International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Ocular Surface Diseases: A Comprehensive Review of Dry Eye, Uveitis, Glaucoma, and Age-Related Macular Degeneration

Gaurav P. Aswar[1], Pooja R. Hatwar[2], Dr. Ravindra L. Bakal[3], Om N. Ajmire[4]

[1,2,3,4]Department of Pharmaceutics, Shri Swami Samarth Institute of Pharmacy, At Parsodi, Dhamangaon Rly, Dist -Amravati (444709) Maharashtra, India.

Abstract:
Ocular surface diseases, including dry eye, uveitis, glaucoma, and age-related macular degeneration, are a significant cause of visual impairment and blindness worldwide. These conditions are complex and multifactorial, involving various risk factors such as age, genetics, and environmental factors. Dry eye disease, characterized by inflammation and damage to the ocular surface, is a prevalent condition affecting millions of people globally. Uveitis, glaucoma, and age-related macular degeneration are other significant ocular surface diseases that can lead to severe visual impairment if left untreated. Understanding the anatomy of the eye, including the eyelid and ocular surface, is crucial in diagnosing and managing these conditions. This review aims to provide a comprehensive overview of ocular surface diseases, their risk factors, and treatment. We discuss the importance of preoperative ocular surface evaluation and the role of inflammation in ocular surface diseases. A thorough understanding of these conditions is essential for developing effective treatment strategies and improving patient outcomes.

Keyword: Anatomy of eye, Ocular surface diseases, Dry eye disease

1. Introduction

Dry eye disease, a broad range of ocular disorders, is a lack of tear film. Homeostasis brought on by hyperosmolarity and tear film instability, which cause symptoms such inflammation and injury to the ocular surface [1]. In addition to the neurosensory system innervating the ocular surface and the Meibomian and lacrimal glands helping to stabilize the tear film, dry eye disease (DED) is a multifactorial condition of the ocular surface that is characterised by chronic self-perpetuating inflammatory damages of the cornea, conjunctiva, and covering tear film [2]. In DED, the ocular surface is compromised, and the presence of inflammation renders the eyes vulnerable to recurrent ocular integrity breaches [3]. Keratoconjunctivitis sicca, also referred to as dry eye disease (DED), is a widespread eye illness that affects millions of individuals worldwide, with a prevalence of 5 to 50%. "A multifactorial disease of the ocular surface characterised by a loss of homeostasis of the tear film and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles," is how the Tear Film & Ocular Surface Society (TFOS) Dry Eye Workshop II (TFOS DEWS II) defined dry eye in 2017. The

impact of this condition has grown globally in recent years, especially among younger people [4]. Because of its distinct structure and ongoing exposure to the outside world, the ocular surface develops a persistent symbiotic microbiota that is essential to preserving the immunological balance of the surface. Numerous eye conditions can result from a disturbed microenvironment. About 150 times more microbial genes than human genes are found in the gut, which the National Institutes of Health (NIH) in the United States has intensively investigated as a crucial mucosal region for understanding the human microbiome [5]. Ocular surface inflammation is the primary reason behind the loss of tear film homeostasis, although there are other contributing factors as well (Wei and Asbell 2014). The following are additional potential mechanisms: High glucose levels in tears cause advanced glycation end products (AGEs) to accumulate and epithelial cells to undergo apoptosis. causes corneal neuropathy and damage to the ocular surface. causes the glands to secrete less and blink less frequently [6]. Air pollution is immediately exposed to the eye. According to research conducted in the developing countries, household air pollution is linked to eye conditions including cataracts. Additionally, age-related macular degeneration (AMD) and cataracts are linked to cigarette smoking [7]. More than 90% of the tear film is made up of the mucogel aqueous layer, which is mostly made up of water (98%) along with proteins, growth hormones, and salts. It supports the functions of hydration, lubrication, refraction, and infection protection and is secreted by the lacrimal and auxiliary lacrimal glands. The ocular surface is flushed and dirt and other harmful chemicals are removed by the turnover and outflow of tears during blinking [8]. While the fibrotic phase might continue indefinitely, the active phase usually lasts 6 to 18 months. The clinical activity score (CAS) is a crucial instrument for tracking the severity of the disease. It has been demonstrated that the CAS, which has a score range of 0 to 10, may predict how well anti-inflammatory treatments would work.

- The following seven make up the CAS:

Components include: Chemosis (conjunctival oedema); swollen caruncle (flesh body at the medial angle of the eye); redness of the eyelids; redness of the conjunctiva; swelling of the eyelids; and pain behind the globe for the past four weeks as well as pain when moving the eyes [9].

2. Anatomy of eye

There are three categories for the human face's anatomy: upper, middle, and lower. The upper face contains the eye and periorbital region. Therefore, to comprehend how cosmetics affect the eye, an understanding of anatomy is required.

2.1 The eyelid

The eye is mainly shielded from mechanical stress by the eyelid, a thin layer of skin. The eyelid's ability to provide necessary nutrients and facilitate the even distribution of tears throughout the eye, followed by their drainage through the lacrimal puncta, is another crucial function. The eyelid also controls the amount of light entering the eye through squinting and keeps the globe in the proper orbital position [10].

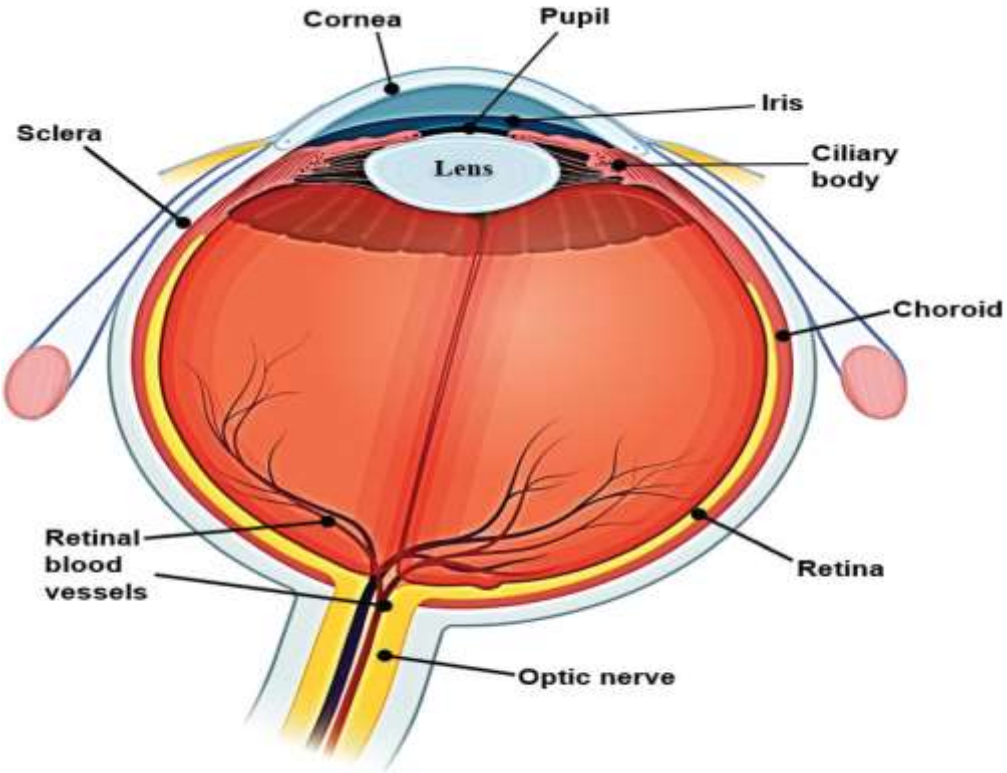

Figure 1: Anatomy of eye [11]

3. Ocular surface diseases

3.1.Dry eye

Dry eye is a complex condition affecting both the ocular surface and the tear. Discomfort, blurred vision, and unstable tear film with possible ocular surface injury are the primary symptoms. The cornea, conjunctiva, meibomian glands, lacrimal glands, and neural network make up the intricate system that is the ocular surface. The microbiome is among the numerous elements that need to be taken into account. Many immune cell types ensure protection of the ocular surface. mucosal immune systems linked to the conjunctiva (CALT) and lacrimal drainage tissue make up ocular surface-associated lymphoid tissue (EALT). Both the innate and adaptive immune systems control the activation of the ocular surface immune system [12].

3.2.Uveitis

Redness, discomfort, photophobia, and loss of visual acuity are some of the clinical manifestations of uveitis, a disease that is characterised by inflammation of the uvea, a structure in the eye made up of the choroid, iris, and ciliary body, as well as the neural retina. According to reports, uveitis is more frequent in women than in men, affecting 115.3 out of every 100,000 people in the US and having a comparable lifetime incidence globally [13]. Visual impairment can result from uveitis (UVT), an inflammatory eye illness that affects the iris, retina, vitreous, choroid, and ciliary body, among other areas of the eye. Based on the circumstances that cause it, UVT is classified as either infectious or noninfectious [14]. It is yet unknown how changes in gut microbiota impact uveitis on a cellular level. Autoreactive T cells' disruption of the blood-retinal barrier is thought to target ing retinal antigens, potentially brought on by gut commensal bacteria [15].

3.3.Glaucoma

Glaucoma is the second most common cause of blindness globally and a debilitating neurological diseas-

e. Axons of the retinal ganglion cells (RGCs), which are essential to the development of this illness, lose their inherent ability to regenerate when they die or malfunction [16]. This disease has been linked to environmental factors, specifically pollution, UVR, and temperature. It can be divided as follows:

- Chronic open-angle glaucoma
- acute glaucoma [17].

3.4.Cataract

A complicated interaction between internal and external factors can lead to cataract development, with ageing being the most important risk factor. One of the main causes of vision impairment worldwide is senile cataracts. Aggregation and mutation of lens proteins brought on by cumulative oxidative stress, lipid peroxidation, and DNA damage are the basic causes of this age-related eye disorder, which entails degenerative changes in lens cells [18]. Clear avascular ocular lenses originate from lens epithelial cells (LECs). LECs go to the lens equator and create lens fibres, which progressively compress and condense to cause opacity and lens nucleus hardness. Cataracts and posterior capsular opacification can be caused by aberrant proliferation, posterior displacement, and loss of LEC homeostasis [19].

3.5.Diabetic retinopathy

It has been proposed that OSA's increased oxidative stress and inflammation impact energy metabolism, raise insulin resistance and dysglycemia, and ultimately raise the risk of type II diabetes. It was observed that greater insulin levels were linked to reduced oxygen saturation during sleeping, even in people without diabetes. Even lean or non-obese people with OSA have higher insulin levels than age-, sex-, and BMI-matched controls, indicating that OSA may be an independent risk factor for diabetes, even though some of the association between the two conditions may be mediated by common risk factors, most notably obesity [20].

3.6.Age-related macular degeneration

With incidence rates of 10% in those over 65 and >25% in those over 75, AMD is an eye condition that is highly correlated with age [21]. The primary cause of vision loss in developed nations is age-related macular degeneration (AMD), a disorder that affects central vision. The etiology and progression of AMD have been linked to both hereditary and environmental factors, including smoking. Anti-vascular endothelial growth factor (anti-VEGF) injections can be used to improve visual acuity, stop further vision loss, or even prevent vision loss altogether, however in certain circumstances, fast vision loss may occur due to choroidal neovascularisation [22]. AMD is frequently divided into early, middle, and late phases in clinical epidemiology. In contrast to other stages of AMD, late-stage AMD is treated differently and frequently results in visual impairment and even irreversible loss of central vision. The macular region experiences extracellular aggregate (drusen) buildup and pigmentary abnormalities in the early and intermediate stages of AMD [23].

3.7.Pigmentary retinopathy

The migration and proliferation of RPE cells or macrophages harbouring melanin pigments to the retina is known as pigmentary retinopathy (PR). Patients with mitochondrial illness may see pigmentary alterations in their retina. The conditions with the best explanations are neuropathy, ataxia, and retinitis pigmentosa (NARP) and mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS). People who have Mitochondrial encephalopathy, lactic acidosis and stroke may frequently experience night blindness, decreased visual acuity, and narrowed visual fields. Usually appearing in youth or early adulthood, these signs and symptoms get worse with time [24].

3.8.Age-Related Retinal Diseases

Accelerated loss of retinal neurones and their axons is a characteristic of age-related neurodegenerative eye illnesses, such as glaucoma. These illnesses are connected and have similar biological processes brought on by recurrent light damage and the oxidative stress overexpression that results. As people age, the incidence and prevalence of primary open-angle glaucoma rise dramatically [25].

4. Preoperative Ocular Surface Evaluation

A thorough examination of the lids and adnexa, using both objective and subjective tests to determine the condition of the tear film, should be part of the preoperative evaluation.

4.1.Fluorescein staining

The evaluation of corneal staining influences subsequent decision-making and aids in the assessment of pre-existing punctate keratopathy. It aids in determining the tear breakup time and whether dellenor conjunctivochalasis is present, which can result in exacerbated symptoms. If missing prior to surgery because of disruptions in tear film stability. Before undergoing cataract surgery, patients with moderate to severe dry eye need to have their ocular surface further evaluated and optimised. If an aqueous tear shortage is found, it must be treated by ruling out any systemic causes and, if necessary, referring the patient to a rheumatologist [26].

4.2.Corneal and Conjunctival Staining

An Invasive procedure called corneal and conjunctival staining uses a dye, such as sodium fluorescein, rose bengal, or lissamine green, to assess damage to the ocular surface. Patients handle fluorescein well, and a single application doesn't hurt. The staining pattern may be obscured by the dye suspended in the tear film, but it must be examined right away to avoid erroneous recording due to stromal diffusion. Because fluorescein is not fluorescent at concentrations above 2%, the amount of dye administered should be kept to a minimum, especially in dry eyes [27].

5. Risk Factors of eye

5.1.Age

Epidemiological studies have consistently demonstrated a positive association between aging and the onset of dry eye disease, independent of ethnicity. According to several population-based cross-sectional studies, as people age, the frequency and intensity of dry eye disease's clinical signs and symptoms rise. In fact, a variety of physiological and environmental factors can cause changes in systemic hormonal and neurosensory regulation, tear film homeostatic disturbances, and ocular surface inflammatory pathways, leading to dry eye disease, which is acknowledged as a complex and multifactorial degenerative condition [28].

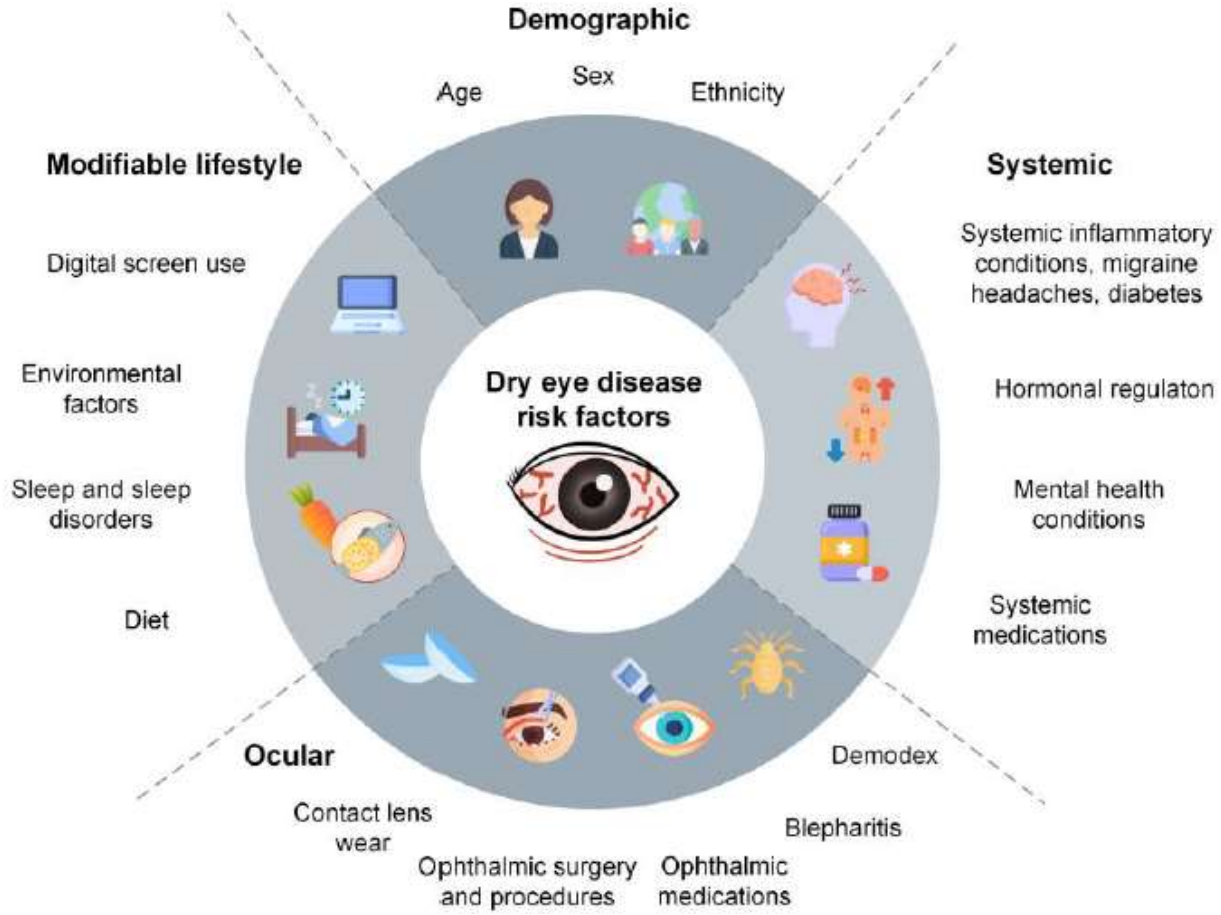

Fig 2: Dry eye disease risk factor [28]

5.2.Covariates

The Total Population Registe used to collect baseline data for each person, including sex, age, country of birth, date of death, county of residence, and emigration [29].

5.3.Uveitis

The intensity and rate of progression of the disease, the anatomic space affected, the exclusion of alternative aetiologies, and the underlying known or suspected disease process all influence how uveitis is treated. Topically, ophthalmologists will first topical steroids can be used to relieve inflammation in non-infectious anterior uveitis, while dilating eye drops can lessen pain, stop synechiae production, and lower the risk of glaucoma. Systemic glucocorticoids may be used as a treatment for significant anterior inflammation (2+ or more AC cells) [30].

5.4.Intermediate uveitis

Intermediate uveitis (IU), which includes inflammation in the vitreous cavity (sometimes known as "vitritis"), frequently manifests as painless floaters and decreased VA. Even though IU may be idiopathic, there should be a lower bar for physician referral for systemic evaluation because recognised connections include lymphoma, sarcoidosis, and MS. The degree of symptoms or the existence of CMO determines whether to treat; in mild situations, monitoring is permissible while treating any underlying systemic causes. Topical steroids are typically less effective than AAU. Intravitreal injections can be used for local steroid therapy [31].

Conclusion:

Ocular surface diseases are a significant public health concern, and understanding their complex pathophysiology is crucial for developing effective treatment strategies. Dry eye disease, uveitis, glaucoma, and age-related macular degeneration are complex conditions that require a comprehensive approach to management. By understanding the risk factors, including age, genetics, and environmental factors, healthcare professionals can provide better care for patients with ocular surface diseases. Preoperative ocular surface evaluation is essential in preventing complications and improving patient outcomes. Further research is needed to elucidate the underlying mechanisms of ocular surface diseases and to develop novel therapeutic approaches. By working together, we can improve the diagnosis, treatment, and management of ocular surface diseases and reduce the burden of visual impairment and blindness worldwide.

Reference

1. Hisey EA, Galor A, Leonard BC. A comparative review of evaporative dry eye disease and meibomian gland dysfunction in dogs and humans. Vet Ophthalmol. 2023:16-30.
2. Chen Y, Dana R. Autoimmunity in dry eye disease-An updated review of evidence on effector and memory Th17 cells in disease pathogenicity. Autoimmun Rev. 2021;20(11):102933. Doi: 10.1016/j.autrev.2021.102933. Epub 2021 Sep 9. PMID: 34509656; PMCID: PMC8530974.
3. Kate A, Deshmukh R, Donthineni PR, Sharma N, Vajpayee RB, Basu S. Management of corneal perforations in dry eye disease: Preferred practice pattern guidelines. Indian J Ophthalmol. 2023;71(4):1373-1381. Doi: 10.4103/IJO.IJO_2826_22. PMID: 37026269; PMCID: PMC10276684.
4. Scarpellini C, Ramos Llorca A, Lanthier C, Klejborowska G, Augustyns K. The Potential Role of Regulated Cell Death in Dry Eye Diseases and Ocular Surface Dysfunction. Int J Mol Sci. 2023:1;24(1):731. Doi: 10.3390/ijms24010731. PMID: 36614174; PMCID: PMC9820812.
5. Song J, Dong H, Wang T, Yu H, Yu J, Ma S, Song X, Sun Q, Xu Y, Liu M. What is the impact of microbiota on dry eye: a literature review of the gut-eye axis. BMC Ophthalmol. 2024 19;24(1):262. Doi: 10.1186/s12886-024-03526-2. PMID: 38898418; PMCID: PMC11186098.
6. An Q, Zou H. Ocular surface microbiota dysbiosis contributes to the high prevalence of dry eye disease in diabetic patients. Crit Rev Microbiol. 2023;49(6):805-814. Doi: 10.1080/1040841X.2022.2142090. Epub 2022 Nov 21. PMID: 36409575.
7. Grant A, Leung G, Freeman EE. Ambient Air Pollution and Age-Related Eye Disease: A Systematic Review and Meta-Analysis. Invest Ophthalmol Vis Sci. 2022:2;63(9):17. Doi: 10.1167/iovs.63.9.17. PMID: 35960515; PMCID: PMC9396677.
8. 8.Koh S, Rao SK, Srinivas SP, Tong L, Young AL. Evaluation of ocular surface and tear function – A review of current approaches for dry eye. Indian J Ophthalmol. 2022;70(6):1883-1891. Doi: 10.4103/ijo.IJO_1804_21. PMID: 35647953; PMCID: PMC9359282.
9. Johnson BT, Jameyfield E, Aakalu VK. Optic neuropathy and diplopia from thyroid eye disease: update on pathophysiology and treatment. Curr Opin Neurol. 2021:1;34(1):116-121. Doi: 10.1097/WCO.0000000000000894. PMID: 33278144; PMCID: PMC7853658.
10. Yazdani M, Elgstøen KBP, Utheim TP. Eye Make-up Products and Dry Eye Disease: A Mini Review. Curr Eye Res. 2022;47(1):1-11. Doi: 10.1080/02713683.2021.1966476. Epub 2021 Sep 19. PMID: 34365876.

11. Shi Y, Hu Y, Jiang N, Yetisen AK. Fluorescence Sensing Technologies for Ophthalmic Diagnosis. ACS Sens. 2022 Jun 24;7(6):1615-1633. doi: 10.1021/acssensors.2c00313. Epub 2022 May 31. Erratum in: ACS Sens. 2025:24;10(1):573. doi: 10.1021/acssensors.4c03522. PMID: 35640088; PMCID: PMC9237824.
12. Napolitano P, Filippelli M, Davinelli S, Bartollino S, dell'Omo R, Costagliola C. Influence of gut microbiota on eye diseases: an overview. Ann Med. 2021;53(1):750-761. Doi: 10.1080/07853890.2021.1925150. PMID: 34042554; PMCID: PMC8168766.
13. Donabedian P, Dawson E, Li Q, Chen J. Gut Microbes and Eye Disease. Ophthalmic Res. 2022;65(3):245-253. Doi: 10.1159/000519457. Epub 2021 Dec 16. PMID: 34915517; PMCID: PMC9198007.
14. Zhao Y, Qiu P, Shen T. Gut microbiota and eye diseases: A review. Medicine (Baltimore). 2024:27;103(39):e39866. Doi: 10.1097/MD.0000000000039866. PMID: 39331938; PMCID: PMC11441905.
15. Song J, Dong H, Wang T, Yu H, Yu J, Ma S, Song X, Sun Q, Xu Y, Liu M. What is the impact of microbiota on dry eye: a literature review of the gut-eye axis. BMC Ophthalmol. 202419;24(1):262. doi: 10.1186/s12886-024-03526-2. PMID: 38898418; PMCID: PMC11186098.
16. Campagnoli LIM, Varesi A, Barbieri A, Marchesi N, Pascale A. Targeting the Gut-Eye Axis: An Emerging Strategy to Face Ocular Diseases. Int J Mol Sci. 2023:28;24(17):13338. Doi: 10.3390/ijms241713338. PMID: 37686143; PMCID: PMC10488056.
17. Echevarría-Lucas L, Senciales-González JM, Medialdea-Hurtado ME, Rodrigo-Comino J. Impact of Climate Change on Eye Diseases and Associated Economical Costs. Int J Environ Res Public Health. 2021:5;18(13):7197. Doi: 10.3390/ijerph18137197. PMID: 34281132; PMCID: PMC8297364.
18. Tang Y, Fang C, Shi J, Chen H, Chen X, Yao X. Antioxidant potential of chlorogenic acid in Age-Related eye diseases. Pharmacol Res Perspect. 2024;12(1):e1162. Doi: 10.1002/prp2.1162. PMID: 38189160; PMCID: PMC10772849.
19. Du Y. The Hippo signalling pathway and its impact on eye diseases. J Cell Mol Med. 2024;28(8):e18300. Doi: 10.1111/jcmm.18300. PMID: 38613348; PMCID: PMC11015399.
20. Lee SSY, Nilagiri VK, Mackey DA. Sleep and eye disease: A review. Clin Exp Ophthalmol. 2022;50(3):334-344. Doi: 10.1111/ceo.14071. Epub 2022 Mar 16. PMID: 35263016; PMCID: PMC9544516.
21. Wang X, Wang T, Lam E, Alvarez D, Sun Y. Ocular Vascular Diseases: From Retinal Immune Privilege to Inflammation. Int J Mol Sci. 2023:28;24(15):12090. Doi: 10.3390/ijms241512090. PMID: 37569464; PMCID: PMC10418793.
22. Kalloniatis M, Wang H, Phu J, Tong J, Armitage J. Optical coherence tomography angiography in the diagnosis of ocular disease. Clin Exp Optom. 2024;107(5):482-498. Doi: 10.1080/08164622.2024.2323603. Epub 2024 Mar 7. PMID: 38452795.
23. Li J, Li C, Huang Y, Guan P, Huang D, Yu H, Yang X, Liu L. Mendelian randomization analyses in ocular disease: a powerful approach to causal inference with human genetic data. J Transl Med. 2022:26;20(1):621. Doi: 10.1186/s12967-022-03822-9. PMID: 36572895; PMCID: PMC9793675.
24. Anand S, Trounce IA, Gangoda L. Role of extracellular vesicles in mitochondrial eye diseases. IUBMB Life. 2022;74(12):1264-1272. Doi: 10.1002/iub.2687. Epub 2022 Nov 11. PMID: 36308309; PMCID: PMC10947567.

25. Choi YK. An Altered Neurovascular System in Aging-Related Eye Diseases. Int J Mol Sci. 2022:15;23(22):14104. Doi: 10.3390/ijms232214104. PMID: 36430581; PMCID: PMC9694120.
26. Priyadarshini K, Sharma N, Kaur M, Titiyal JS. Cataract surgery in ocular surface disease. Indian J Ophthalmol. 2023;71(4):1167-1175. Doi: 10.4103/IJO.IJO_3395_22. PMID: 37026248; PMCID: PMC10276679.
27. McGinnigle S, Naroo SA, Eperjesi F. Evaluation of dry eye. Surv Ophthalmol. 2012;57(4):293-316. Doi: 10.1016/j.survophthal.2011.11.003. PMID: 22726587.
28. Britten-Jones AC, Wang MTM, Samuels I, Jennings C, Stapleton F, Craig JP. Epidemiology and Risk Factors of Dry Eye Disease: Considerations for Clinical Management. Medicina (Kaunas). 2024:5;60(9):1458. doi: 10.3390/medicina60091458. PMID: 39336499; PMCID: PMC11433936.
29. Bergman D, Ebrahimi F, Sun J, Norin C, Mollazadegan K, Ludvigsson JF. Inflammatory eye disease is a risk factor for future microscopic colitis: A nationwide population-based matched case control study. United European Gastroenterol J. 2024;12(8):1081-1090. Doi: 10.1002/ueg2.12623. Epub 2024 Jul 4. PMID: 38963730; PMCID: PMC11485298.
30. Corbitt K, Nowatzky J. Inflammatory eye disease for rheumatologists. Curr Opin Rheumatol. 2023:1;35(3):201-212. Doi: 10.1097/BOR.0000000000000933. Epub 2023 Mar 20. PMID: 36943695; PMCID: PMC10461883.
31. Miller JR, Hanumunthadu D. Inflammatory eye disease: An overview of clinical presentation and management. Clin Med (Lond). 2022;22(2):100-103. doi: 10.7861/clinmed.2022-0046. PMID: 35304367; PMCID: PMC8966833.