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UNLOCKING THE FACTORS THAT CAUSE EARLY CATARACT

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ABSTRACT
Cataract is one of the reversible blindness in this world. Cataracts, a leading cause of blindness, result from various factors beyond aging. While senile cataracts are common in the elderly, their diverse forms suggest multiple causes. Childhood cataracts are a leading cause of blindness in underdeveloped nations, particularly India, where they account for 7.4-15.3% of all blindness cases. Risk factors include smoking, UV-B radiation, diabetes, steroid use, heavy alcohol consumption, electric shock, and genetic conditions like Down syndrome and hereditary cataracts. Metabolic disorders such as galactosemia, infections like TORCH, and chronic diseases including chronic kidney disease, atopic dermatitis, hepatitis C, Wilson's disease, celiac disease, systemic lupus erythematosus, Fabry disease, and Marfan syndrome also contribute. Myopia, hypertension, and trauma, particularly in children, increase risk. Notably, high-dose vitamin C supplements may elevate cataract risk, unlike lower doses in multivitamins. Understanding these factors emphasizes the need for targeted prevention and early intervention to manage cataract risk and reduce vision impairment globally. In this review article we mainly find different types of factors that cause cataract.

INTRODUCTION
There are two types of blindness, Irreversible blindness and reversible blindness; the main aim is to avoid reversible blindness, to control the warden of blindness. Cataract is one of the reversible blindness in this world. According to the previous study there are 70 million facing childhood blindness and childhood cataracts accounting for approximately 10 million, which is almost 14% of the total [1]. A timely diagnosis and surgical intervention are critical for recovering vision and improving the overall health of affected youngsters.
Cataracts are classified into different categories according to their location and cause. There are several forms of cataracts: congenital cataract, nuclear sclerotic, subcapsular cataract, cortical cataract, Christmas tree cataract.

- **Congenital cataract**: - Congenital cataract is a lens opacity that appears at birth or develops shortly after in the postnatal era. It may be unilateral (affecting only one eye) or bilateral (affecting both eyes). Congenital cataract, which arises during critical phases of visual development, can cause considerable vision loss and, more significantly, severe amblyopia (lazy eye). Long-term follow-up and therapy are critical for affected individuals, as the underlying cause of congenital cataracts, cannot be determined in a large majority of instances. This emphasizes the significance of initiatives such as Vision 2020: Right to Sight, a global campaign aimed at eliminating preventable blindness globally. One of the primary goals of this project is to address the causes of childhood blindness, such as congenital cataract [2].

- **Nuclear sclerotic cataract**- is primarily an age-related disease produced by changes that occur with age. It is frequently associated with myopia, which causes a secondary increase in the refractive index, allowing some older individuals to read without glasses, a phenomenon known as "second sight." In some situations, a hypermetropic shift can occur. Nuclear sclerosis is distinguished by a yellowish tint caused by the deposition of urochrome pigment, which is most apparent under oblique slit lamp light. While retro illumination reveals a strong red reflex, a thorough examination is required to distinguish between the nucleus and cortex. In severe situations, the nucleus may appear brown or even black [3].

- **Subcapsular cataracts**- come in two types:
  (1) Anterior subcapsular cataract- This type of cataract develops behind the anterior lens capsule and is linked to fibrous metaplasia of the lens epithelium.

  (2) posterior subcapsular cataract- It is in front of the posterior capsule and appears granular or plaque-like on an oblique slit lamp examination. Retro illumination gives these cataracts a black and vacuolated appearance due to enlarged migrating

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epithelial cells. Because they are placed at the eye's nodal point, posterior subcapsular cataracts have a considerable impact on vision, resulting in symptoms like glare, halos, and photophobia [4].

- **Cortical cataracts**- may damage the anterior, posterior, or equatorial cortex of the lens. They appear as clefts and vacuoles between lenticular fibers, resulting in cortical hydration. This produces distinctive wedge-shaped (cuneiform) or radial spoke-like opacities, which are frequently first seen in the inferonasal quadrant. Glare and photophobia are two common symptoms related to cortical cataracts [5].

- **Christmas tree cataract**- is a rare kind of cataract distinguished by its unique look. Polychromatic, needle-like opacities are typical of the lens' deeper cortex and nucleus. The name comes from its distinctive colors and structure, which resembles a Christmas tree. This type of cataract may not have a substantial impact on vision in the early stages, but it can cause visual impairment as it progresses. Because of its rarity, further research is required to completely understand its causes and the best treatment choices [6].

Previous research has indicated that delayed presentation for therapy among children with childhood cataract is a common problem in low-income nations. These delays have been connected to a variety of causes, including socio-demographic and cultural concerns, as well as health-care system issues. It is critical to examine the precise causes of such delays in our environment to develop effective interventions and increase access to timely care [7].

India faces a tremendous difficulty with roughly 280,000 to 320,000 visually handicapped children, resulting in an estimated $3.5 billion in economic losses. Improving community awareness, assuring early detection by healthcare practitioners, and permitting timely intervention by ophthalmologists are all critical steps toward addressing this issue. With these initiatives, we may aspire to eliminate preventable childhood blindness by 2020 [8]. Childhood cataract-induced blindness is a huge challenge, resulting in substantial economic loss, societal burden, and morbidity. Cataracts blind an estimated 200,000 children worldwide, with 20,000 to 40,000 children born with congenital cataracts each year. However, the prevalence of this illness varies around the globe [9].

Congenital cataracts involve a wide range of causes, and the exact cause in many children is unknown. But some of known reasons are genetic predispositions, metabolic abnormalities, and environmental influences, which can result in severe vision impairment and have a significant impact on a child's development, learning, and quality of life. It is the most widespread visual loss in children. However, autosomal dominant inheritance is frequently found in these circumstances, which means that a parent with a gene mutation has a 50% probability of passing it on to their child. Various genes have been related to this illness, which can arise as solitary cases or as part of larger syndromes. Understanding these genetic variables is critical for diagnostics and genetic counseling [10].

Untreated cataracts in children lead to tremendous social, economic, and emotional burden to the child, family, and society. Blindness related to pediatric cataract can be treated with early identification and appropriate management. Most cases are diagnosed with routine screening whereas some may be diagnosed after the parents have noticed leukocoria or strabismus [11]. Early diagnosis and treatment are crucial for visual prognosis. It can be associated with various ocular and systemic abnormalities. Many genes have been identified in the molecular etiology of congenital cataract. Most mutations have been reported in the crystalline genes [12]. To estimate the occurrence of early cataract among patients with Down's syndrome and to evaluate the clinical characteristics of the cases [13]. To reduce the impact of childhood cataracts on blindness, we must increase access to eye care, enhance public awareness of the need for early identification, and engage in research to better understand the problem and develop viable therapies [14].

Prevalence

Childhood cataracts are the leading cause of blindness in underdeveloped nations such as India, accounting for 7.4-15.3% of all cases. This disorder not only impairs vision but also shortens children's quality-adjusted life expectancy. Higher prevalence is associated with lower living standards, with incidence rates stable across genders and education levels. According to studies, 67% of mothers with afflicted children experienced health concerns throughout their pregnancy, with 22% needing medication. Furthermore, 22% of congenital cataracts relate to systemic illnesses, whereas 27% include ocular impairment, which is frequently detected accidentally during routine eye exams [15,16].

Childhood blindness is responsible for around 70 million blind-person-years, with childhood cataracts accounting for approximately 10 million (14%) of them. This demonstrates the huge influence of childhood cataracts on worldwide blindness and emphasizes the importance of effective prevention and treatment efforts to address the problem [17]. Pediatric cataracts are a curable illness that is the major cause of childhood blindness, accounting for 7.4% to 15.3% of cases. Pediatric cataracts have a considerable impact, accounting for many avertable disability-adjusted life years (DALY). This stresses the need of early detection and intervention in pediatric cataract management in order to avoid long-term vision impairment and improve the quality of life for affected children [18,19].

The annual incidence of pediatric cataract ranges from 1.8 to 3.6 occurrences per 10,000 children, whereas the median frequency is at 1.03 cases per 10,000 children, with a range of 0.32 to 22.9 cases per 10,000. Notably, the prevalence of juvenile cataract is higher in low-income economies, with rates ranging from 0.63 to 13.6 cases per 10,000 children, as opposed to high-income

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economies, where rates range from 0.42 to 2.05 cases per 10,000 children. Furthermore, research shows that there is no substantial difference in prevalence based on gender or laterality of the illness. This report emphasizes the global burden of pediatric cataract and the inequalities in prevalence across economic situations [20].

It was discovered that during pregnancy, 67% of women claimed a history of illness, with 22% reporting that they had used drugs during this time. These data indicate a high prevalence of mother health concerns and drug use during pregnancy, which may have consequences for the child's health. Understanding the maternal health background is critical for evaluating the risks associated with childhood diseases, such as pediatric cataracts [21,22]. Congenital cataract is associated with ocular abnormalities in 27% of cases and systemic abnormalities in 22%. Diagnosis is frequently accidental, with 41% of cases discovered during routine examinations, whereas leukocoria and strabismus account for 24% and 19% respectively [23].

The timing of the insult during development is essential since it affects which area of the lens is impacted. Congenital cataract has a genetic component in 8.3% to 25% of cases, with roughly 75% demonstrating an autosomal dominant inheritance pattern. This emphasizes the importance of genetic variables in the etiology of congenital cataracts, underlining the need for a family history examination in affected individuals [24]. India bears a major burden of around 280,000 to 320,000 visually handicapped children, resulting in an estimated economic loss of $3,500 million. This emphasizes the critical need for effective interventions and resources to address childhood blindness and visual impairment in the country, which can have far-reaching social and economic consequences for affected individuals and families [25,26].

Childhood cataracts provide enormous obstacles, resulting in large economic losses, social hardships, and health concerns. Currently, cataracts cause blindness in an estimated 200,000 children worldwide, with 20,000 to 40,000 infants born with congenital cataracts every year [27,28]. Childhood cataracts occur at varying rates around the world. For example, a study of blind students in West African schools discovered that lens-related anomalies caused 15.5% of blindness. In contrast, the percentages are significantly higher in Southern Africa, where 35% of blindness is caused by these conditions in Malawi, and Eastern Africa, where 33% of blindness is reported in Ethiopia. Meanwhile, in South America, Chile has a lesser prevalence of 9.2%, while South India in Asia has a 7.4% rate [29,30,31].

Types of Cataracts

- **Senile cataract-** Cataracts have long been connected with aging, hence the name "senile cataract." However, the variety of morphological forms and their unique positions inside the lens, as well as the fact that cataracts can occur at any age, indicate that aging is not the only reason. This complexity calls into question the idea that senile cataracts are solely the result of aging [32].
- **Cortical cataract-**Cortical cataracts may be caused by recurrent internal deformations in the lens during accommodation, as well as alterations in lens proteins (figure 1). Wilhelm Schoen initially introduced the hypothesis that accommodation pressures could contribute to cortical cataract formation in a speech at Leipzig University in 1896 [33,34]. This theory has been revisited by researchers such as Fisher and Pau. Angra et al. observed that shear pressures in the lens cortex may disturb the physiological milieu, making it vulnerable to variables such as UV radiation and oxidative stress, which decrease transparency. Recent research suggests that emmetropes and hyperopes, who accommodate more than myopes, have a higher incidence of cortical cataracts than myopes [35,36,37].

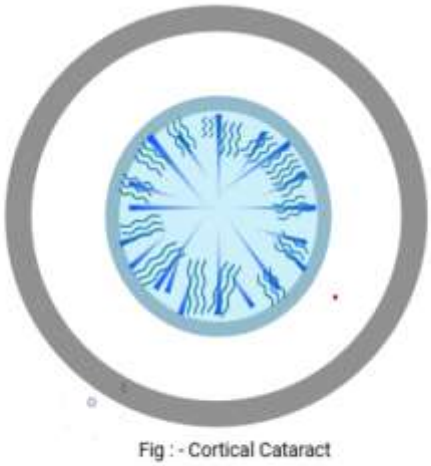


Fig 1 Cortical Cataract

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- **Nuclear sclerosis cataract-**As humans age, the nucleus of the crystalline lens becomes opaque and hard, resulting in nuclear sclerotic cataract (figure 2). These cataracts are the most common cause of cataract surgery in Western nations. Cataract surgery is the most common surgical treatment in the United States, costing more than $3 billion per year [38].

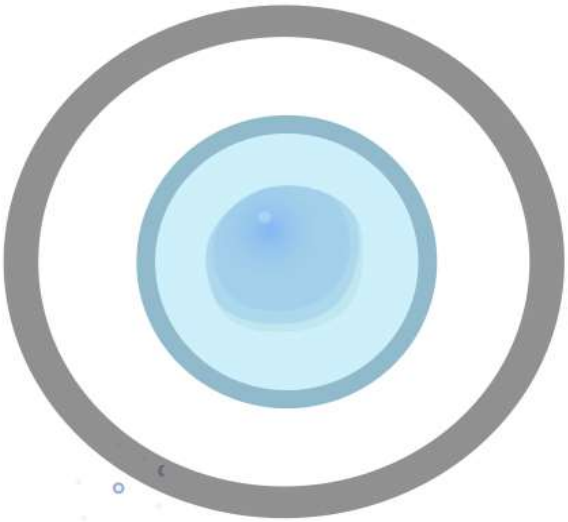


Fig: - Nuclear Cataract

Fig 2 Nuclear Cataract

Factors that cause cataract

- **Age: -** The combined impacts of aging and population increase are increasing the burden of blindness worldwide. A major cause of blindness, cataracts are mostly age-related, and the risk rises with increasing life expectancy. Cataracts and associated vision impairments are predicted to become more common as the population's share of elderly people rises. This emphasizes how important it is to make eye care and cataract treatment more accessible, particularly in aging cultures [39].

- **Smoking: -** West and Valmadrid examined many research on smoking as a risk factor for nuclear cataracts[i] [40]. In eight of the ten trials examined, the researchers discovered a consistent link between smoking and nuclear cataract. Key findings include the strength of the link, a lesser cataractogenic effect in former smokers compared to current smokers, indicating some reversibility, and a clear dose-response relationship [41,42]. Smoking was found to be responsible for up to 17% of nuclear cataracts in the population [43]. These findings reinforced the message of "Stop Smoking" ads, emphasizing not only the risk of lung cancer, heart disease, and chronic obstructive pulmonary disease, but also the additional risk of vision impairment caused by cataracts.

- **UV-B radiation: -** McCarty and Taylor's evaluation of 22 research discovered a direct correlation between lifetime UV exposure and increased cortical cataract prevalence. The most compelling data came from studies that measured individual UV-B exposure and dose response. Individual actions in places with equal sunlight can result in a UV-B exposure differential of up to 18 times. UV radiation is responsible for around 10% of the population's risk of cortical cataract, with the WHO estimating that it causes 20% of all cataract-related blindness worldwide [44].

- **Diabetic: -**The link between "sugar cataracts" and metabolic illnesses like diabetes mellitus and galactosemia has been known for centuries, with early case reports indicating the relationship long before medical therapies were created. This association was eventually validated through biochemical and experimental study, which helped us to understand the underlying mechanisms. Clinical studies have also demonstrated that people with diabetes had a higher prevalence and faster development of some cataract forms, including cortical cataracts and posterior subcapsular opacities. These data imply that elevated blood sugar has a major influence on the eye lens, leading to cataract development at a younger age than the general population [45,46]. According to research, diabetes accounts for approximately 4% of all cataract cases, emphasizing its function as [47].

- **Uses of steroids: -** Reviews by Hodge et al. and West and Valmadrid have found a strong link between steroid use and the development of posterior subcapsular cataracts, which is backed by biological plausibility and

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consistent findings across studies. Systemic and topical steroids have been found to be important risk factors for cataract formation, and inhaled steroids have also been linked to an increased risk [48]. However, Hodge et al. determined that the population-attributable risk of cataracts from steroid usage is rather modest, as most people do not use steroids on a regular basis.

- **Uses of alcohol: -** Several studies have suggested that alcohol is a risk factor for cataracts, namely posterior subcapsular opacities, although these findings should be regarded with caution due to inherent biases [49]. Many studies did not report on alcohol intake, despite the fact that it was frequently gathered, which could indicate that there is no substantial link. Furthermore, participants may have underreported their alcohol consumption out of embarrassment, or health-conscious persons may be less inclined to indulge in heavy drinking. Drinking habits vary by culture, which may alter the outcomes. The Beaver Dam Eye Study discovered a complex pattern, with severe drinking associated with injury and moderate alcohol consumption appearing to have a protective effect [50].

- **Electric shock: -** A careful analysis of the existing literature clearly supports the idea that electric cataracts can form as a result of an electric current coming into contact with a specific place on the skull or close to the eye. This syndrome has been well recognized as a possible side effect of electrical injury. However, based on our data, we infer that electric cataracts do not usually manifest as a delayed-onset impact after an electrical damage. In fact, our findings indicate that the development of electric cataracts is neither common nor expected in the aftermath of electrical damage. As a result, we do not find evidence to support the need for routine cataract screening for all patients who experience electrical harm, as the risk of acquiring electric cataracts appears [51].

- **Down syndrome: -** According to research, the frequency of cataracts, a common visual ailment in children with Down syndrome, can vary greatly, from 6% to as high as 50%. These cataracts, which may be inherited or develop over time, can have a major impact on vision. Children with Down syndrome frequently have various eye-related conditions in addition to cataracts. People with hyperopia, or farsightedness, frequently struggle to focus on close things. Involuntary, rhythmic eye movements, or nystagmus, can also happen. Another common disorder that can result in misalignment or crossed eyes is strabismus, which is characterized by improper eye alignment. Additionally, children with Down syndrome are more likely to have entropion, a condition in which the eyelids turn inward, irritating the eye [52].

- **Hypertension: -** Identifying risk factors for cataract is critical, as multiple studies have shown that hypertension contributes significantly to its development. Elevated blood pressure has been associated to increased C-reactive protein (CRP), a sign of systemic inflammation. Because cataracts are associated with severe inflammation, hypertension may aid in their development via inflammatory pathways. The link between hypertension and cataract pathogenesis emphasizes the need of controlling blood pressure to potentially lower cataract risk. Inflammation-driven pathways are thus critical to the evolution of cataracts in hypertensive people [53,54].

- **Norrie disease: -** Dense congenital cataracts, retinal folds, retinal detachment, vitreous hemorrhage, and bilateral retrolental masses made of hemorrhagic vascular and glial tissues are the hallmarks of Norrie disease, an X-linked recessive condition. It is caused by mutations in the X chromosomes NDP gene. Developmental delays and sensorineural hearing loss are also linked to this issue. Although the severity of these symptoms might vary, controlling the disorder's effects on development, hearing, and vision requires early identification and care [55].

- **Nance-horan syndrome: -** Males are the main victims of Norrie syndrome (NHS), an X-linked recessive condition that manifests as cataract–oto–dental syndrome, which includes bilateral dense stellate or nuclear cataracts, microcornea, anteverted and simplex pinnae, and dental abnormalities. Female carriers usually have milder symptoms, such as presenile cataracts, a small corneal diameter, and punctate opacities along the posterior Y-suture of the lens. The degree of these systemic and ocular symptoms, which are typical of NHS, can differ from person to person, with men typically exhibiting more severe symptoms [56].

- **Hereditary: -** In 8.3% to 25% of instances, congenital cataracts are inherited, with 75% of cases having an autosomal-dominant pattern [57]. These cataracts, which include crystalline aculeiform, Coppock-like, Volkmann-type, zonular with sutural, posterior polar, anterior polar, cerulean, zonular pulverulent, and myotonic dystrophy 1-like cataracts, have varying penetrance.

- **Galactosemia:-** Mutations in GALK1, galactose-1-phosphate uridyltransferase, or UDP-galactose-4-epimerase cause galactosemia, which is characterized by elevated serum galactose levels. Osmotic damage and "oil droplet cataracts," which usually manifest as nuclear cataracts but may also manifest as anterior or posterior subscapular cataracts, are the results of galactitol

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buildup. A diet devoid of galactose can reverse these cataracts. In addition to lesser cataracts, galactokinase deficiency is associated with jaundice, vomiting, failure to thrive, and intellectual impairment [58].

- **Torch infection: -** Congenital cataracts are often connected with congenital infections, specifically TORCH infections (Toxoplasma, Rubella, Cytomegalovirus, Herpes, and Syphilis), of which rubella is the most common. Other eye conditions such pigmentary retinopathy, microphthalmos, glaucoma, iris dystrophy, and chorioretinitis can also be symptoms of these infections. The type of infection and the time of exposure during pregnancy affect the severity and variety of eye symptoms. Babies with rubella, in particular, are known to experience serious eye problems [59]. In the Indian subcontinent, TORCH infections are common; up to 20% of patients are seropositive [60].

- **Myopia: -** Three prospective and eight cross-sectional studies were conducted to investigate the link between myopia and cataracts (both incident and prevalent). These research sought to establish whether myopia is a risk factor for the development or occurrence of cataracts in various groups. The findings help to comprehend the potential link between myopia and cataract production [61]. Nine of eleven studies indicated a significant link between myopia and posterior subcapsular cataract (PSC). This shows that myopia could considerably raise the likelihood of acquiring PSC [62].

- **POAG: -** Our findings indicate that genetic variables linked to primary open-angle glaucoma (POAG) and myopia may be causal risk factors for age-related cataract [63].

- **HBMI: -** This study identified new genetic loci associated with cataracts, however more research is needed to investigate the causal pathways of cataract formation. Previous research has identified clinical and behavioral risk factors for cataracts, including type 2 diabetes, high blood pressure, and a high body mass index (HBMI) [64].

- **Renal disease (CKD): -** Recent research have looked into the relationship between chronic kidney disease (CKD) and ocular disorders such retinopathy and cataracts. CKD patients may be at a higher risk of cataracts due to variables such as hypocalcemia, oxidative stress, and higher amounts of circulating urea. These factors can cause water collection in the lens, which contributes to cataract formation. Understanding these pathways can aid in managing cataract risk in CKD patients [65].

- **Atopic dermatitis (eczema):-** Atopic dermatitis is associated with a variety of ocular problems, including conjunctivitis, keratoconus, iritis, cataracts, and retinal detachment. Cataracts affect around 10% of those who have atopic dermatitis. This link emphasizes the importance of vigilant eye monitoring in individuals with atopic dermatitis in order to recognize and manage any ocular disorders. Early intervention can help avoid or treat issues like cataract development [66].
- **Hepatitis c virus (HCV): -** When compared to the age-matched general population, patients with age-related cataracts had noticeably higher hepatitis C virus (HCV) seropositivity. This implies that HCV infection could play a role in the onset or advancement of cataracts. The results show that HCV may be a risk factor for cataract development [67].

- **Wilson's disease: -** Cataracts arise in Wilson's disease as a result of copper deposits behind the lens capsule, giving the condition its distinctive sunflower appearance. Unlike traditional cataracts, these deposits do not severely reduce visual acuity. The cataract comprises a central disc with spreading petal-like fronds that may be seen with the naked eye. Sunflower cataracts are prevalent in 2% to 20% of people with Wilson's disease and are a prominent ocular symptom of the ailment [68].

- **Celiac disease: -** Mollazadegan and colleagues carried out population-based cohort research to determine the risk of cataracts in people with biopsy-proven celiac disease (CD). Their findings revealed that people with CD are more likely to develop cataracts. This lends support to the theory that CD may lead to cataract formation, emphasizing the importance of monitoring eye health in these patients [69].

- **Traumatic: -** Children's traumatic cataracts in India have different causes than in Western countries. Bow and arrow occurrences are the primary cause of open-globe injuries, which happen three times more frequently than closed-globe injuries [70].

- **Systemic lupus erythematosus: -** One known consequence of systemic lupus erythematosus (SLE) is cataract development. In this population, the prevalence of cataracts ranges greatly, from 5% to 32%. The length of illness, the usage of corticosteroids, and the existence of additional underlying medical disorders are some of the variables that affect this difference. Long-term steroid medication can raise the risk of lens opacification, which is frequently linked to cataracts caused by SLE [71].

- **Fabry disease: -** Fabry cataract like cataracts caused by head trauma or cortisone, Fabry's cataract is

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characterized by subcapsular opacities along the posterior lens suture lines. Soon after it develops, this kind of cataract usually results in severe vision abnormalities. Patients frequently noticeably lose their visual acuity and become more sensitive to light [72]. To control symptoms and stop more vision damage, early intervention is crucial.

- **Mafran syndrome: -** Although the overall prevalence of cataracts in Marfan syndrome is not higher than in the general population, they usually appear earlier in life. Early-onset lens opacities, which can seriously impair vision, are the condition's defining feature. Localized globular lens opacities and posterior subcapsular cataracts are the two most prevalent types of cataracts observed in people with Marfan syndrome [73].

- **Vitamin c: -** A recent prospective research of women discovered that high-dose vitamin C supplements, but not multivitamins containing lower doses of vitamin C, were associated with a higher incidence of age-related cataract extraction. This shows that excessive vitamin C intake may be linked to cataract formation. In contrast, lesser levels found in multivitamins did not produce the same impact. These findings emphasize the possible hazards of taking large doses of vitamin C for eye health [74].

CONCLUSION

Cataracts are caused by a complex interplay of factors that result in the clouding of the eye's natural lens, which has a significant impact on vision and life quality. This review emphasises the multifaceted nature of cataract genesis, highlighting the importance of age, genetic predispositions, and environmental factors such as UV exposure. Lifestyle factors such as smoking, alcohol consumption, and nutrition, as well as systemic conditions like diabetes mellitus, all increase the risk of cataract development. Medications, particularly corticosteroids, are significant contributors. The underlying mechanisms of oxidative stress and inflammation provide important insights into potential intervention targets. A thorough understanding of these factors is essential for developing effective prevention and treatment plans. Public health initiatives focused on education, lifestyle changes, and regular eye screenings, combined with advances in medical research, hold promise for reducing the prevalence and impact of cataracts worldwide.

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