Congenital cataracts – a literature review

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ABSTRACT
Congenital cataracts are clouding of the crystalline lens inside the eye, which is present at birth and leads to a decrease in vision. It is one of the three leading causes of blindness in children, responsible for up to 27.6% of cases. The etiology of congenital cataracts varies. The main causes include heredity, chromosomal aberrations, metabolic diseases, and intrauterine infections. Early diagnosis and treatment of congenital cataracts are essential in the prevention of irreversible loss of vision. The red reflex test is an excellent tool in the screening of congenital cataracts and should be performed on each newborn. Congenital cataract therapy differs from adult cataract therapy, being based primarily on early surgical intervention. Long-term post-operative rehabilitation is also an important part of care.

KEY WORDS:
infants, congenital cataracts, pediatric ophthalmology, eye disease.

INTRODUCTION
Cataracts in general are a clouding of the crystalline lens inside the eye, which leads to a decrease in vision [1]. Congenital cataracts are a lens opacity that is present at birth or diagnosed in the first year of life and may be unilateral or bilateral. They are the most common cause of lifelong visual loss in children worldwide [2].

Although the most common etiology of congenital cataracts is hereditary (especially autosomal dominant inheritance), this condition has diverse etiologies. Research carried out by Fkih et al. showed that metabolic diseases and intrauterine infections (such as congenital rubella syndrome, toxoplasmosis) also can cause congenital cataracts [3]. For this reason, parents should be questioned about their family history, pregnancy, and the child's other health problems. Also, due to the fact that congenital cataracts may be a part of a multisystem disorder, patients, their parents and siblings should be observed for any dysmorphic features [4]. Approximately 70% of congenital cataract cases are isolated traits, while 15% of cases are associated with other ocular anomalies such as microcornea and microphthalmia [5].

Qin et al.'s analysis of 41 cases of congenital cataracts diagnosed prenatally among women undergoing anatomic survey at four referral centers showed that prenatal diagnosis of congenital cataracts provides vital information for counseling and subsequent management [6]. Nevertheless, early diagnosis on the postnatal ward or in the community also can result in good levels of visual function [2].

The most important factor of visual outcome is the timing of surgery when dense cataracts are present. Good outcomes have been reported in children undergoing surgery before 6 weeks of age in children with unilateral cataracts and before 10 weeks of age in bilateral cases [2].

The aim of this article is to highlight the importance of early diagnosis and implementation of treatment in infants with congenital cataracts, which is one of the main causes of blindness in children.
METHODS

A PubMed and UpToDate search was conducted using the keywords “congenital cataracts AND surgery” (1924 results), “inherited cataracts” (1070 results) and “congenital cataracts AND red reflex” (39 results) for articles published in the period 1990-2022. After a screening process of studies published before April 2023, a total of 56 articles were selected in this paper. Articles were analyzed with a particular emphasis on the most recent publications. Other criteria included the number of citations and the size of the study group. Studies not available in English were excluded. Nevertheless, due to the nature of this review, a systematic methodology was not involved.

ETIOLOGY

Congenital cataract has a varied etiology. It can occur as an isolated inherited trait, can be a component of a more extensive syndrome or disease, including for instance diabetes and cholesterol metabolism diseases, or result from undetermined causes [2, 14].

Congenital cataracts are often inherited, mostly autosomal dominant (AD), less often autosomal recessive (AR), and sometimes X-linked. Chromosomal aberrations, such as Down syndrome, Marfan syndrome, other trisomies (13, 18), and deletions (5p, 18p, 18q), also may be the cause [2, 15, 16].

It is important to pay attention to the molecular basis of congenital cataracts. Thanks to recent advances in molecular genetics, mutations in genes encoding many different proteins have been identified. The same mutation in one gene can lead to different cataract phenotypes, while the expression of different genes can result in the same cataract pattern [17–19].

Gene mutations, leading to the development of the disease, can be divided into four main groups:

1. Mutations in genes encoding crystallins:
   - We distinguish α, β and γ crystallins. Alpha-crystallins have distinct protective roles in preventing the precipitation of denatured proteins and promoting resistance of cells to stress. Alpha-crystallins are members of the small heat shock protein family and they function as chaperonins [20–22]. Beta and gamma crystallins are part of a large protein family that includes spoor coat proteins in bacteria [23]. Also, the taxon-specific crystallins have been discovered, which are associated with various metabolic enzymes and together form a class called enzyme-crystallins [24].

2. Mutations in genes encoding lens membrane proteins:
   - Lens membrane proteins are important in intercellular communication such as connexins, which take part in lens microcirculation and are responsible for delivering nutrients toward the center of the lens and draining unwanted byproducts to the periphery, and aquaporins, which function mainly as water channels [20, 25, 26].

3. Mutations in genes encoding cytoskeletal structural proteins:
   - Beaded filament structural proteins (BFSP) belong to intermediate filament proteins and together with crystallins form part of the highly organized cytoskeleton and play a role in lens development [20]. They are made up of BFSP1 (filensin) and BFSP2 (phakinin). These proteins are encoded by their corresponding genes – BFSP1 and BFSP2 [23]. Mutations in both genes, BFSP1 and BFSP2, can cause variety of types of congenital and pediatric cataracts with both AD and AR inheritance pattern [18, 27, 28].

4. Other possible examples of mutations in genes: ITX3 (paired-like homeodomain 3), PAX6 (paired box 6), and HSF-4 (heat shock protein factor-4) [26].

A complete list of possible mutations is provided in Cat-Map, which is an online chromosome map and reference database for inherited and age-related forms of cataract. The most common causative groups are mutations in genes encoding crystallins (33%), developmental and transcription factors (26%), connexins (18%), membrane proteins and transporters (11%), intermediate filament proteins (4%) and others (Figure 1) [27, 29].

In addition, the metabolic basis can be distinguished, including disorders such as hyperglycinuria, diabetes, and galactosemia [30, 31].
Some of the non-genetic causes of congenital cataract are: intrauterine infections with herpes simplex virus (HSV), rubella virus, Toxoplasma gondii, and others, physical trauma, radiation and drug exposure (e.g. steroids) during pregnancy [2, 20].

Congenital cataracts may also be a part of a multisystem disorder. Common syndromes associated with congenital cataracts are Alport syndrome, Hallermann-Streiff-Francois syndrome, Lowe syndrome, Smith-Lemli-Opitz syndrome and others.

All of the above are the primary known causes of congenital cataracts; however, many cases, especially unilateral congenital cataracts, remain idiopathic [4, 32].

**DIAGNOSIS**

Congenital cataracts are a rare disease, but one which may lead to irreversible loss of vision. Thus, early diagnosis and appropriate management are essential in the prevention of lifelong visual impairment [33].

In the diagnosis of congenital cataracts medical history and physical examination are crucial. Pediatricians should pay attention to the risk factors of CC (congenital cataracts). They include a family history of hereditary or congenital cataracts, trisomy 21, prematurity and maternal exposure during pregnancy to viruses such as rubella or cytomegalovirus (CMV) [34]. In cases of bilateral cataracts with no family history, it is recommended to do a urine test for reducing sugars, screening for toxoplasmosis, rubella, CMV and herpes simplex virus, a VDRL test and a blood test for calcium, phosphorus, glucose and galactokinase levels. An extensive systemic workup is not necessary for patients with unilateral cataracts, who are otherwise healthy [35, 36]. Depending on the severity of a lens opacity the signs of the congenital cataracts may differ. Some children may be asymptomatic over years and show noticeable abnormalities such as microcornea, megalocornea and aniridia [37]. The first symptoms that are often noticed by parents are leukocoria and the occlusal sign of Franceschetti, which is characterized by repetitive pressing of the eye with fingers [38]. Untreated dense unilateral congenital cataracts lead to amblyopia and may cause strabismus and nystagmus. Therefore, by physical examination unilateral cases of CC are more emergent than bilateral cases [16, 34]. Visual deprivation amblyopia may be a result of a dense central opacity. The other types of congenital cataracts cause anisometropia due to high degrees of astigmatism. These abnormalities indicate the need for an ophthalmologist to perform an eye evaluation for congenital cataracts [2, 34] (Figure 2).

The red reflex test is an important component of the newborn examination, which should be performed in the maternity ward. According to a study conducted by Magnusson et al., it helps to diagnose three times more cases in comparison with no congenital cataracts screening [39]. The red reflex test can be performed through undilated pupils using a direct ophthalmoscope. It is recommended to do the examination in a darkened room. In some countries the red reflex test is performed with a flashlight or penlight instead of an ophthalmoscope; however, it is believed to be a less sensitive screening method. During the examination, the light of an ophthalmoscope is projected onto both eyes simultaneously from approximately 50 cm away. The red reflex should be equal and bright for each pupil. Any difference between the eyes, an absence of the red reflex or an abnormal color are indications for urgent referral to an ophthalmologist. Additionally, patients with a positive family history of congenital cataracts should undergo complete eye evaluation [40–42]. In most countries, it is recommended to perform the red reflex test at least twice: in the neonatal period and at 6–8 weeks of life [43].

A more advanced technique of congenital cataracts diagnosis is genetic testing, which can be performed for...
a fetus at early gestational stages. However, genetic testing is most helpful when prior to pregnancy the specific mutation involved in CC is known. Therefore, that diagnostic method is used in inherited cataracts with a known genetic cause. Next generation sequencing (NGS) is a method of genetic testing which provides an accurate high-throughput genotype-based approach to molecular diagnosis of congenital cataracts [44].

It is possible to detect congenital cataracts by ultrasoundographic prenatal imaging. Prenatal detection of CC should be an indication for a detailed fetal anatomy survey in searching for other abnormalities that may be associated with congenital cataracts [45].

The ophthalmologic evaluation consists of a slit lamp examination of both eyes, checking intraocular pressure, and an ultrasound examination of the posterior pole if not visible. By the slit lamp examination morphology and severity of the cataract are revealed. In addition, any associated abnormalities of the cornea or anterior segment should be documented. Full retinal examination is performed if there is a view of the retina. Otherwise, ultrasonography is carried out. By identifying the morphology and the size of the cataracts it is possible to adjust a personalized treatment [36].

**TREATMENT**

The treatment of congenital cataracts is distinct from that of age-related cataracts in adults. While in adults, it can be delayed without adversely affecting the outcome of vision, in infants, however, it must be removed prior to the first year of life; otherwise, the child will not fully regain vision following surgery. The management of cataracts in children is more complex than in adults, as it involves balancing the risks associated with early surgery against the need to promote optimal visual development during a critical period when amblyopia can occur [46].

Early surgical intervention is the main treatment for congenital cataracts. It involves the removal of the cloudy lens and gives a good chance for the child's vision to develop properly [20, 47].

The exact optimal timing for the operation is still to be determined. The age of the child when undergoing surgery is important because early surgery for bilateral cataracts can minimize deprivation amblyopia. In addition, if the surgery is performed more than four weeks after birth, it will increase the risk of strabismus and nystagmus. However, cases of aphakic glaucoma following cataract surgery within the first four weeks have also been described, so it is recommended that the procedure be performed when patients are 28 days old [48, 49]. Current recommendations state that unilateral cataracts should be treated at 4–6 weeks and bilateral cataracts at 6–8 weeks (some reviews extend this time to 10 weeks) [49, 50].

Prior to the operation, the ophthalmologist will apply drops to the eye in order to dilate the pupils and paralyze accommodation. A small cut is made on the outer edges of the cornea, in order to remove natural lens, and leaving the back of the capsule intact. Commonly used surgical procedures for congenital cataracts are lensectomy and extra-capsular cataract extraction (ECCE). In lensectomy the majority of the lens, including the posterior capsule, and anterior vitreous are removed. This creates a permanently clear visual axis. However, it requires a vitrectomy machine, and there is a potential increased risk of late retinal detachment due to manipulation of the vitreous. Pediatric surgeons have traditionally used a 20-gauge vitrector to remove cataracts in infants, but this can lead to complications due to the large instruments. Smaller incisions with 25- or 23-gauge vitrectors have advantages such as better wound healing and stability, potentially enabling sutureless surgery. However, the use of smaller gauges may limit maneuverability, make certain procedures more difficult, and increase operation times. Transcorneal 23G vitrectomy has shown fewer complications in pediatric cataract surgery. In general, for routine congenital cataracts, the 23G vitrectomy is preferred due to its small incision size, anterior chamber stability, and instrument stiffness. During ECCE in children, the elastic anterior capsule makes performing continuous curvilinear capsulorhexis (CCC) difficult. A small capsulorhexis (4–5 mm) or a can-opener capsulotomy can be done [47, 51].

The intraocular lens (IOL) is implanted in some of the cases, with the aim of improving vision after the surgery and to avoid aphakia. In the older population, operations without implantation of an IOL are rarely performed due to the lack of accommodation and hypermetropia in such an eye [49]. The available research suggests that IOL insertion is appropriate in most older children who have cataracts but need surgery. However, a difference is apparent in regard to the advisability of IOL implants during the first years of life. Because the majority of the eye's axial growth occurs during the first two years of life, it is difficult to choose an IOL power for an infant [52].

After cataract surgery, long-lasting rehabilitation is important (Figure 3). Immediately after surgery, spectacle correction should be introduced so that visual stimuli can reach the retina and allow vision to develop.

Visual recovery includes IOL, glasses, and contact lenses. In children, glasses still have a significant role because the power of an IOL is often inaccurate for the current refractive error; as a result, frequent adjustments to the child's refractive error are necessary with glasses [53]. In the case of unilateral cataracts, it is a challenge to compensate for postoperative aphakia with an ocular correction due to the phenomenon of anisometropia – the condition where the eyes have a different refractive power. In such a situation, a contact lens for the aphakic eye is used. In bilateral cataracts, there is no problem associated with anisometropia [50, 54]. In the majority of cases of unilateral cataracts, and occasionally in cases of poorer vision in one eye in bilateral cataracts, a temporary patch over
the stronger eye is employed. Occlusion therapy attempts to enhance vision in the weaker eye by forcing the brain to recognize the visual signals from that eye, which it may have previously ignored [53, 55, 56].

CONCLUSIONS

Congenital cataracts are one of the main causes of blindness in children. Congenital cataracts have a varied etiology, and it is not possible to determine the cause in every case. Unilateral cataracts are usually isolated sporadic incidents. The timing of surgery is the most important factor in the visual outcome so early diagnosis and implementation of treatment are crucial for children's eyesight. Early diagnosis and implementation of treatment are crucial for optimal visual development, prevention of amblyopia, normal sensory input, development of binocular vision, depth perception and cognitive growth. Timely intervention provides infants with the best opportunity to achieve good visual outcomes and overall well-being. For this reason, prospective parents should be questioned about family history, pregnancy and the child's other health problems. Also, due to the fact that congenital cataracts may be a part of a multisystem disorder, patients, their parents and siblings should be observed for any dysmorphic features.

DISCLOSURE

The authors declare no conflict of interest.

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