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Born with Clouded Eyes: A Literature Review on Congenital Cataract in Pediatric Ophthalmology

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ABSTRACT

There are about 70 million cases of childhood blindness and congenital cataract is one of the most major cause of blindness in children. This disease appears at birth or early phase after postnatal and can be seen by the appearance of lens opacity. Congenital cataract can occur in one or both eyes. The epidemiology of congenital cataracts varies across different populations, with the condition presenting as either isolated or part of a syndrome associated with other systemic abnormalities. The etiology of congenital cataracts is multifactorial, encompassing genetic factors, prenatal infections, metabolic disorders, and other environmental influences. In many cases, the precise cause may remain unclear. Diagnosis is typically made through clinical examination, with early detection being crucial for effective management. Management often involves surgical intervention to remove the cataract and may include the use of corrective measures, such as intraocular lenses or visual rehabilitation. Timely intervention and follow-up care are essential to optimize visual outcomes and minimize the risk of long-term visual impairment. This review aims to provide an overview of congenital cataracts in children, discussing the condition's definition, epidemiology, potential causes, diagnostic approaches, and management strategies, with an emphasis on improving outcomes through early intervention.

Keywords: congenital cataract; pediatric; ophthalmology.

INTRODUCTION

Congenital cataract is lens opacity that presents at birth or early in the postnatal period. It may be unilateral or bilateral. Because it occurs during early vision development, it causes serious vision loss and, more importantly, severe amblyopia [1]. Congenital cataracts have been an issue in the current global health. The research showed that the highest incidence in Asia (7.43/10,000) was usually diagnosed after 1 year of age. The research also showed that congenital cataracts were more frequently bilateral and the most common type was total cataracts the cause of 62.2% of cases of congenital cataracts were idiopathic and the prevalence of inherited cataracts was 22.3% [2].

Unfortunately, there was not enough data and research on the epidemiology of congenital cataracts in Indonesia. The research was conducted at RSUD Provinsi Nusa Tenggara Barat using secondary data showed that in the 2018-2019 period, 40 children had congenital cataracts. Most of the cataract sufferers were female (52.5%); living outside the city of Mataram (92.5%) with an age distribution of under 12 months (95%) and the rest over 12 months [3]. Of 195 children aged 0- 15 years old that were examined in Sumba and Yogyakarta, 113 children were experiencing blindness and 35,31% of cases were caused by problems in the eye lens [4].

The research in 2014 showed that DNA sequencing, high-resolution imaging, and new tools in pediatric surgery have improved the medical screening, detection, and management of congenital cataracts [5]. Research in 2015 showed in their study that early screening for congenital cataracts has been developed worldwide to optimize the management of affected children. Prenatal imaging diagnosis by ultrasound and, if needed, genetic testing, can be performed for a fetus at early gestational stages [6]. Based on the research in 2015, Microincision cataract aspiration combined with posterior capsulotomy, anterior vitrectomy, and primary intraocular lens (IOL) implantation is now recognized as the optimal surgical option for the management of a large part of pediatric cataracts [7]. In the research, posterior capsulotomy and anterior vitrectomy are particularly important to reduce posterior capsule opacification

(PCO) and recommended until 4–8 years, a presumed cooperative age for the procedure. Primary IOL implantation is usually performed in children older than 2 years of age. However, IOL implantation in children younger than 2 years of age remains a matter of controversy, despite the increasing evidence of safety for the procedure [8] The study suggested that the implantation should be performed at the age of 3 months old for unilateral cataracts and 7 months old for bilateral cataract [9].

DEFINITION

Congenital cataract is a disease that causes vision loss. This disease appears at birth or early phase after postnatal and can be seen by the appearance of lens opacity. Congenital cataracts can occur in one or both eyes. Because this disease happens to occur in early vision development, this may cause severe vision loss, such as amblyopia [1].

Congenital cataracts can be classified into several categories, including hereditary and non-hereditary classifications. The hereditary classification refers to cases where the cataract is caused by genetic factors, often running in families. On the other hand, the non-hereditary classification encompasses cases where the cataract is not associated with genetic factors and may be caused by environmental factors or other underlying conditions. In clinical settings, the morphological classification is commonly utilized. This classification focuses on the specific characteristics and appearance of the cataract, helping clinicians in diagnosis and treatment planning. By understanding the different classifications of congenital cataracts, healthcare professionals can better assess and manage these conditions for optimal patient care [1].

Hereditary pediatric cataracts exhibit various classifications, each associated with different underlying conditions. These classifications include isolated cataracts as well as those linked to metabolic diseases such as galactosemia, Wilson's disease, and diabetes. Renal diseases like Alport syndrome and Lowe syndrome can also be associated with hereditary cataracts. Additionally, musculoskeletal diseases (e.g., myotonic dystrophy, chondrodysplasia puncta), dermatological diseases (e.g., incontinentia pigmenti, Cockayne syndrome, Rothmund-Thomson syndrome), craniofacial anomalies (e.g., Hallerman-Streiff syndrome, Rubinstein-Taybi syndrome, Smith-Lemli-Opitz syndrome), and genetic anomalies (e.g., trisomy 13, 18, 21; 5p deletion, 11p deletion, Norrie disease, Nance-Horan syndrome) may also contribute to the development of hereditary cataracts.

Non-hereditary pediatric cataracts, on the other hand, can arise from various factors such as trauma, congenital infections (TORCH), drug use (e.g., steroids), radiation exposure, or exposure to teratogens.

Additionally, in clinical practice, the morphological classification of pediatric cataracts is commonly employed. This classification system helps categorize cataracts based on their specific characteristics and appearance. Examples of morphological classifications include anterior cataracts (such as anterior polar, anterior pyramidal, and anterior subcapsular cataracts), central cataracts (including nuclear, sutural, lamellar, cerulean, Christmas tree, pulverulent, aculeiform, polymorphic, crown-shaped, cuneiform, and coralliform cataracts), posterior cataracts (such as posterior lenticonus, posterior subcapsular, posterior polar, and oil droplet cataracts, persistent hyperplastic primary vitreous, and Mittendorf dots), and total cataracts (involving the entire lens, often without identifiable morphology at onset unless accompanied by additional ocular findings). Congenital Morgagnian and membranous cataracts may also fall into the category of total cataracts.

EPIDEMIOLOGY

Based on a meta-analysis in 2016 conducted using 27 eligible studies published from 1983 to 2014, the pooled prevalence was 4.24/10.000 people and based on the WHO is categorized as a rare disease. In Asia, congenital cataract has the highest incidence with a rate of 7.43/10,000. Followed by, the USA with the rate of 4.39/10.000, Europe with the rate of 3.41/10.000, and Australia with the rate of 2.25/10.000 [2].

Regarding the epidemiology of congenital cataract classification, such as laterality, morphology, comorbidity, and etiology. Bilateral cataracts accounted for 54.1% laterality. The three most common congenital cataracts were total (31.2%), nuclear (27.2%), and posterior subcapsular (26.8%) [1]. Based on the comorbidity, isolated cataracts were reported to account for 62.3%, cataracts with ocular disorders for 22.7%, and cataracts with systemic disorders for 17.3%. Hereditary cataracts accounted for 22.3%, and non-hereditary cataracts accounted for 11.5%. Lastly, idiopathic cataracts are accounted for 62.2% [10]. There is not much specific research regarding the epidemiology of Congenital cataracts in the world nor Indonesia due to limited public awareness and health system for rare diseases.

ETIOLOGY

According to a 2020 journal article., the etiology of congenital cataracts exhibits considerable diversity. The primary cause of congenital cataracts is idiopathic, accounting for 62.2% of cases. The remaining cases can be categorized into two groups: hereditary (22.3%) and non-hereditary (11.5%) congenital cataracts. Non-hereditary congenital cataracts are frequently linked to trauma and infections, with rubella and herpes simplex virus identified as the most prevalent causes [10].

When considering the lateralities of congenital cataracts, it is observed that bilateral cases are commonly associated with genetic and systemic diseases. On the other hand, unilateral cases are often linked to local anomalies, such as persistent fetal vasculature (PFV). PFV occurs when the embryonic hyaloid vasculature fails to regress completely, leading to congenital ocular dysgenesis.

Pediatric cataracts can have various causes, ranging from genetic defects that can be inherited to insults that occur during the development of the lens either in the fetal period or during childhood, as well as associations with systemic syndromes. The autosomal dominant type of inheritance is commonly observed in cases of hereditary cataracts. Genetic screening studies conducted in Australia have identified a total of 51 genes and loci that are implicated in pediatric cataracts. Mutations in genes responsible for coding transcription proteins such as PAX6, FoxE3, C-MAF, PITX3, MIP, and CRYAA, among others, are frequently observed. Additionally, mutations in crystallin and connexin genes are also commonly seen in the majority of pediatric cataract cases [11].

Congenital cataracts are mostly caused by mutations in protein structure. This may lead to severe functional consequences. The mutations that cause congenital cataracts are divided into some groups [1].

In humans, crystallin proteins make up over 90% of the soluble proteins found in the lens. They constitute nearly 35% of the lens mass and play a crucial role in maintaining its optical transparency and high refractive index. Crystallins are classified into three subgroups, namely α-, β-, and γ-crystallins, based on their elution order during gel exclusion chromatography [1]. These proteins are considered to be inherently stable and are synthesized in the lens fiber cells, which do not possess nuclei.

Crystallins are water-soluble proteins that have a very important role in the lens structure as the major component of lens protein. These proteins have been associated with various phenotypes of congenital cataracts. About 50% of autosomal dominant cataracts are caused by crystallin mutations. The β and γ crystallins can also be considered a single family. Not only in the eyes, crystallins are also located in the extraocular tissue. The function of crystallins is to stabilize the lens and transparency. Crystallins have various effects, such as antiapoptotic, antidegradation, and antioxidants. The example of crystallin mutations is detected in numerous genes. Such as *CRYAA, CRYAB, CRYBB1, CRYBB2, CRYBB3, CRYBA1, CRYGC, CRYGD*, and *CRYGS* [1].

The cell membrane protein that functions as the intercellular communication. Such as connexins, aquaporins, and other cell membrane proteins are associated with the mutations that cause congenital cataracts. About 25% of mutations of congenital cataracts are associated with connexin genes. Specifically, connexin 46 and 50, and LIM-2 proteins. Connexin proteins are essential components of gap junctions, which play a crucial role in facilitating intercellular communication and nutrient transfer in the avascular lens. They are responsible for transporting small biomolecules such as ions, nutrients, and metabolites between cells.

The cytoskeletal components are filensin and CP49, which produce beaded filaments. Cataract has been linked to mutations in the BFSP-2 (beaded filament structural protein 2) gene that encodes CP49 [1]. The arrangement of lens cells is a result of the interplay between the cytoskeleton, crystallin proteins, and cytoplasm. The cytoskeleton comprises a diverse set of proteins within the cytoplasm that serve various functions, including providing structural support, enabling cell movement, and determining and maintaining cell volume and shape. Within lens cells, there are three distinct filament types, distinguished by their diameter, subunit composition, and molecular organization: microfilaments, microtubules, and intermediate filaments.

Additionally, mutations in the developmental regulatory genes PITX3 (paired-like homeodomain 3), PAX6 (paired box 6), and HSF-4 (heat shock protein factor-4) can result in congenital cataracts [1]. In Japan, documented by Narumi *et al* in 2014, showed that congenital cataract with microcornea and/or iris coloboma was caused by the MAF (MAF bZIP transcription factor) gene mutation c.908A>C [12].

DIAGNOSIS AND MANAGEMENT

The diagnosis of congenital cataracts has been developed worldwide. The earlier the diagnosis will result in the more positive visual outcome regarding the management or surgery. A diagnosis can be performed during early gestational stages, by prenatal imaging using ultrasound and if needed, genetic testing.

When evaluating a patient with a pediatric cataract, it is important to conduct a thorough history, ocular examination, and systemic examination. The history should include details such as the age of onset, duration of symptoms, antenatal and perinatal history, developmental milestones, and any associated systemic abnormalities. Trauma, previous treatment, or surgery should also be considered [11].

Examining the ocular health of family members, particularly parents and siblings, can reveal undiagnosed lenticular changes that suggest an inherited cause of pediatric cataracts. Autosomal dominant forms are the most common, but the X-linked recessive pattern may also be present in children with Lowe syndrome and Nance-Horan syndrome [13].

A consultation with a pediatric specialist is necessary to eliminate any potential systemic associations or genetically transmitted disorders. Measurement of head circumference is important, particularly in cases where congenital cataracts are linked to dysmorphic syndromes such as Trisomy 21, Hallermann-Streiff-Francois syndrome, Lowe's Oculo-Cerebro-renal syndrome, Cri-du-chat syndrome (5p deletion), Nance-Horan syndrome, and Edward syndrome. If the attending physician or parents are unsure about when they first noticed the white reflex in the eye or the onset of the cataract, reviewing the family album can provide helpful information.

During the ocular examination, various assessments are conducted to evaluate a patient with pediatric cataracts. Visual acuity is measured using different tests depending on the age of the child. For preverbal children, the Bruckner test, cover test, resistance to occlusion, monocular fixation, fixation preference, vertical prism test, forced choice preferential looking, Teller acuity cards, optokinetic nystagmus, and pattern VEP are used. Verbal children undergo tests such as the detection acuity test, Catford drum test, STYCAR graded ball test, recognition acuity test, and direction identification test [11] A slit-lamp examination is performed to examine the anterior segment of the eye for any associated findings like microcornea, anterior segment dysgenesis, iris coloboma, cataract morphology, microspherophakia, ectopia lentis, or pre-existing posterior capsular defect. Intraocular pressure is measured to rule out glaucoma, particularly associated with congenital rubella syndrome [14]. Pupillary reactions are observed to gain an understanding of the health of the optic nerve head.

Additionally, direct and indirect ophthalmoscopy is performed to examine the posterior segment of the eye for any associated abnormalities, including vitreous hemorrhage, remnants of primary vitreous, fundal coloboma, optic or macular hypoplasia, and other related conditions. This comprehensive ocular examination helps in assessing and managing pediatric cataracts effectively.

Laboratory investigations play a crucial role in the evaluation of pediatric cataracts, helping to identify underlying conditions and genetic defects associated with the condition. These investigations include various blood and routine tests. A complete hemogram is performed to assess blood cell counts and detect any abnormalities. Blood sugar levels are evaluated to assess glucose metabolism, while urine routine microscopy examines urine for potential irregularities. Additional tests are conducted on a case-by-case basis, depending on the patient's history and examination findings. These tests may involve assessing serum calcium levels for hyper or hypoparathyroidism, conducting VDRL tests to screen for syphilis, and measuring antibody titers for TORCH infections, including Toxoplasmosis, Rubella, Cytomegalovirus, and Herpes simplex virus. Specific tests may be conducted to identify certain genetic disorders associated with pediatric cataracts. These can include red cell galactokinase or uridyl transferase tests for galactosemia, urine protein analysis for Alport syndrome, urine amino acid testing for Lowe syndrome, and urine sodium nitroprusside or plasma homocysteine testing for homocystinuria. Urine/serum copper tests may be performed to assess Wilson's disease, and karyotyping can be conducted to detect genetic defects [11].

Ocular investigations are essential in the evaluation of pediatric cataracts to accurately diagnose and differentiate them from other posterior segment pathologies.

One such investigation is B-scan ultrasonography, which is performed to rule out conditions that may mimic congenital cataracts, such as retinoblastoma, persistent hyperplastic primary vitreous, coats disease, and others. This helps in identifying the underlying cause of leukocoria, a common symptom associated with pediatric cataracts [15]. Ultrasound biometry is another valuable tool used in ocular investigations for pediatric cataracts. It provides important optical parameters like axial length (AL), anterior chamber depth (ACD), and lens thickness (LT), which are crucial for calculating the intraocular lens (IOL) power accurately. These measurements assist in determining the appropriate IOL for surgical intervention [16]. Keratometry is performed using handheld keratometers to assess corneal curvature. However, obtaining accurate readings relies on the child's cooperation during the procedure.

These ocular investigations aid in the precise diagnosis, treatment planning, and management of pediatric cataracts by differentiating them from other ocular conditions and providing essential measurements for IOL power calculation.

One of the treatment options for pediatric cataracts is mydriasis, which involves the use of 2.5% phenylephrine. This medication is specifically chosen for its mydriatic action, which is the dilation of the pupil. Mydriasis is employed in cases where there is a partial or nonamblyogenic cataract, allowing vision through the non-opacified area of the lens. By dilating the pupil, this treatment approach aims to improve visual access to the unaffected parts of the lens [11].

Surgery is recommended when certain criteria are met, including the presence of visually significant opacity in the lens. This may involve cataracts that cause vision equal to or worse than 20/60 or when the optic disc is not visible using an indirect ophthalmoscope. Additionally, surgery may be considered for central cataracts with a diameter of 3 mm or larger, posterior subcapsular cataracts, nuclear cataracts, bilateral cataracts, and cataracts associated with strabismus or nystagmus. These factors indicate the need for intervention to address the cataract and improve visual function [16].

If the cataracts lead to a high risk of amblyopia, surgical intervention is needed at the age of 6 weeks for unilateral cases and before the age of 8 weeks for bilateral cases. The best surgical choice for the treatment of a significant portion of children's cataracts is currently understood to be microincision cataract aspiration in conjunction with posterior capsulotomy, anterior vitrectomy, and primary intraocular lens (IOL) implantation.

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