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Cataract and genetic diseases

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Abstract

Despite the decreasing number of cases, cataract is still the leading cause of visual impairment and blindness worldwide. The search for the causes of this disease, its risk factors and the relationship with systemic diseases is the subject of many studies and attracts the attention of scientists around the world.

One of the most common cause of cataract and probably the most frequently reported in the literature, is aging. Other commonly described causes of cataracts are external factors and acquired diseases. Although genetic diseases are not the most common disorders associated with the occurrence and development of cataract, this review takes a broader look at this particular aspect, describing the relationship between cataracts and a group of genetic diseases. The links between cataracts and genetic diseases have been investigated. This review focuses on the diseases most frequently reported in the literature to be associated with cataracts, such as Down syndrome, myotonic dystrophy, neurofibromatosis type 2, Marfan syndrome, Wilson disease and Alport syndrome. The associations of cataracts with various genetic diseases, confirmed in previously published studies, were described. Despite the fact that it is difficult to distinguish individual factors influencing the development of cataract, the analyzed literature examples allowed to demonstrate that cataract in the course of the genetic disorders discussed in this review is not accidental.

Keywords: cataract, risk factors, genetic diseases

Introduction and purpose:

Cataract is a congenital or degenerative eye disease that leads to clouding of the lens and is one of the causes of blindness. Although number of people affect by cataract is decreasing, it is still main reason of global blindness, particularly in the developing countries[1,2].

The pathogenesis of cataract is multifactorial and not fully understood. However, in recent years, much has been discovered about the pathophysiology, epidemiology and risk factors affecting the development of cataract. Moreover, cataract has been associated with many systemic diseases and genetic disorders.

The most common cause of cataract is aging, but it can also result from trauma, radiation exposure or exist from birth. Risk factors include smoking, ultraviolet (UV-B) exposure, diabetes, excessive sunlight exposure, steroid and alcohol use [3] . Non-modifiable and modifiable risk factors can be distinguished (*Table 1.*).

With so many variables that can cause cataract and such a high burden of the disease, identifying risk factors is crucial for early diagnosis and stopping the progression of the disease.

Table 1. Non-modifiable and modifiable risk factors of cataract[4].

Non-modifiable risk factors	**Modifiable risk factors**
Aging (most common cause)	Smoking
Female sex	Alcohol intake
Race	Ultraviolet radiation
Myopia	Nutrition

Many connections between genetic diseases and cataract have been recognized, and although these are not the primary causes of that disorder, we believe they are just as significant. Among the genetic diseases that are linked to cataract described in the literature, those most frequently discussed have been selected for the review.

Material and methods:

A review of the PubMed database, supported with Google Scholar search, was performed. The articles were searched with the use of keywords such as “cataract”, ”genetic diseases”, “risk factors”, and chosen strictly focusing on the investigated connections (cataract-genetic disorders). The papers included in this review were selected based on the relevance of the research described, close relationship to the topic and publication date. Articles published over the last 10 years (2014-2024) were selected, but in some cases older studies were cited due to lack of appropriate sources.

Epidemiology:

Cataract is a leading cause of vision impairment and blindness globally. According to World Health Organization estimates, 94 million people worldwide suffer from cataract [2] . Furthermore, the WHO predicts that population growth and aging will raise the likelihood that more people may get visual impairment[2]. The prevalence of cataract increases with age but exact values varies depending on the region in which the study was performed: from 3-9% at age 55–64 years to 92-96% at age 80 years and older[5,6].

State of knowledge:

Down syndrome

Down syndrome is a syndrome of birth defects caused by the presence of extra genetic material of chromosome 21. Although Down syndrome is associated with mental disability and a characteristic phenotype, the course of the disease can also result in ocular manifestations one of which is cataract[7,8,9,10].

Among children with Down syndrome , the prevalence of cataract ranges from 1,4% to as much as 50%[8,10]. Such sizable differences may be due to both different diagnostic criteria and the inclusion of congenital and acquired cataract. However, studies seem to unequivocally show that bilateral cataract is more common in people with Down syndrome compared to the general population[7].

Early detection and treatment of cataract among the population of children with Down syndrome is especially important, as delay can result in visual impairment or even blindness. However, it is important to keep in mind that not all cataract cases require surgery[8].

Myotonic dystrophy

Myotonic dystrophy is a genetic disease characterized by progressive muscle weakness and prolonged muscle spasms. This is the most common form of muscular dystrophy, which occurs with a prevalence of 1/8,000 [11,12]. The muscles of the face, neck, forearms, hands, lower legs and feet are affected first and most often. However, ophthalmic symptoms may be the first sign of the disease, of which cataract is the most common. It is also important to keep in mind patients whose symptoms appeared at a late age or are so discreet that they do not cause a sense of illness, and the only symptom may be cataract.

It is now established that myotonic dystrophy manifests in at least two genetically different forms: type 1 (DM1) and type 2 (DM2) [13]. The cataract caused by myotonic dystrophy is generic and manifest as punctate opacities on direct ophthalmoscopy. Slit lamp examination reveals that they are situated in the posterior lens capsule and have a multicolored iridescent look, both of which are very suggestive of DM1 or DM2[14].

Neurofibromatosis type 2 (NF2)

Neurofibromatosis type 2 is an autosomal-dominant genetic disease with a prevalence of 1/60,000 [15] . Although NF2 is characterized by bilateral synchronous or metachronous schwannoma-type tumors of the auditory organ, patients are predisposed to developing lesions in the nervous system, skin and eyes. Among the ocular lesions we can distinguish Hamartoma of the retina , Epiretinal membranes and above all cataract, which is the most common and occurs with a frequency of 60-81% in patients suffering from NF2[16].

Cataract that is particular to this disease can only be diagnosed in patients under 50 years of age. These cataract include opacities in the peripheral cortical region of the lens and posterior subcapsular or capsular regions of the lens.

Around 80% of patients with NF2 develop juvenile posterior subcapsular cataract. An explanation for the pathophysiology of juvenile posterior subcapsular cataract could be that NF2-deficient posterior lens vesicle cells accumulate in front of the posterior capsule because they are unable to vertically elongate to form primary lens fiber cells due to abnormal adherence junctions[17].

In addition in 10-25% of cases, cataract impair vision and may require extraction[16].

Marfan syndrome

Marfan syndrome is an autosomal dominant genetic disorder of connective tissue caused by a mutation in the fibrillin-1 (FBN1) gene, which causes skeletal, cardiovascular and ocular symptoms. This disease's prevalence is estimated to be 1/5000 [18] . Of all the ocular manifestations, the most characteristic lesion is ectopia lentis, which is the most common and occurs with a frequency of 60-80% in people with Marfan syndrome [19] . However, it is important to remember that this is not the only ocular lesion that can occur in the course of this disease.

Although cataract is not a hallmark of Marfan syndrome, there are reports of cataract occurring in people with the condition. Compared to the general population, there is a significantly higher chance of having vision-threatening conditions like cataract. Common forms of cataract in Marfan syndrome include localized globular lens opacities and posterior subcapsular cataract[20].

Wilson disease

Wilson's disease is one of the rare autosomal recessively inherited genetic disorders. As a result of mutations in the ATP7B gene, the excretion of copper from the body is impaired, resulting in excessive accumulation of this metal in the body - mainly in the liver, brain, kidneys and cornea, leading to damage to these organs.

Among all the possible ocular manifestations seen in patients with Wilson's disease, the most common are Kayser-Fleischer ring and sunflower cataract (SC) [21,22] . A thin, centralized opacification encompassing one-third to half of the anterior lens pole surface area is the hallmark of a sunflower cataract, which is situated directly under the anterior capsule [23] . A central disk with radiating petal-like spokes that give the cataract its name is caused by copper deposition in the lens capsule[21].

Typically, sunflower cataract do not cause visual impairments. It can only be detected by a slit-lamp examination and cannot be seen with an ophthalmoscope or the naked eye. When treated with copper chelating agents, sunflower cataract usually regress[21].

Alport syndrome

Alport syndrome (AS) is a congenital, genetic kidney disease with additional hearing and vision disorders. Although the incidence of Alport syndrome is 1/50,000 [24] , it should be emphasized that it is the most common of the congenital nephropathies.

AS is caused by the abnormal structure of one of the components of connective tissue, type IV collagen, which is an important element of the structure of the ear, eye and kidney glomeruli. Lack of collagen IV in the cornea, lens capsule, and retina of the eye causes corneal opacities, anterior lenticonus, fleck retinopathy, and temporal retinal thinning[4].

Cataract is not the most common form of ocular lesions in this disease, nevertheless, it has been shown that it can occur in the course of Alport syndrome. Cataract develop as a result of the healing of small spontaneous ruptures that occurs due to partial splitting in the lens capsule caused by a lack of the aforementioned collagen[25].

Conclusions:

A number of links between cataract and genetic diseases proven by research have been demonstrated. As shown in this review, despite the fact that it is not the most common cause of cataract, they are important and should not be ignored. At the same time, in the complexity of symptoms and the course of diseases occurring simultaneously, it is difficult to distinguish individual factors and follow cause-effect relationships. Although many connections already have been proven, there are still many assumptions and speculations that need clarification. In authors' opinion, this aspect requires further research and advanced analysis in order to gain more knowledge and acquire broader perspective in this field.

Author's contribution:

Conceptualization, MK, and NSD; check, MO, PC and KC; formal analysis, NSD,WM,MN and KZ; investigation, MK,NSD and MRS; data curation, MO,MN, PC and KZ; writing - rough preparation, MK,MRS,AM and KC; writing - review and editing, MK,AM; supervision, MK; project administration, MK.

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