Rocco et al.* have noted that this pattern of vision deficits is similar to the one in Alzheimer’s disease and is observed from the fifth decade of life in adults with DS.\textsuperscript{6,8}

11.2. **Depth perception**

The image on the retina is a two-dimensional representation of a three-dimensional world. In individuals with DS, stereopsis is very poor, not due to retinal damage, but likely as a result of cortical involvement.\textsuperscript{6} Impaired depth perception makes operating stairs and escalators difficult as well as participating in sports and other leisure activities.

11.3. **Colour Vision**

Individuals with DS have a diminished ability to discriminate colour\textsuperscript{6} that interferes with the ability to
recognize and discriminate objects from one another and to see objects in a background.

Deficits in vision have implications in learning, cognitive functioning, and adaptive behavior. Adults with visual impairment show diminished independent living skills, communication and language, initiative and social skills.6,13

12. Other ocular features

Glaucoma has been described in 7% of cases.11

Although DS children were believed to be more susceptible to retinoblastoma, its incidence is quite infrequent (1.7%).11

Compared to Caucasian children with DS, Asian children show a higher incidence of epiblepharon, the highest rates of exotropia and almost no cases of Brushfield spots or keratoconus.12

RELATION WITH AGE AND INTELLECTUAL IMPAIRMENT

1. Age

The number and severity of ophthalmic disorders increases with age. Also, while refractive errors and strabismus are more prevalent in younger individuals, cataracts and blepharitis are more common in older ones.5,10

2. Intellectual Impairment

The prevalence of ophthalmic disorders increases substantially with the severity of intellectual impairment. Evenhuis et al. observed visual impairment in 4.5% of individuals with mild or moderate intellectual disability but in 74% of individuals with severe or profound intellectual disability.4 McCulloch et al. diagnosed strabismus in 25% of patients with mild intellectual disability compared to 60% of individuals with profound disability. Furthermore, esotropia was typically found in milder disabilities, whereas exotropia was most common in severe disabilities.4

3. Sex

There is no association between sex and the prevalence of an ophthalmic disorder.4,8

FOLLOW-UP

Children, particularly with Down’s syndrome, can be challenging to examine as they require developmentally appropriate vision testing procedures, a distraction-free environment and extra time with trained professionals to optimize the evaluation.5

All newborn children with DS should be examined for congenital cataract and other eye anomalies by a trained Ophthalmologist.9 The first formal ophthalmologic review should occur in the first six months of life and patients should be followed annually until the age of five and every six months after that. This review must include orthoptic assessment, cycloplegic refraction, and fundus examination.5,9 Adults should be reviewed at least every two years and with increasing frequency with advancing age.5

Distance and near vision should be checked at every review and a prescription for near correction or bifocals considered at all ages; detail vision is likely to remain poorer than expected throughout life even when appropriate glasses are worn.

CONCLUSION

Individuals with Down’s syndrome are at a greater risk of visual impairment.2 Early awareness and detection of ophthalmic manifestations of DS can decrease its complications and sight threatening conditions. Therefore, ophthalmologic evaluation must be included in the routine medical care of all patients with DS, since a delay in the diagnosis and treatment of ophthalmologic disorders can lead to visual impairment and adversely affect their quality of life.2,7

Early detection should be emphasized near the Family Physicians and the Pediatricians, as proper assessment of visual functioning and correction when possible would lead to improved developmental and functional outcomes for children and adults with Down’s syndrome.5,6
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CONTACT

Diogo Hipólito Fernandes
Ophthalmology Department
Lisbon Central Hospital Centre
Alameda Santo António dos Capuchos
1169-050 Lisboa
E-mail: cdiogo777@gmail.com

None of the authors has any financial/conflicting interests to disclose.