A CROSS-SECTIONAL STUDY OF CORRELATION OF CLIMATIC DROPLET KERATOPATHY WITH DRY EYE, SERUM PROTEINS, SERUM CALCIUM AND LIPID PROFILE.

By

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Dissertation submitted to the

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VIJAYAPURA, KARNATAKA

In Partial fulfillment of requirements for the degree of

MASTER OF SURGERY
In
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List of abbreviations

Abbreviations	Full expansion
A/G Ratio	Albumin/Globulin Ratio
CDK	Climatic Droplet Keratopathy
CsA	Cyclosporin A
DED	Dry eye disease
DNA	Deoxy
ECM	Extracellular matrix
HDL	High density lipoprotein
IL-6	Interleukin-6
LDL	Low density lipoprotein
LFA	Lymphocyte function associated antigen -1
MGD	Meibomian Gland Dysfunction
MMP	Matrix metalloproteinase
MDA	Malondialdehyde
MS	Mass spectrometry
NAC	N- Acetyl cysteine
OX-LDL	Oxidised low-density lipoprotein
PKP	Penetrating keratoplasty
ROS	Reactive Oxygen species
SIRT1	Sirtutin activators
T-BUT	Tear-film Break-up time
TG	Triglyceride
TNF-α	Tissue necrosis factor-alpha
UV	Ultraviolet
VLDL	Very low-density lipoprotein
4HNE	4- Hydroxynonenal

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ABSTRACT

Background: Climatic Droplet Keratopathy (CDK) is a progressive degenerative condition of the cornea with unclear pathogenesis, though environmental and systemic factors are suspected contributors. This study aimed to explore associations between CDK and dry eye syndrome, serum protein, calcium levels, and lipid profile, to uncover potential systemic and environmental links to disease severity.

Methods: A cross-sectional observational study was conducted at a tertiary care center over 18 months, involving 32 CDK patients and 32 matched controls. Participants underwent comprehensive ocular assessments, including Schirmer's tests and Tear Film Break-Up Time (TBUT), alongside biochemical analyses of serum proteins, calcium, and lipid profile. CDK severity was graded using slit lamp biomicroscopy findings. Statistical analysis was performed using SPSS v22.0.

Results: CDK was significantly more prevalent in older males and those with farming occupations. Bilateral involvement was noted in 81.3% of cases. A significant association was found between CDK and abnormal TBUT (95.3% in cases vs. 56.3% in controls, $P<0.001$) and reduced Schirmer's II scores ($P=0.001$), indicating impaired tear film function and basal tear secretion. Serum calcium levels were inversely correlated with CDK severity ($P=0.015$), while a significantly lower HDL level was observed in cases compared to controls ($P<0.001$). VLDL levels also varied significantly with CDK grade ($P=0.011$). However, serum total protein, albumin, A/G ratio, total cholesterol, LDL, and triglyceride levels did not show statistically significant differences.

Conclusion: The study highlights significant associations between CDK and tear film instability, reduced basal tear secretion, low HDL, altered VLDL levels, and declining serum calcium with disease progression. These findings support a multifactorial etiology of CDK involving ocular surface dysfunction and systemic metabolic alterations, particularly in rural male populations with high environmental exposure.

INTRODUCTION

Climatic Droplet Keratopathy (CDK): An underestimated corneal Degeneration

Climatic Droplet Keratopathy (CDK) is a progressive degenerative disease of the cornea characterized by the accumulation of golden-yellow granular deposits in the anterior stroma, leading to stromal opacification and subsequent visual impairment [1]. This condition predominantly affects populations residing in harsh climatic conditions with high levels of ultraviolet (UV) radiation, dust exposure, high temperatures, and low humidity [2,3]. Despite its global prevalence, particularly in arid and high-altitude regions, limited research has been conducted on the precise pathogenesis of CDK and its correlation with systemic factors such as dry eye, serum proteins, serum calcium levels and lipid profile.[4].

The etiology of CDK remains multifactorial, involving environmental, genetic, and systemic influences. The most widely accepted hypothesis suggests prolonged exposure to UV radiation leads to oxidative stress and protein denaturation, resulting in the accumulation of proteinaceous deposits in the cornea [5]. The prevalence of climatic droplet keratopathy (CDK) in India appears to be influenced by environmental factors, with higher occurrence in rural and arid regions where prolonged exposure to UV radiation, dust, and dry conditions may contribute to its development. While CDK is more commonly reported in rural areas with harsh climatic conditions, urban environments with rising air pollution and increased particulate matter exposure may also play a role in disease progression, highlighting the impact of environmental stressors on ocular health. [6].

Dry eye disease (DED) is a common ocular condition that results from either decreased tear production or increased tear evaporation, leading to ocular surface damage and inflammation. Studies have postulated a strong association between CDK and DED, given the shared environmental risk factors such as UV radiation and desiccating wind exposure [6]. Further large-scale studies are required to elucidate the precise mechanism linking CDK and DED.

The proteinaceous nature of the deposits found in CDK has been a subject of interest in ophthalmological research. Proteomic analyses of corneal deposits have identified the presence of extracellular matrix (ECM) proteins, immunoglobulins, and oxidative stress markers, suggesting an inflammatory and degenerative pathophysiology. Kaji et al. conducted an immunohistochemical study and found evidence of D-β-aspartic acid-containing proteins in CDK lesions, supporting the hypothesis of protein denaturation due to chronic UV exposure [07].

A review by Serra et al. highlighted that the proteins found in CDK deposits share similarities with amyloid-like aggregates, indicating a possible role of protein misfolding and aggregation in disease progression [08]. Additionally, systemic factors such as serum albumin levels and the albumin/globulin (A/G) ratio have been implicated in various degenerative ocular disorders. However, their direct correlation with CDK remains unexplored, necessitating further clinical and biochemical investigations.

Calcium homeostasis plays a crucial role in maintaining corneal transparency and cellular function. Dysregulation of calcium metabolism has been implicated in various corneal degenerations like calcific band keratopathy, calcareous degeneration and CDK. Histopathological studies have demonstrated Von Kossa-positive calcium deposits in the corneal stroma of CDK patients, suggesting a role of calcium deposition in disease pathogenesis [09]. Investigating the correlation between serum calcium levels and CDK may provide valuable insights into novel therapeutic and preventive strategies for this condition.

Lipid peroxidation, a process in which reactive oxygen species (ROS) degrade polyunsaturated fatty acids in cell membranes, plays a key role in the pathogenesis of CDK. UV radiation promotes oxidative stress and lipid peroxidation, leading to cellular damage and the formation of abnormal protein-lipid aggregates in the cornea, contributing to the progression of CDK. Investigating the systemic lipid levels may give us valuable information on its systemic association with CDK.

Early identification and management of CDK may prevent severe visual impairment, particularly in vulnerable populations exposed to extreme climatic conditions. Understanding the correlation between CDK, DED, serum proteins, and serum calcium holds significant clinical relevance. The findings from this study may contribute to public health policies aimed at preventing CDK, particularly in regions with high UV exposure. Implementing awareness programs on ocular protection and routine screening for corneal degenerations may significantly reduce the disease burden.

REVIEW OF LITERATURE

Definition and Historical Background

Climatic Droplet Keratopathy (CDK) is a degenerative corneal disease characterized by the deposition of golden-yellow proteinaceous material in the anterior corneal stroma, leading to progressive visual impairment [1]. First described in regions with extreme environmental conditions, CDK has been predominantly observed in populations exposed to prolonged ultraviolet (UV) radiation, high temperatures, and airborne particulates [2].

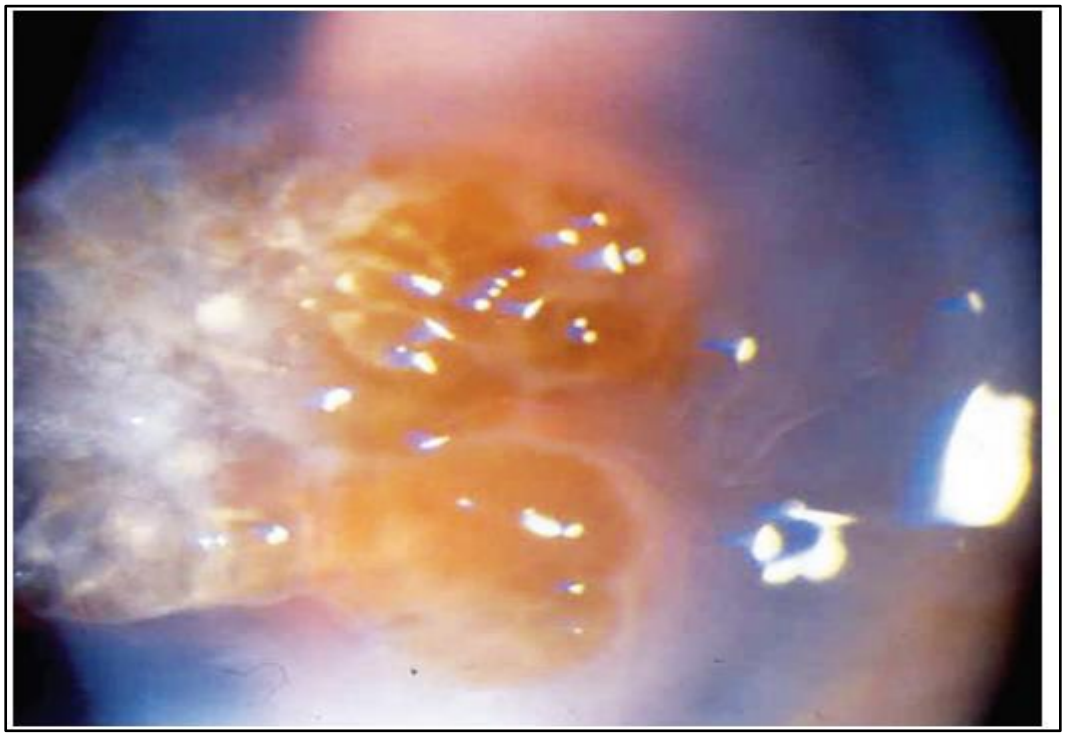


Figure 1: Aggregates of large yellow-golden globules in a patient with CDK(1)

Historically, CDK was initially misclassified as a variant of spheroidal degeneration due to its histopathological similarities [3]. However, advancements in immuno-histochemical and proteomic analyses have differentiated it as a distinct corneal pathology with a multifactorial etiology [4]. Early reports from Labrador and Arctic regions indicated a higher prevalence among outdoor workers and indigenous populations [5], reinforcing the role of chronic environmental exposure in its pathogenesis.

Further research demonstrated that corneal stromal degeneration in CDK is associated with oxidative stress-induced protein aggregation and extracellular matrix (ECM) alterations [6]. Recent studies employing confocal microscopy and histochemical staining techniques have confirmed the presence of D-β-aspartic acid-containing proteins [7], suggesting that prolonged oxidative damage leads to irreversible protein misfolding and deposition [8].

Epidemiology and Global Distribution

CDK has been reported in various geographical locations, with a high prevalence in desert regions, high-altitude areas, and coastal zones [9]. Populations residing in these areas exhibit increased exposure to environmental stressors such as UV radiation, wind, dust, and extreme temperatures [10]. Studies from South America, Africa, and Asia have indicated a higher prevalence of CDK among agricultural workers, fishermen, and construction laborers [11]. A significant association between geographical location and disease severity has been noted in epidemiological surveys [12].

Pathophysiology of CDK

The primary pathogenic mechanisms involved in CDK include oxidative stress, chronic inflammation, and protein aggregation [13]. UV radiation leads to the generation of reactive oxygen species (ROS), which cause corneal damage and stromal protein denaturation [14]. Additionally, chronic exposure to environmental pollutants and irritants exacerbates the inflammatory response, promoting the accumulation of proteinaceous material in the anterior stroma [15].

ETIOPATHOGENESIS OF CLIMATIC DROPLET KERATOPATHY

Role of Ultraviolet (UV) Radiation in Corneal Degeneration

Ultraviolet (UV) radiation is widely recognized as a major environmental factor contributing to the development of Climatic Droplet Keratopathy (CDK) [15]. Chronic UV exposure induces oxidative stress, DNA fragmentation, lipid peroxidation, and apoptosis of corneal epithelial cells [16]. Furthermore, UV radiation alters stromal proteins via oxidative crosslinking and carbonylation, leading to reduced corneal transparency and the formation of insoluble protein deposits [1].

Impact of Chronic Environmental Exposure (Dust, Heat, Humidity)

Long-term exposure to harsh climatic factors such as dust, wind, high ambient temperatures, and low humidity disrupts ocular surface homeostasis and promotes the accumulation of proteinaceous material in the anterior stroma [9]. These stressors also compromise the tear film and contribute to evaporative dry eye disease, aggravating epithelial cell damage and inflammation of the corneal surface [6].

Pathological Changes in Corneal Stroma

Histopathological investigations have revealed the presence of amyloid-like protein aggregates, irregular collagen fibril arrangements, and disorganization of the extracellular matrix (ECM) in affected corneal tissue [3]. These structural alterations result in progressive stromal opacity, increased light scattering, and gradual vision loss [4].

Cellular and Molecular Mechanisms of Protein Aggregation

Excessive generation of reactive oxygen species (ROS) in the cornea damages keratocytes and leads to collagen degradation and misfolded protein accumulation [14]. Immunohistochemical analyses have demonstrated abnormal deposition of ECM proteins and formation of amyloid-like structures in the anterior stroma [15]. Additionally, proteomic studies have identified D-β-aspartic acid residues in stromal deposits, indicative of chronic oxidative damage and age-related racemization of long-lived corneal proteins [16].

3.CORRELATION OF CLIMATIC DROPLET KERATOPATHY WITH DRY EYE SYNDROME

Pathophysiology of Dry Eye in CDK Patients

Climatic Droplet Keratopathy (CDK) is strongly associated with Dry Eye Disease (DED) due to the chronic impact of environmental exposure, oxidative stress, and corneal surface degradation [17]. CDK patients frequently present with tear film instability, increased evaporation, and epithelial surface damage which are hallmarks of ocular surface dysfunction [18]. The following mechanisms contribute to DED in CDK cases:

- Reduced tear production**:** Chronic oxidative stress and inflammatory damage to the lacrimal glands reduce aqueous tear output, particularly in individuals from high UV and dusty environments like desert or high-altitude areas [17].
- Increased tear evaporation**:** Disruption of the tear film lipid layer, often linked to Meibomian gland dysfunction, leads to shorter tear film breakup time (TBUT < 10 seconds), worsening evaporative dry eye symptoms [19].
- Corneal epithelial barrier dysfunction**:** Repeated environmental insult impairs the corneal epithelium, increasing surface permeability and promoting chronic inflammation [19].
- Inflammatory cytokine release**:** CDK patients often exhibit elevated tear levels of cytokines such as IL-6, TNF-α, and matrix metalloproteinase-9 (MMP-9), intensifying the inflammatory response and epithelial degradation [17,19].
- Schirmer's Test Abnormalities**:** Schirmer's values under 5 mm in ocular surface disorder patients indicate severe aqueous deficiency, often accompanied by tear hyperosmolarity and cell damage [20].

Clinical Evidence Linking CDK and Dry Eye

Prevalence Studies and Epidemiological Evidence

- A study in Chile found that 70% of CDK patients had symptoms of DED, such as foreign body sensation, irritation, and photophobia [17].
- An Argentinian survey revealed correlations between Schirmer's test, TBUT, and CDK lesion severity, confirming a tear dysfunction-CDK link [18].
- A Tibetan study among high-altitude residents showed decreased TBUT and increased CDK prevalence, emphasizing UV-induced ocular surface stress [19].

Comparative Analysis of Tear Film Parameters in CDK vs. Control Groups

- In Mongolia, TBUT in CDK patients averaged 7.5 seconds, compared to 12.5 seconds in healthy controls—confirming tear instability [18].
- A case-control study in China showed significantly higher tear osmolarity in CDK patients, suggesting hyperosmolarity-driven inflammation [20].

  A North Indian hospital study reported 42% lower Schirmer's scores in CDK patients compared to controls, indicating aqueous tear deficiency [21].

Histopathological and Biochemical Correlations

Recent biochemical studies strengthen the CDK–DED link:

- Elevated levels of MMP-9 and MMP-2 in CDK tear samples indicate ECM degradation due to chronic inflammation [17].
- Confocal microscopy shows subclinical corneal nerve loss in CDK patients, suggesting neurotrophic DED involvement [18].
- Oxidative stress markers such as malondialdehyde (MDA) and 4-hydroxynonenal (4-HNE) are elevated in CDK-related tear samples, supporting the role of lipid peroxidation in ocular surface breakdown [19].

Clinical Presentation and Classification of Climatic Droplet Keratopathy (CDK)

Climatic Droplet Keratopathy (CDK) is a progressive degenerative corneal disorder characterized by the accumulation of small, golden-yellow proteinaceous globules in the subepithelial and anterior stromal layers of the cornea, particularly near the limbus [1]. These deposits can spread toward the central cornea, leading to decreased visual acuity. They involve Bowman's layer and can disrupt epithelial and stromal architecture, causing corneal opacification and vision deterioration [1].

Primary vs. Secondary CDK

Two distinct clinical subtypes of CDK are described:

- **Primary CDK**:
  - Occurs without prior corneal pathology
  - Characterized by bilateral, symmetrical, band-like golden-yellow globules
  - Typically no vascularization or scarring
- **Secondary CDK**:
  - Associated with pre-existing ocular trauma, surgery, or vascularization
  - Often unilateral or asymmetrical
  - May involve deeper stromal layers and corneal scarring [1]

Table no 1 :Clinical Differentiation Table: Primary vs. Secondary CDK

Feature	**Primary CDK**	**Secondary CDK**
Laterality	Bilateral	Unilateral or bilateral
Distribution	Band-shaped	Scattered deposits
Corneal Scarring	Absent	Present
Vascularization	Absent	Present
Involvement	Subepithelial deposits	Deep stromal invasion
Associated Conditions	None	Corneal trauma, surgery, vascularization
Symmetry	Symmetrical	Asymmetrical

Epidemiological and Gender Differences:

- CDK is more frequent in men, likely due to greater occupational outdoor exposure.
- In regions such as Saudi Arabia, the use of protective face coverings in women is associated with lower CDK incidence.
- Recurrence of CDK has been documented post-penetrating keratoplasty (PKP), with new deposits forming in corneal grafts [21].

Clinical Features and Staging of CDK

Early Manifestations:

- Small subepithelial deposits near the nasal and temporal limbus
- Often asymptomatic; patients may report mild irritation or photophobia

Progressive Features:

- Coalescence of deposits into a horizontal band
- Involvement of Bowman's layer and anterior stroma
- Increased corneal thickness, opacity, and in secondary CDK, neovascularization [22]

Advanced CDK:

- Central corneal involvement reducing visual acuity
- Irregular corneal surface causes glare and poor contrast sensitivity
- Severe opacification may require surgical intervention [22]

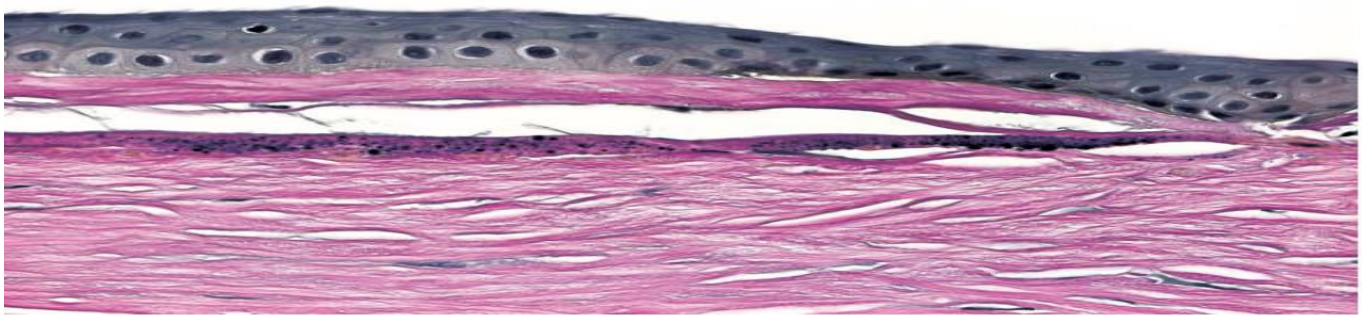


Figure 02 : Bowman's layer deposits of CDK (original magnification x 400 elastic stain)(1)

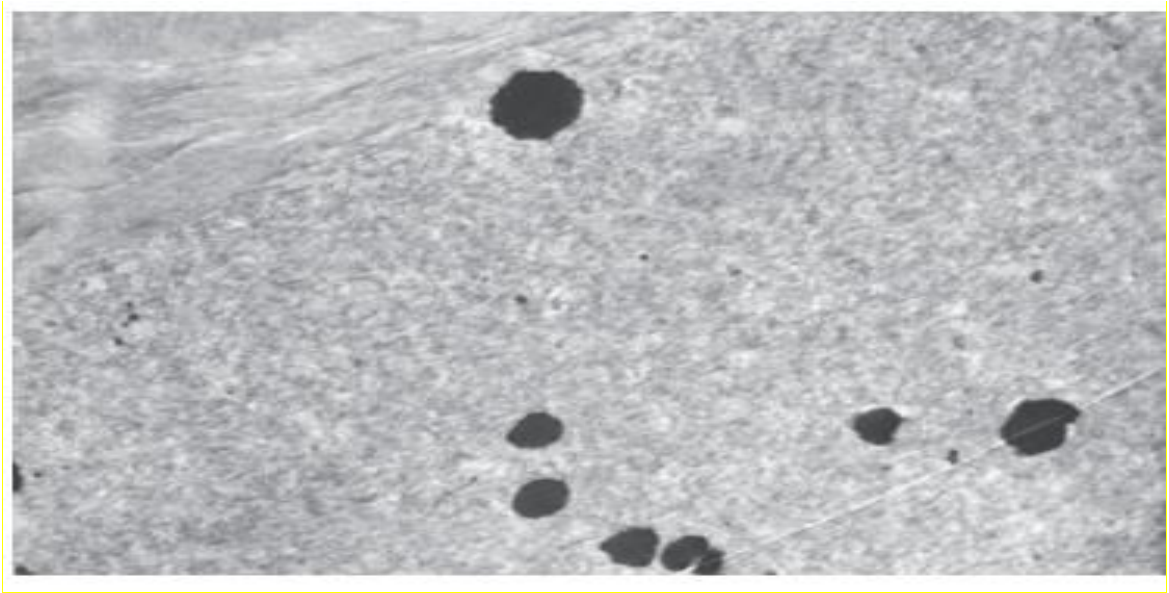


Figure 03: Ultrastructural appearance of irregularly shaped-electron dense extracellular deposits of CDK (original magnification x 1,000)(1)

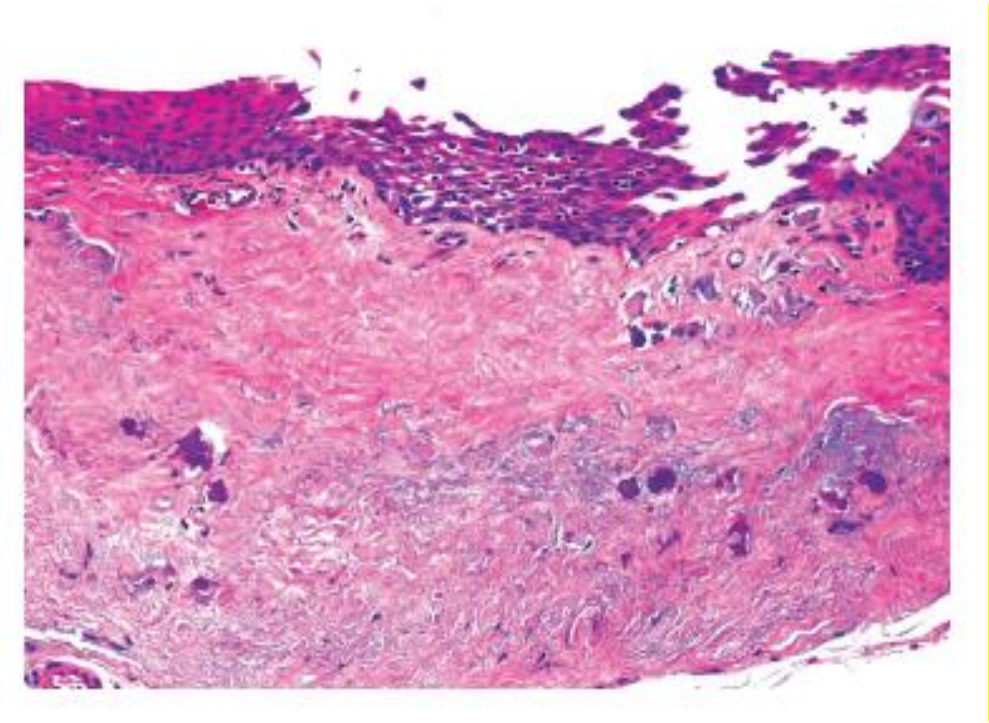


Figure 04: Similar CDK deposits in a pterygium (original magnification x 200 hematoxylin and eosin stain)(1)

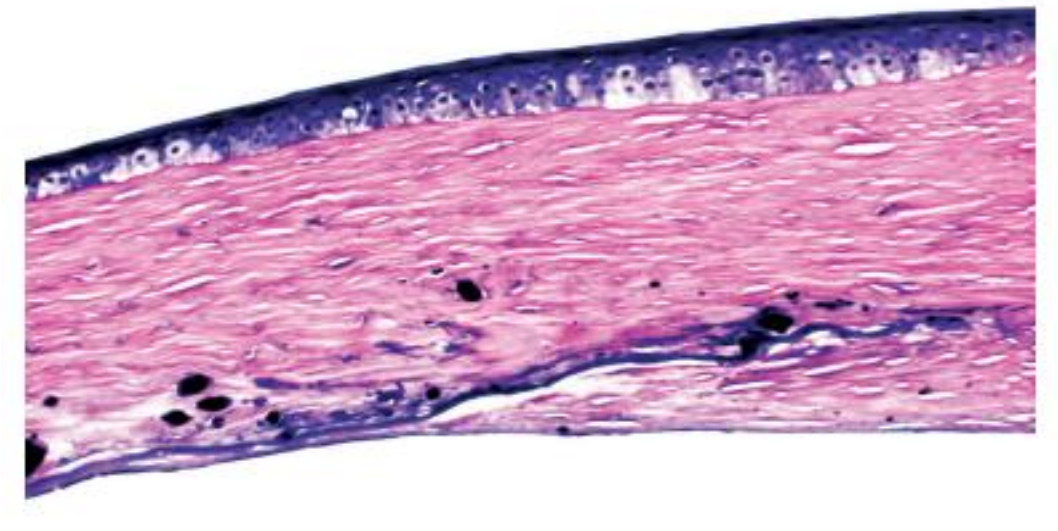


Figure 05: Climatic droplet keratopathy deposits within the deep stroma in a cornea with full thickness corneal scar (original magnification x 200 elastic stain)(1)

Lattice Lines and Corneal Amyloidosis in CDK

Fine lattice-like lines (~1–3 mm) have been noted in some CDK patients, resembling patterns seen in lattice corneal dystrophy. These are often bilateral, without recurrent erosions [23]. Amyloid deposition has also been observed in some CDK-affected corneas, though its pathogenic significance remains unclear. Environmental microtrauma (sand, UV) may play a contributory role [23].

Grading and Classification of CDK [21]

Standard Three-Grade Classification:[2]

Grade 1:

- Mild deposition of subepithelial spherules near the limbus.
- No visual impairment or corneal vascularization.

Grade 2:

- Increased spherule deposition forming a band-shaped opacity.
- No involvement of the central cornea, with mild visual disturbances.

Grade 3:

- Extensive yellow aggregates reaching the central cornea, significantly reducing vision.

Alternative Severity-Based Grading System:[21]

- Trace CDK: Few small corneal deposits affecting only one eye or confined to the interpalpebral region.
- Grade 1: Deposits in the medial and lateral interpalpebral strip, sparing the central cornea.
- Grade 2: Central cornea affected but without vision loss.
- Grade 3: Central cornea involvement with reduced vision.
- Grade 4: Formation of elevated nodules, indicating severe CDK progression.

Implications for Clinical Management

- Artificial Tears**:** Preservative-free lubricants alleviate dryness and restore tear stability [24]
- Lipid-Based Tear Substitutes: Improve TBUT by enhancing the lipid layer and reducing evaporative loss [24]
- Anti-inflammatory Therapy: Topical corticosteroids and cyclosporine A reduce cytokine levels (e.g., IL-6, TNF-α), improving symptoms [25]
- UV Protection: Wraparound sunglasses with UV filters are recommended to minimize progression [21]
- Omega-3 Supplementation: Oral omega-3 fatty acids enhance tear lipid content and improve meibomian gland function [26]

ASSOCIATION OF CLIMATIC DROPLET KERATOPATHY WITH SERUM PROTEINS

Composition of Corneal Deposits

Proteomic investigations have revealed that CDK-associated corneal deposits include extracellular matrix components, oxidative stress biomarkers, and immunoglobulins—indicative of chronic degenerative changes [27]. These findings support the hypothesis that environmental insults initiate a cascade of protein degradation, immune activation, and stromal remodeling:

- Collagen degradation products reflect progressive stromal instability due to enzymatic breakdown.
- Lipid peroxidation markers such as malondialdehyde (MDA) and 4-hydroxynonenal (4-HNE) suggest sustained oxidative injury.
- Immunoglobulin accumulation highlights a role for humoral immune responses in deposit formation and corneal opacity [27].

A reduced albumin/globulin (A/G) ratio has been proposed as a systemic biochemical marker in CDK. Albumin acts as an antioxidant and anti-inflammatory agent; its relative reduction may correlate with disease severity, pointing to systemic inflammation and metabolic imbalance in CDK patients [28].

Immunohistochemical Localization of Proteins

Histological and immunohistochemical studies of CDK corneas confirm: Amyloid-like protein deposits**,** confirmed by Congo red and thioflavin-T staining

- Oxidative protein modifications, including carbonylated and nitrosylated residues
- Increased expression of MMP-9, IL-1β, and TNF-α in corneal and tear fluid samples, linking chronic inflammation to stromal remodeling and neovascularization [29,30]

These features are reminiscent of protein misfolding diseases in other ocular conditions (e.g., cataracts and AMD) and strongly suggest that CDK is driven by a combination of oxidative stress and unresolved inflammation**.**

Emerging evidence supports the potential for anti-inflammatory and antioxidant therapies to halt or reverse corneal degeneration in CDK, though more targeted clinical trials are needed [30].

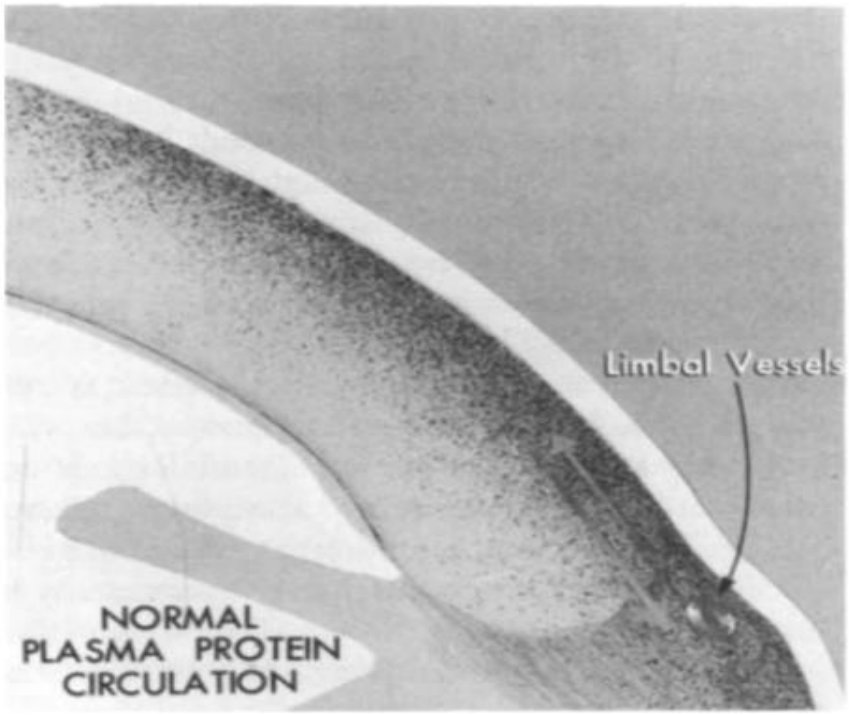


Figure 6*:Plasma proteins – Albumin and globulin diffuse from limbal vessels into cornea(9)*

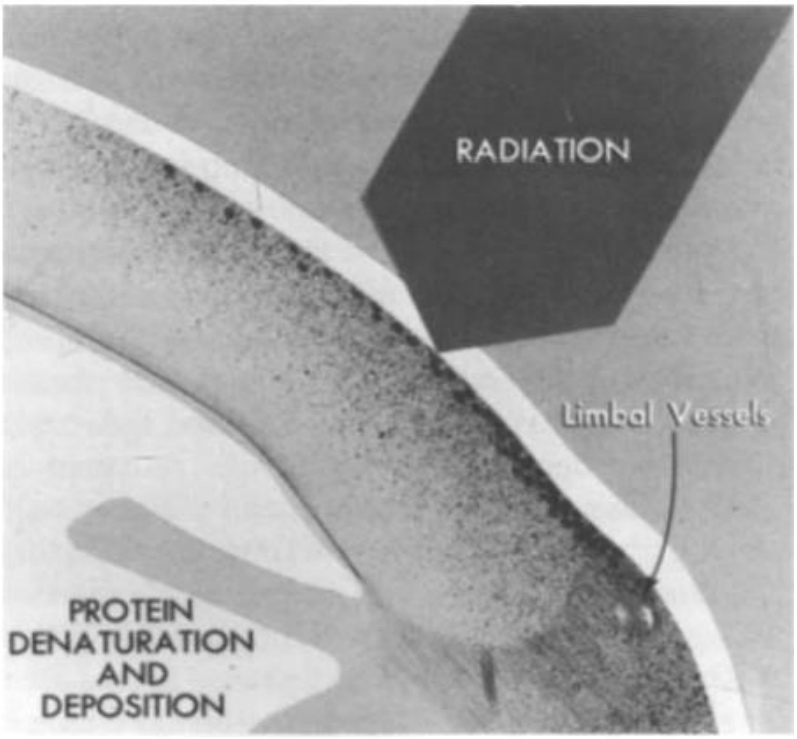


Figure 7*: Proteins are denatured by UV radiation with accumulation as droplets(9)*

SERUM CALCIUM AND ITS ROLE IN CDK PATHOGENESIS

Calcium is a vital regulator of corneal transparency, epithelial repair, nerve activity, and tear film stability. Disruption in calcium homeostasis has been implicated in various ocular surface disorders, including Climatic Droplet Keratopathy (CDK) [1,31].

Pathophysiological Role of Calcium in Corneal Health

Calcium supports:

- Corneal epithelial renewal and wound healing via calcium-mediated signaling cascades [32]
- Prevention of ECM overaccumulation, maintaining corneal clarity [33]
- Tight junction integrity and intercellular adhesion, critical for barrier function [34]

Dysregulated Calcium Metabolism and Corneal Calcification

When calcium regulation is impaired:

- Abnormal calcium deposits form in CDK lesions, exacerbating stromal opacity [35]
- Von Kossa staining confirms calcium accumulation, especially in advanced CDK [1]

These findings establish a link between local calcium dysregulation and chronic corneal degeneration in CDK.

Association Between Serum Calcium Levels and CDK

Because calcium homeostasis is systemic, serum calcium levels may reflect disease status in ocular pathology.

Hypocalcemia and Its Impact

- Low serum calcium levels are associated with increased oxidative stress and ECM degradation [36]
- CDK severity appears to correlate with systemic hypocalcemia, especially in advanced cases [36]
- Calcium-related enzymes involved in epithelial repair and anti-inflammatory defense become compromised [36]

Serum Calcium Analysis in CDK Patients

Comparative biochemical studies reveal:

- Hypocalcemia is more pronounced in patients with severe corneal lesions [36]
- Elevated tear calcium levels in CDK patients imply abnormal epithelial transport or leakage [37]

Clinical and Therapeutic Implications

Understanding calcium's role has therapeutic potential:

- Dietary supplementation with calcium and vitamin D may improve systemic and ocular health [37]
- Topical calcium modulators could prevent stromal calcification and enhance epithelial healing [32]
- Future therapies may target calcium ion channels to restore epithelial barrier function [33]

LIPID PROFILE AND ITS INFLUENCE ON CLIMATIC DROPLET KERATOPATHY

Lipid metabolism plays a critical role in ocular surface health, particularly in maintaining the tear film's lipid layer — vital for hydration, tear stability, and environmental protection. Recent evidence suggests that dyslipidemia may contribute to the progression of Climatic Droplet Keratopathy (CDK**)** by impairing lipid-mediated ocular surface defenses [38].

Impact of Dyslipidemia on Corneal Health

Dyslipidemia — characterized by elevated LDL, triglycerides, and low HDL — alters tear film composition, increases oxidative stress, and promotes inflammation.

Mechanisms Linking Dyslipidemia to CDK:

1. Tear Film Instability:
    - The meibomian glands produce lipids essential for reducing tear evaporation.
    - Dyslipidemia leads to meibomian gland dysfunction (MGD), destabilizing the tear film and worsening CDK [39].
2. Oxidative Stress and Lipid Peroxidation:
    - Elevated LDL levels trigger lipid peroxidation, producing reactive species like MDA and 4-HNE, which damage corneal cells.
    - Oxidized LDL (ox-LDL) induces cytokines such as IL-6 and TNF-α, exacerbating inflammation and stromal damage [40].
3. Extracellular Matrix Dysfunction and Opacity:
    - Chronic lipid imbalance disrupts ECM remodeling and leads to droplet deposition in the corneal stroma, impairing transparency [41].

Clinical Evidence Supporting Dyslipidemia as a Risk Factor for CDK**:**

- A study conducted among Kazhaks showed occurrence of CDK with high fat diet secondary to oxidative stress. [42].
- A fatty diet with minimal nutrients resulting in dyslipidemia is shown to increase oxidative stress systemically. [43].

Clinical Correlation Between CDK and Lipid Profile

Hyperlipidemia as a Risk Factor:

- A population-based study in Kazakh adults found that hyperlipidemia increases CDK risk, especially in outdoor workers [41].
- Higher LDL and triglyceride levels are correlated with greater CDK severity, highlighting lipid imbalance as a pathogenic factor [42].

Lipid Peroxidation and Oxidative Stress:

- CDK patients exhibit elevated MDA and 4-HNE in tear film samples, indicating lipid peroxidation [40].
- This oxidative damage disrupts ECM structure, promotes inflammation, and accelerates CDK [40].

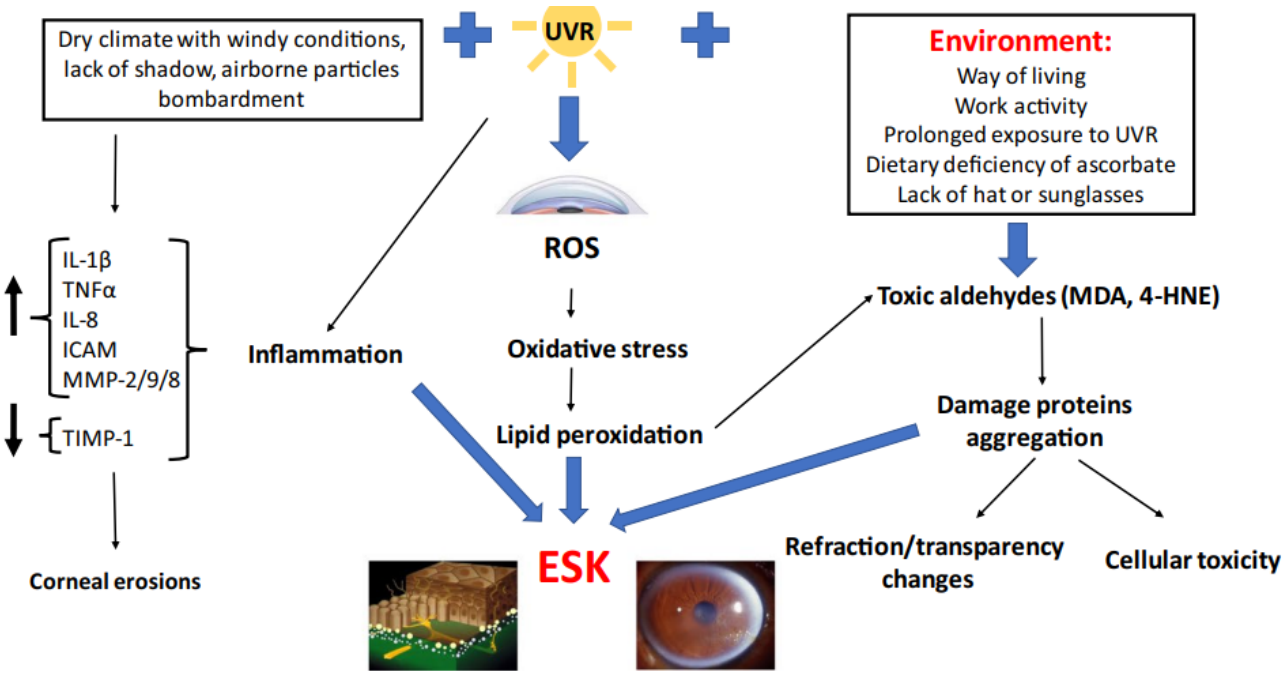


Figure 8 : Schematic diagram demonstrating lipid peroxidation and formation of CDK(5)

Treatment Implications:

- Statins have been explored for reducing systemic inflammation and lipid peroxidation in CDK. Preliminary results are promising [43].
- Omega-3 fatty acid supplementation improves tear lipid profile and may reduce oxidative damage in CDK [44].

DIAGNOSTIC TECHNIQUES IN CDK RESEARCH

Accurate diagnosis of Climatic Droplet Keratopathy (CDK) is vital for assessing disease severity and understanding its pathogenesis. Modern diagnostic strategies include imaging techniques, biochemical biomarker assays, and proteomic tools, all of which help to identify links between oxidative stress, lipid metabolism**,** and protein aggregation [45].

Slit Lamp Biomicroscopy and Confocal Microscopy

Slit Lamp Biomicroscopy: The Clinical Cornerstone

Slit lamp examination remains the primary method for diagnosing CDK, offering real-time visualization of corneal changes. It allows clinicians to observe subepithelial deposits, corneal haze, and tear film irregularities across disease stages:

- Early CDK**:** Granular subepithelial deposits near the limbus; mild dryness
- Intermediate CDK**:** Central stromal haze, irregular tear film breakup
- Advanced CDK: Dense amber-colored nodules, visual axis involvement [46]

Confocal Microscopy: Microscopic Visualization

Confocal microscopy enables high-resolution imaging of corneal cellular architecture. It has revealed:

- Amyloid-like protein deposits in the anterior stroma
- Altered extracellular matrix (ECM)
- Increased keratocyte apoptosis
- Corneal nerve fiber loss, indicating neurotrophic-like features [47]

In a study conducted conducted among leprosy patients with CDK , fifteen out of 24 eyes showed corneal nerve involvement. [48].

Biochemical and Proteomic Assays

Serum and Tear Biomarkers in CDK

Recent research highlights systemic markers that correlate with CDK severity:

- Albumin and A/G ratio abnormalities: Reflect oxidative damage and systemic inflammation [49]
- Lipid profile disturbances (elevated LDL/triglycerides, low HDL) correlate with CDK progression
- Tear biomarkers such as malondialdehyde (MDA) indicate lipid peroxidation and oxidative stress [50]

Proteomic Tools: Mass Spectrometry and Immunohistochemistry

- Mass spectrometry (MS) has identified oxidized proteins and lipid peroxidation products in CDK lesions, affirming the role of chronic UV-induced damage [46].
- Immunohistochemistry shows amyloid-like deposits and ECM protein misfolding, similar to other protein aggregation disorders [45].

THERAPEUTIC APPROACHES AND PREVENTIVE STRATEGIES

Climatic Droplet Keratopathy (CDK) is a progressive corneal degeneration with a multifactorial etiology involving UV exposure, oxidative stress, dyslipidemia, and chronic inflammation. While there is no cure, modern treatment strategies aim to relieve symptoms, stabilize tear film, reduce inflammation, and slow disease progression [51].

Role of Tear Film Stabilizers and Artificial Tears

Tear film stabilizers and lubricants form the first-line treatment to manage dry eye symptoms in CDK:

- Preservative-free artificial tears prevent ocular surface irritation and maintain hydration.
- Lipid-based eye drops restore the tear film's lipid layer and reduce evaporation [52].
- Hyaluronic acid-based drops promote epithelial healing and improve visual quality [53].

Anti-Inflammatory and Immunomodulatory Therapies

Chronic inflammation in CDK can be managed using:

- Cyclosporine A (CsA) eye drops: shown to reduce ocular surface inflammation and improve tear production in dry eye-related CDK [54].
- Lifitegrast: a lymphocyte function-associated antigen-1 antagonist under investigation for controlling cytokine-driven inflammation and corneal damage in degenerative conditions like CDK [54].

UV Protection and Environmental Modifications

Since UV light is a central factor in CDK pathogenesis:

- **UV-blocking wraparound sunglasses** protect against environmental oxidative stress [51].
- Use of polarized lenses is particularly effective for those in high-risk occupations (e.g., agriculture, fishing) [51].
- Avoidance of dust, wind, and pollutants is advised to minimize ocular surface irritation.

Antioxidant Therapy for CDK Management

To counteract oxidative stress, emerging antioxidant therapies include:

- Topical N-acetylcysteine (NAC) to scavenge ROS and protect corneal cells [55].
- Vitamin C and E supplementation has shown benefit in reducing oxidative damage in corneal tissue [55].
- Coenzyme Q10 eye drops are being studied for improving mitochondrial function and cell survival in oxidative environments [56].

Gene Therapy and Regenerative Medicine

Regenerative strategies are being explored for long-term repair of CDK-related corneal degeneration:

- Gene therapy targeting oxidative stress response genes may improve cellular resilience [57].
- Stem cell therapy using limbal epithelial stem cells aims to restore corneal surface structure [57].
- Amniotic membrane transplantation (AMT) has been effective in epithelial healing and inflammation control in severe CDK [58].

Pharmacological Innovations and Future Drug Development

- Sirtuin (SIRT1) activators are being researched for corneal cell longevity and defense against oxidative aging [59].
- Matrix metalloproteinase (MMP) inhibitors may help preserve ECM structure and prevent stromal degradation [60].
- Statins and omega-3 fatty acids may reduce lipid-induced inflammation and restore lipid balance in CDK [44].

MATERIALS AND METHODS

Study Design

This study was designed as a cross-sectional observational analysis to evaluate the correlation between Climatic Droplet Keratopathy (CDK) and various clinical and biochemical parameters.

Study Center

Participants were recruited from the Outpatient and Inpatient Departments of the Department of Ophthalmology at B.L.D.E. (Deemed to be University), Shri B. M. Patil Medical College, Hospital and Research Centre,

Duration of Study

The study was conducted over a period of **18 months** to ensure an adequate sample size and comprehensive data collection.

Sampling and Sample Size Calculation

The sample size was calculated using **G*Power Software ver 3.1.9.4,** based on the anticipated difference in Tear Film Break-Up Time (TBUT) between patients with Climatic Droplet Keratopathy (CDK) and healthy controls. The following parameters were used for the calculation: **[22]**

- **Effect size (d) = 0.7138**
- **Significance level (α) = 0.05**
- **Statistical power (1−β) = 0.80**
- **Allocation ratio (N2/N1) = 1**

Sample size output:

- Group 1 (CDK patients): 32 participants
- Group 2 (Controls): 32 participants
- **Total sample size: 64 participants**

This calculated sample size ensures 80% power to detect a statistically significant difference in TBUT between the two groups, assuming a 5% significance level.

Inclusion Criteria

For CDK Group (Cases):

- Clinically diagnosed cases of Climatic Droplet Keratopathy (CDK)
- Age> 40 years

Exclusion Criteria :

- History of previous intraocular surgery
- History of ocular trauma or uveitis
- Presence of systemic conditions associated with dry eye, such as Sjögren's syndrome or other autoimmune disorders

Study tool

A standardized and pre-validated **proforma** was employed for data collection[Appendix III] It was designed to systematically record demographic information, detailed clinical findings, and results of relevant laboratory investigations. The use of a uniform data collection tool ensured consistency, reliability, and completeness across all study participants.

Ethical Considerations

- Ethical approval was obtained from the **Institutional Ethics Committee** (IEC) of **B.L.D.E.** (Deemed to be University), Shri B. M. Patil Medical College, Hospital and Research Centre, Vijayapura, prior to the initiation of the study. [Appendix II].
- Written informed consent [Appendix I] was obtained from all participants before their enrollment in the study.
- The study was conducted in accordance with the ethical principles outlined in the **Declaration of Helsinki** for research involving human subjects.
- Strict confidentiality of all patient information was maintained throughout the study in compliance with institutional data protection policies.

Procedure

Patients fulfilling the clinical criteria for CDK diagnosis and willing to provide informed consent were included in the study. A standardized, pre-validated pro forma was used to record demographic details, clinical findings, and investigation results to maintain uniformity in data collection. Strict confidentiality of all patient information was maintained throughout the study, in accordance with institutional ethical guidelines and data protection protocols.

I. Clinical Examination

All participants underwent a comprehensive ophthalmological assessment, which included the following:

- Detailed ocular and systemic history (including environmental exposure and occupational background)
- Best-Corrected Visual Acuity (BCVA) measurement
- Slit lamp biomicroscopy to evaluate corneal deposits and determine disease severity
- Tear Film Break-Up Time (TBUT) test to assess tear film stability
- Schirmer's test to evaluate aqueous tear production
- Fluorescein staining of cornea
- Fundoscopic examination to assess posterior segment health

II. Laboratory Investigations

To evaluate potential systemic associations with CDK, venous blood samples were collected and analyzed in the VITROS 4600 chemistry system for the following biochemical parameters:

- Serum total protein
- Serum albumin
- Serum calcium
- Lipid profile

III. Grading of Climatic Droplet Keratopathy

CDK severity was graded based on slit lamp examination findings, using the following scale:

Table 2: Grading of Climatic Droplet Keratopathy

Grade	Status	Findings
Grade 0	Normal	No abnormal slit lamp findings
Grade 1	Slightly abnormal	Tiny subepithelial deposits at the nasal/temporal limbus
Grade 2	Abnormal	More prominent droplet-like deposits covering >2/3 of the cornea; cornea below the pupil's horizontal line may turn misty
Grade 3	Significantly abnormal	Sheet-like fused sediment covering the cornea in a stripe-like pattern; raised amber nodules may be present

IV. Diagnostic Criteria for Tear Film Dysfunction

The following clinical benchmarks were used to assess tear film abnormalities:

- **Tear Break-Up Time (TBUT)** ≤ 10 seconds was considered indicative of tear film instability

Procedure: Fluorescein dye was instilled into the patient's eye and made to blink to distribute it evenly. Using a cobalt blue filter on the slit lamp, the tear film was observed and the time from the last blink until the appearance of first dark spot was noted.

- **Schirmer's Test**

  Schirmer's test measures tear production and is classified into:

1. Schirmer I (Without Anaesthesia – Basal & Reflex Tear Secretion**)**.

2. Schirmer II (With Anaesthesia – Basal Tear Secretion Only)

Procedure: Excess tears are wiped off carefully. The strip is gently folded at 5mm from one end and placed at the junction of inner two-third and outer one-third of the eye. The wettability of the strip is checked after 5 mins and recorded.

Table 3: Schirmers test- Grading of dry eye

Grade	mm
Normal	>15mm
Mild dry eye	10-15mm
Moderate dry eye	5-10mm
Severe dry eye	<5mm

Patient Interventions

- The study involved only non-invasive diagnostic procedures, including slit lamp biomicroscopy, Tear Film Break-Up Time (TBUT) test, Schirmer's test, Fluorescein staining and serum biochemical investigations.
- No experimental medications or surgical interventions were administered as part of the study protocol.
- Patients diagnosed with advanced-stage CDK requiring therapeutic intervention, such as corneal transplantation or other surgical management, were referred to appropriate specialized services for further care and treatment.

Data Analysis and Interpretation:

Data was entered into Microsoft Excel (Windows 7; Version 2007) and analyses were done using the Statistical Package for Social Sciences (SPSS) for Windows software (version 22.0; SPSS Inc, Chicago). Descriptive statistics such as mean and standard deviation (SD) for continuous variables, frequencies and percentages were calculated for categorical Variables were determined. Association between Variables was analyzed by using Chi-Square test for categorical Variables. Unpaired t Test was used to compare mean of quantitative variables between Cases and Controls. Bar charts and Pie charts were used for visual representation of the analyzed data. Level of significance was set at 0.05

Results

From May 2023 to December 2024, comprehensive ophthalmological evaluations identified 49 cases of Climatic Droplet Keratopathy (CDK). Following a thorough screening process, 17 cases were excluded based on exclusion criteria that included a history of prior intraocular surgeries, ocular trauma, uveitis, or systemic syndromes associated with dry eye disease. The present study was thus conducted on 32 confirmed cases of Climatic Droplet Keratopathy, alongside a matched control group, to evaluate relevant clinical, demographic, and environmental factors. The findings derived from this cohort are detailed in the subsequent sections.

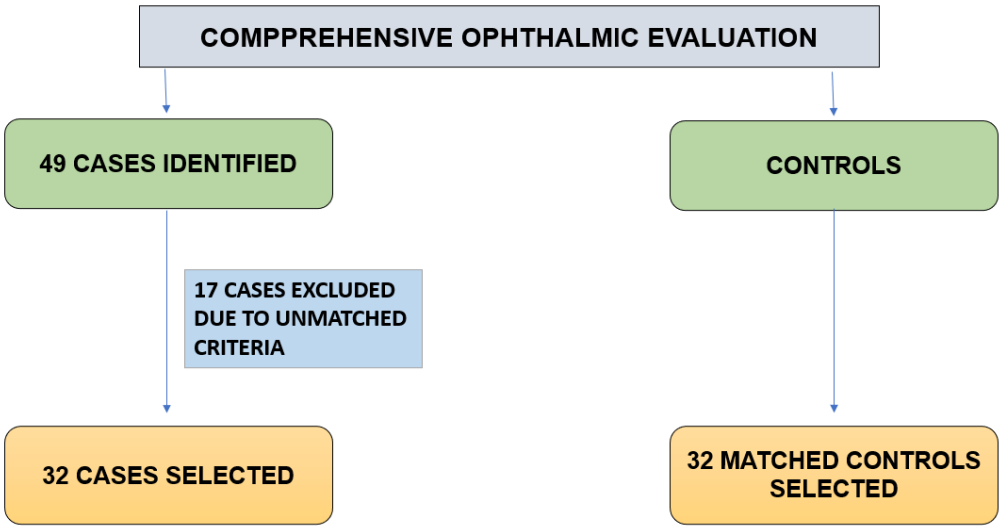


Figure 9 :Flow chart showing number of participants included as cases and controls

Table 4: Comparison of Age between Cases and Controls (N=64)

Age (in Years)	Group	
	Cases (n=32) n (%)	Controls (n=32) n (%)
41-50	2 (6.3)	7 (21.9)
51-60	3 (9.4)	4 (12.5)
61-70	13 (40.6)	15 (46.9)
71-80	10 (31.3)	4 (12.5)
>80	4 (12.5)	2 (6.3)
Mean (SD)	69.41 (9.66)	62.56 (10.89)
Chi-Square Test, P Value = 0.178, Not Significant		

Age distribution was analyzed to determine any significant differences between the case and control groups. Participants were grouped into five age categories.

- The most common age group in both cases and controls was 61–70 years, comprising 40.6% of cases and 46.9% of controls.
- Older age groups (71–80 and >80 years) were more represented among cases (43.8%) compared to controls (18.8%), suggesting a trend toward increased age in the case group.
- In contrast, younger age groups (41–60 years) were more prevalent in the control group (34.4%) than in cases (15.7%).

The mean age of cases was 69.41 years (SD = 9.66), notably higher than that of controls (62.56 years, SD = 10.89), indicating a difference in average age.

However, the Chi-square test yielded a P value of 0.178, which was not statistically significant, suggesting that the age distribution did not differ significantly between the groups.

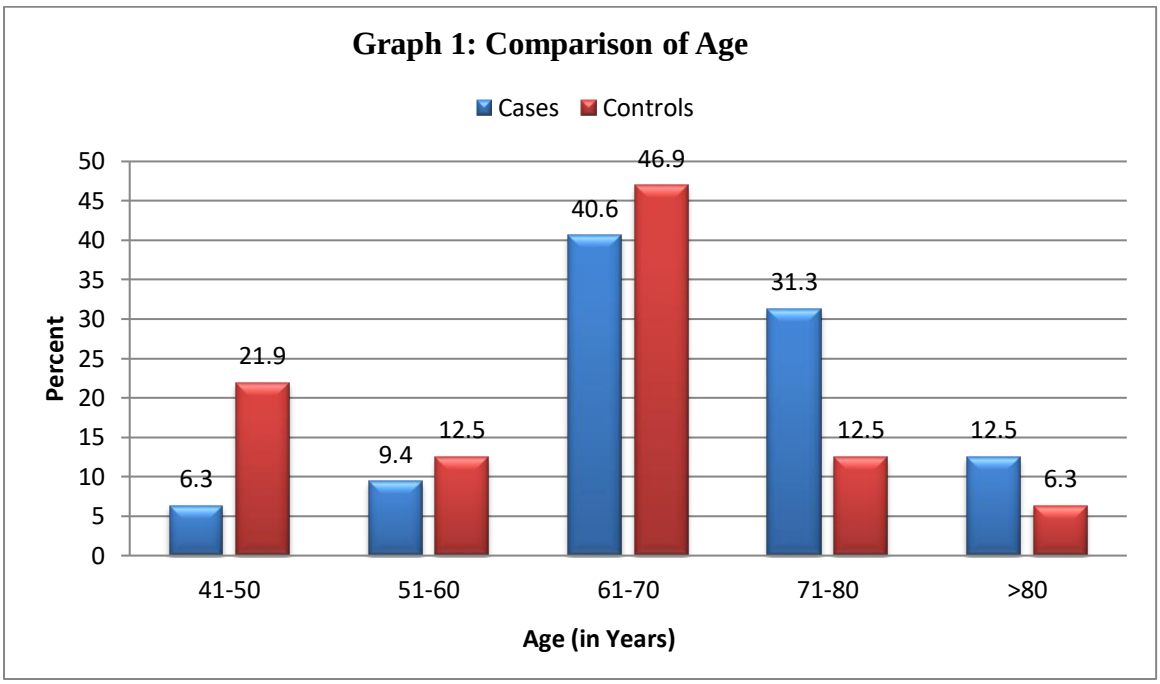


Table 5: Comparison of Gender between Cases and Controls (N=64)

Gender	Group	
	Cases (n=32) n (%)	Controls (n=32) n (%)
Female	9 (28.1)	20 (62.5)
Male	23 (71.9)	12 (37.5)
Chi-Square Test, P Value = 0.006, Significant		

Gender distribution showed a statistically significant difference between cases and controls. Among the cases, a majority were male (71.9%), while females accounted for only 28.1%. In contrast, the control group had a predominantly female composition (62.5%), with males comprising 37.5%.
The disparity in gender proportions was tested using the Chi-square test, yielding a P value of 0.006, indicating a statistically significant association between gender and case/control status.

These findings suggest that male gender may be more associated with the condition under study, warranting further investigation into potential gender-related risk factors or biological mechanisms.

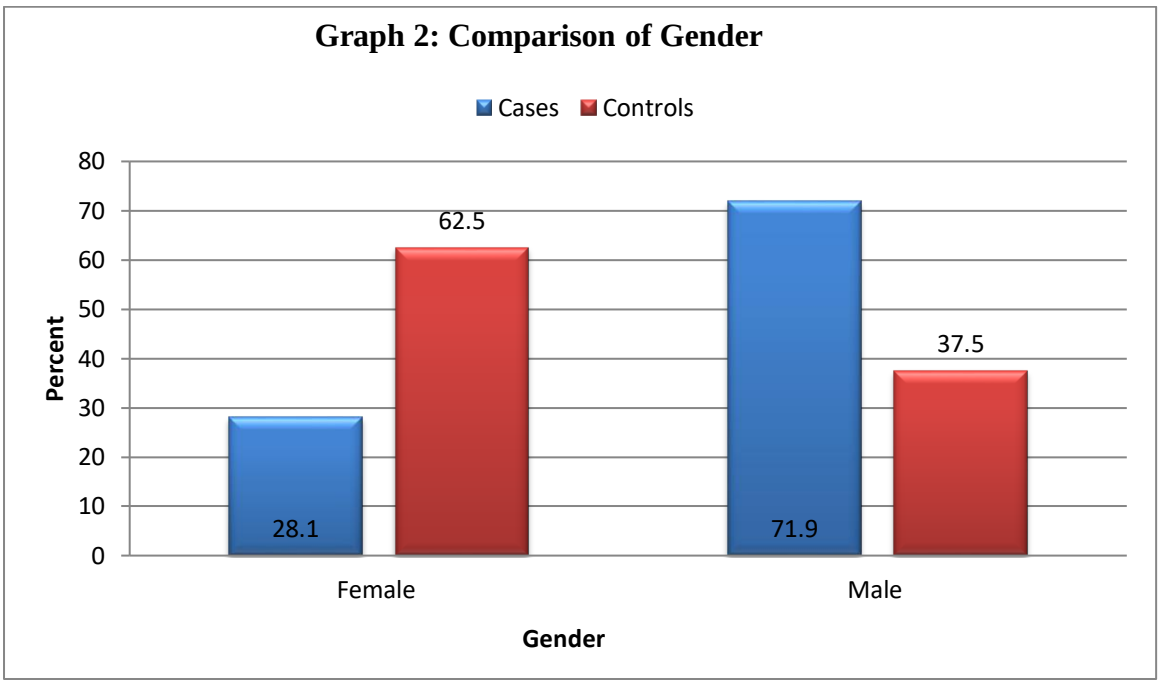


Table 6: Comparison of Occupation between Cases and Controls (N=64)

Occupation	Group	
	Cases (n=32) n (%)	Controls (n=32) n (%)
Businessman		1 (3.1)
Driver	1 (3.1)	1 (3.1)
Farmer	19 (59.4)	13 (40.6)
Housewife	4 (12.5)	8 (25.0)
Shopkeeper	2 (6.3)	
Tailor		1 (3.1)
Unemployed	5 (15.6)	8 (25.0)
Vendor	1 (3.1)	
Chi-Square Test, P Value = 0.319, Not Significant		

Occupational background was compared between cases and controls to identify any significant differences. The most common occupation among both groups was farming, accounting for 59.4% of cases and 40.6% of controls. A greater proportion of controls were housewives (25.0%) and unemployed (25.0%), compared to 12.5% and 15.6% respectively among cases.

Some occupations such as vendor (3.1%) and shopkeeper (6.3%) were reported only among cases, while tailor (3.1%) and businessman (3.1%) were represented only in the control group.

Despite these differences, the Chi-square test yielded a P value of 0.319, indicating that the association between occupation and case/control status was not statistically significant.

These findings suggest that while certain occupational patterns were observed, they did not show a significant relationship with case status in this study population.

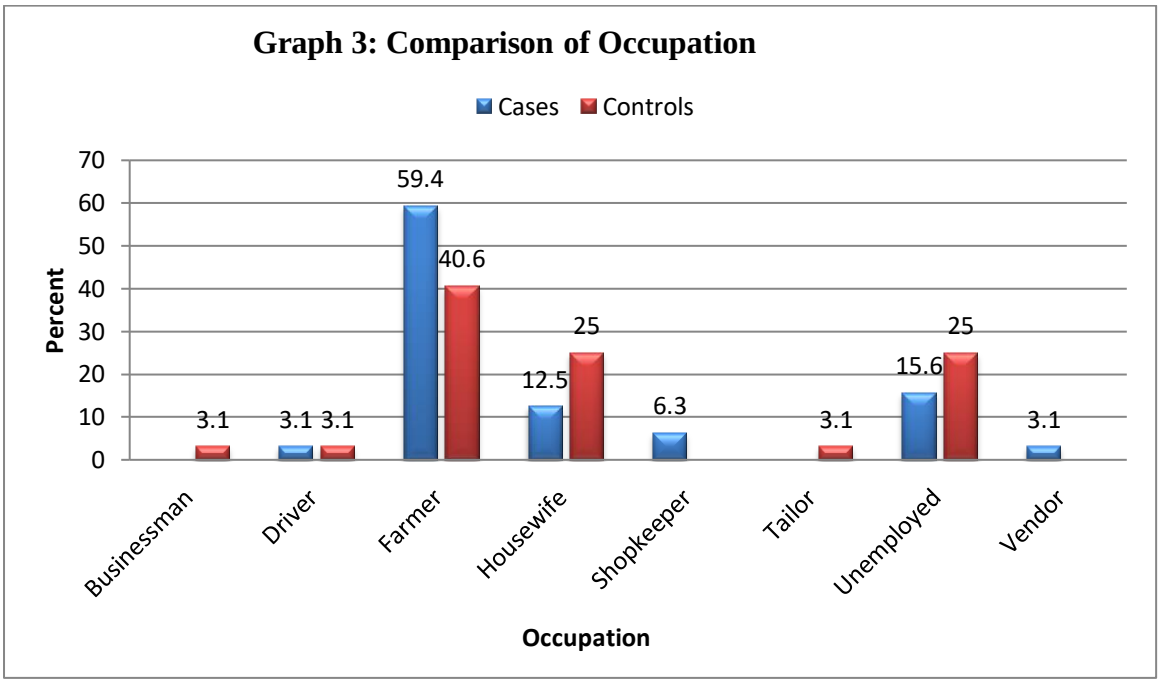


Table 7: Distribution of Study Subjects according to the Laterality among Cases (N=32)

Laterality	No.	Percent
Unilateral	6	18.8
Bilateral	26	81.3

Among the 32 cases studied, the majority demonstrated bilateral eye involvement, with 81.3% of cases presenting symptoms or findings in both eyes. In contrast, only 18.8% had unilateral involvement.

These findings suggest that Climatic Droplet Keratopathy (CDK) predominantly present as a bilateral condition in the affected population.

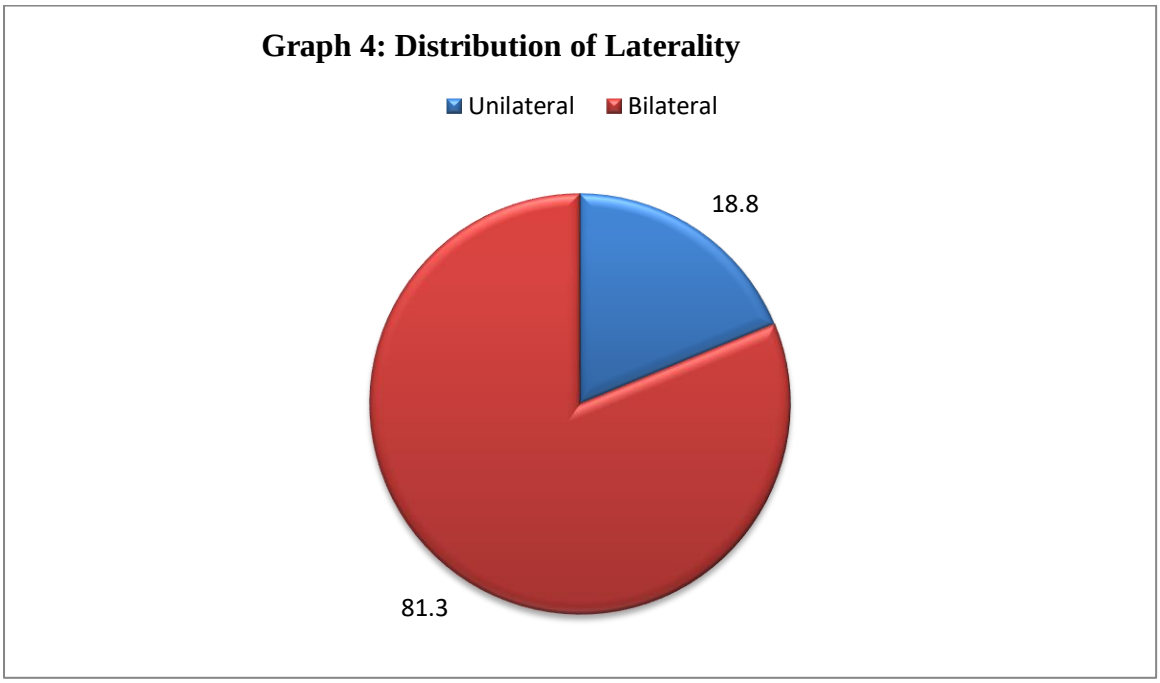


Table 8: Distribution of Study Subjects according to the Symptoms among Cases (N=32)

Symptoms	No.	Percent
Foreign body sensation	22	68.8
Epiphora	21	65.6

Among the 32 cases, the most commonly reported symptom was pricking, experienced by 68.8% of participants. This was closely followed by watering of the eyes, reported by 65.6% of the cases.

These findings highlight that ocular irritation and excessive tearing were prevalent symptoms in the affected individuals, suggesting a common clinical pattern within the case group.

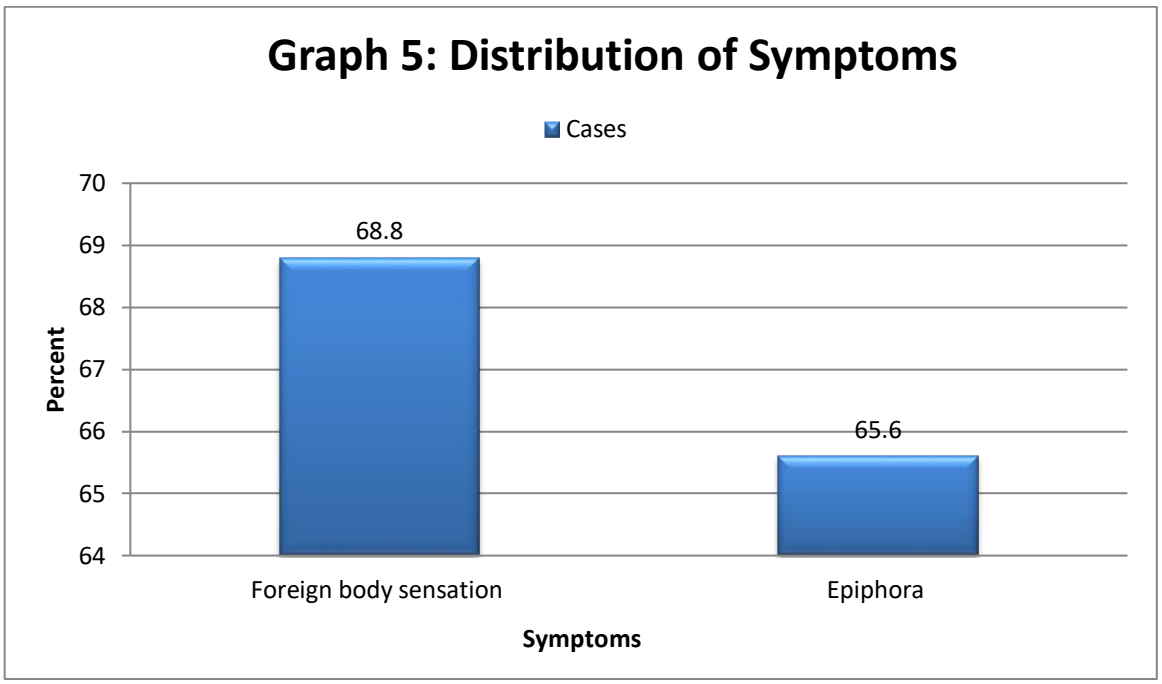


Table 9: Comparison of Comorbidities between Cases and Controls (N=64)

Comorbidities	Group		P Value
	Cases (n=32) n (%)	Controls (n=32) n (%)	
Diabetes Mellitus	5 (15.6)	5 (15.6)	1.000
Hypertension	8 (25.0)	5 (15.6)	0.351
Chi-Square Test, P Value Not Significant			

The distribution of comorbidities, specifically diabetes mellitus (DM) and hypertension (HTN), was compared between the two groups. Both cases and controls had an equal proportion (15.6%) of individuals with DM, indicating no difference in diabetes prevalence.

For hypertension, 25.0% of cases had HTN compared to 15.6% of controls. However, this difference was not statistically significant (P = 0.351).

Overall, the Chi-square test results confirmed that there was no significant association between the presence of these comorbidities and case/control status, suggesting that DM and HTN were evenly distributed across both groups.

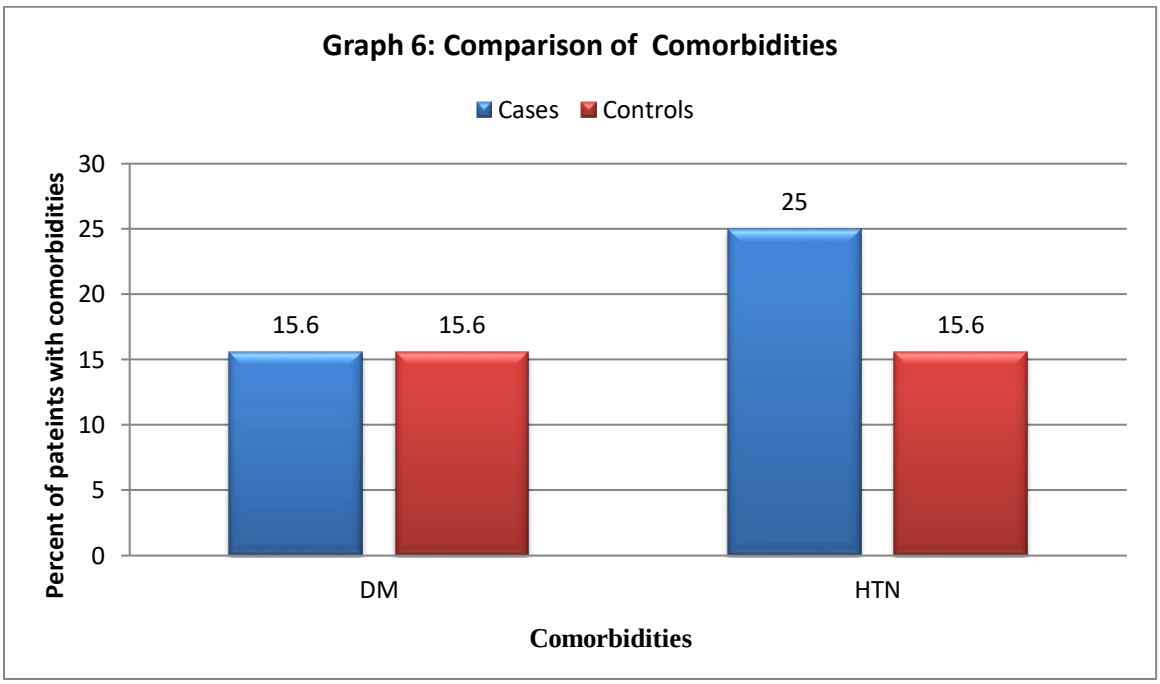


Table 10: Comparison of Addictions between Cases and Controls (N=64)

Addictions	Group		P Value
	Cases (n=32) n (%)	Controls (n=32) n (%)	
Alcohol	1 (3.1)	1 (3.1)	0.059
Smoking	5 (15.6)	2 (6.3)	
Tobacco	4 (12.5)	3 (9.4)	
Chi-Square Test, P Value Not Significant			

Addiction patterns, including alcohol use, smoking, and tobacco consumption, were examined among cases and controls.

- Alcohol consumption was reported by 1 participant (3.1%) in both groups, showing no difference.
- Smoking was more prevalent among cases (15.6%) compared to controls (6.3%).
- Tobacco use was observed in 12.5% of cases and 9.4% of controls.

Although there appeared to be a higher frequency of smoking and tobacco use among cases, the differences did not reach statistical significance, as indicated by the Chi-square test .

These results suggest that while certain addiction behaviors were more frequent in the case group, they were not significantly associated with disease status in this sample.

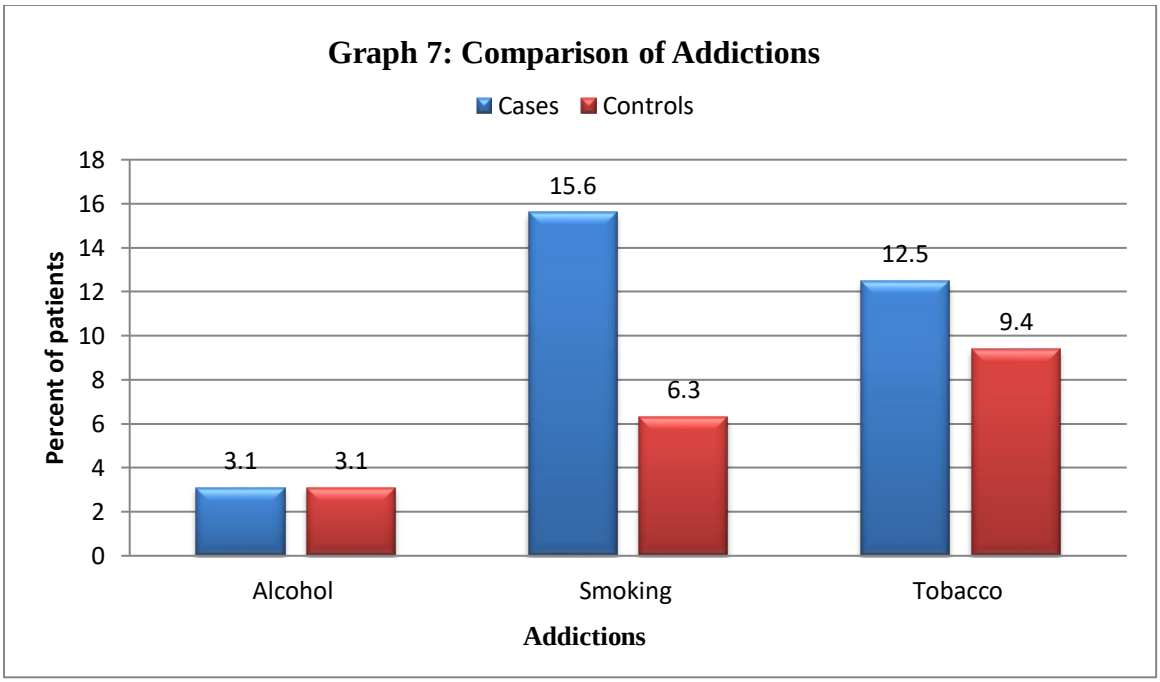


Table 11: Distribution of CDK Grade among Cases (N=64)

Grade	Cases		Total
	Right n (%)	Left n (%)	
0	3 (9.4)	3 (9.4)	6 (9.4)
1	11 (34.4)	11 (34.4)	22 (34.4)
2	6 (18.8)	10 (31.3)	16 (25.0)
3	12 (37.5)	8 (25.0)	20 (31.3)

The severity of Climatic Droplet Keratopathy (CDK) was graded for both eyes of the 32 cases. Grades ranged from 0 (no CDK) to 3 (severe CDK), with distributions summarized for the right eye (RE), left eye (LE), and the total eye count (N=64).

- Grade 1 was the most frequently observed, seen in 34.4% of both eyes (11 eyes each for RE and LE), contributing to a total of 22 eyes (34.4%).
- Grade 3 (severe CDK) was the second most common, with 12 right eyes (37.5%) and 8 left eyes (25.0%), totaling 20 eyes (31.3%).
- Grade 2 accounted for 18.8% of right eyes and 31.3% of left eyes, summing up to 16 eyes (25.0%).
- Grade 0, indicating no CDK, was least frequent, found in only 6 eyes (9.4%) across both sides.

These results indicate that mild to moderate CDK (Grades 1–2) was highly prevalent, with a notable number of cases showing asymmetry in grading between eyes. Only a small proportion exhibited no signs of CDK in one eye.

Graph 8: Distribution of CDK Grade

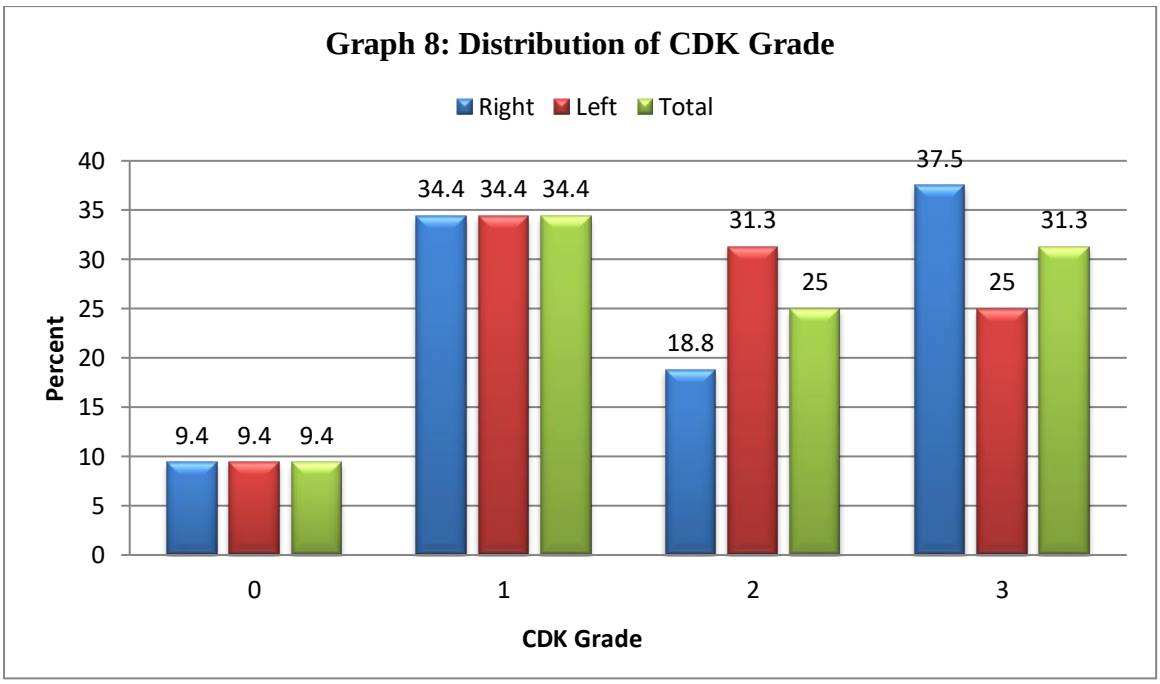


Table 12: Comparison of Lens Status (Both Eyes) between Cases and Controls (N=64)

Status	Group	
	Cases (n=64) n (%)	Controls (n=64) n (%)
1	54 (84.4)	53 (82.8)
2	8 (12.5)	11 (17.2)
3	2 (3.1)	-
Chi-Square Test, P Value = 0.288, Not Significant		

The overall lens status of both eyes (total of 64 eyes per group) was compared between cases and controls. The distribution was as follows:

- Status 1 (Immature Cataract) was the most common finding in both groups, seen in 84.4% of eyes in cases and 82.8% in controls, showing near-identical prevalence.
- Status 2 (Mature Cataract) occurred slightly more in controls (17.2%) compared to cases (12.5%).
- Status 3 (Hypermature Cataract) was observed in 2 eyes (3.1%) among cases, but was absent in controls.

These findings suggest that lens status was generally comparable between groups, with immature cataracts being predominant, and hypermature changes remaining rare and confined to cases.

Graph 9: Comparison of Lens Status in Both Eyes

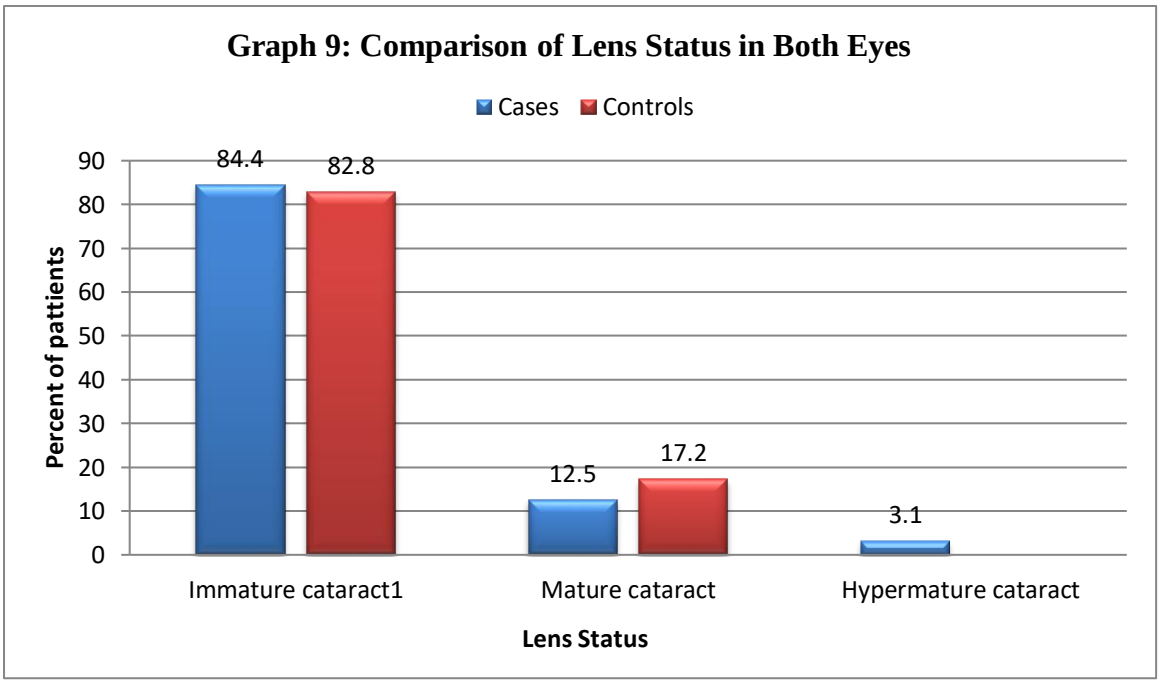


Table 13: Comparison of Schirmer's I Test (Both Eyes) between Cases and Controls

(mm)	Group	
	Cases (n=64) n (%)	**Controls (n=64) n (%)**
0-5	-	-
6-10	3 (4.7)	1 (1.6)
11-15	12 (18.8)	17 (26.6)
>15	49 (76.6)	46 (71.9)
Chi-Square Test, P Value = 0.375, Not Significant		

The Schirmer's I Test, used to assess both basal and reflex tear production, was conducted on both eyes of each subject, resulting in 64 eyes per group.

- The majority of eyes in both groups demonstrated normal tear secretion (>15 mm): 76.6% of cases and 71.9% of controls.
- Tear production in the 11–15 mm range was observed in 18.8% of cases and 26.6% of controls.
- Tear deficiency in the 6–10 mm range was seen in 3 eyes (4.7%) among cases and 1 eye (1.6%) among controls.
- Notably, no eyes in either group fell in the 0–5 mm range, which would indicate severe dry eye.

The Chi-square test yielded a P value of 0.375, indicating that the observed differences in tear secretion levels between the groups were not statistically significant.

These results suggest that tear production profiles were broadly similar between cases and controls, with a high proportion of eyes in both groups demonstrating normal tear output.

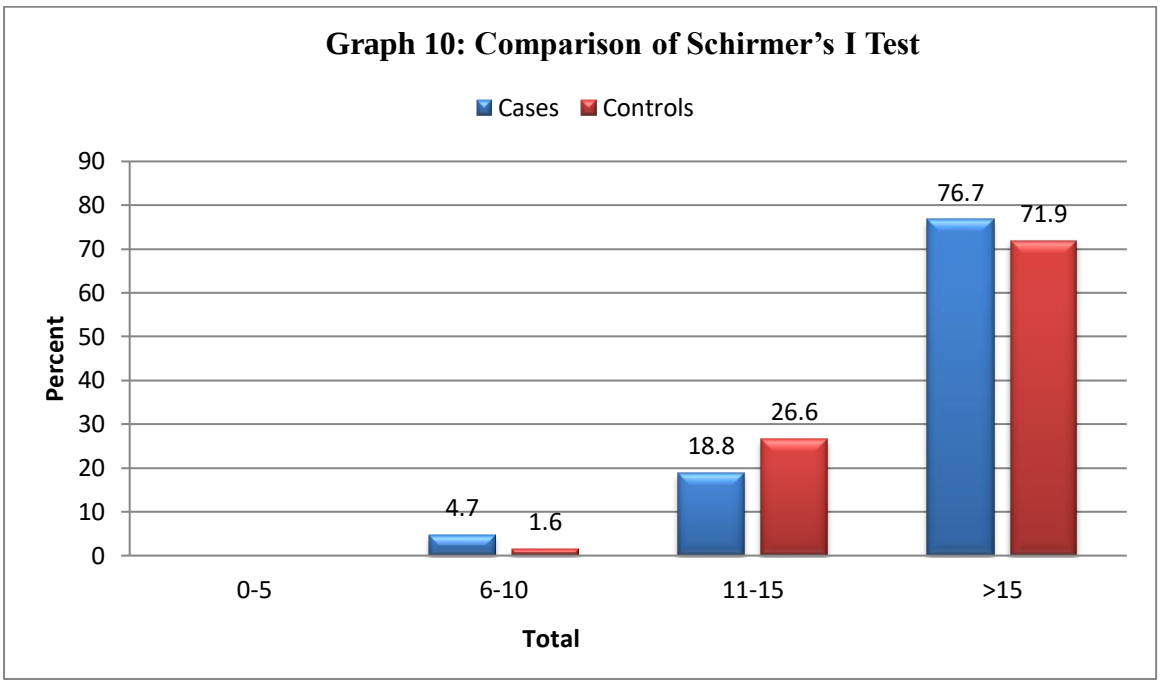


Table 14: Comparison of Schirmer's II Test (Both Eyes) between Cases and Controls

(mm)	Group	
	Cases (n=64) n (%)	Controls (n=64) n (%)
0-5	10 (15.6)	2 (3.1)
6-10	33 (51.6)	18 (28.1)
11-15	19 (29.7)	15 (23.4)
>15	2 (3.1)	29 (45.3)
Chi-Square Test, P Value <0.001, Significant		

The Schirmer's II Test, which measures basal tear secretion, showed a marked difference in tear production between cases and controls.

- Reduced tear secretion (0–5 mm) was observed in 15.6% of case eyes, compared to only 3.1% of control eyes.
- The 6–10 mm range, indicating moderate dryness, was the most common in cases, found in 51.6% of eyes, while only 28.1% of control eyes fell into this category.
- Tear secretion between 11–15 mm was seen in 29.7% of cases and 23.4% of controls.
- Notably, normal or excessive tear secretion (>15 mm) was observed in only 3.1% of case eyes, whereas a significant 45.3% of control eyes demonstrated this level.

The Chi-square test yielded a P value of <0.001, indicating a highly significant difference in tear production between the two groups. These findings reveal that cases exhibited significantly reduced reflex tear secretion compared to controls, suggesting a possible association between the condition under study and impaired lacrimal gland function.

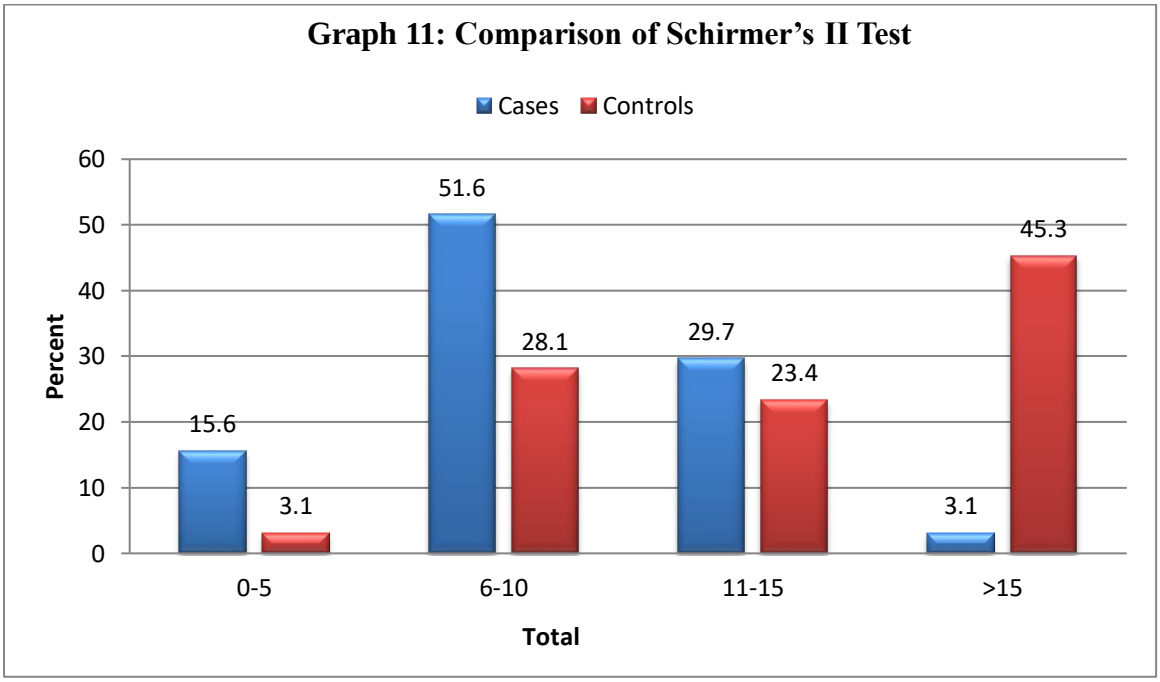


Table 15: Comparison of TBUT (Both Eyes) between Cases and Controls

(sec)	Group	
	Cases (n=64) n (%)	Controls (n=64) n (%)
Abnormal	61 (95.3)	36 (56.3)
Normal	3 (4.7)	28 (43.7)
Chi-Square Test, P Value <0.001, Significant		

The Tear Break-Up Time (TBUT) test, an indicator of tear film stability, showed a significant difference between cases and controls.

- An abnormal TBUT (indicative of tear film instability) was observed in 95.3% of eyes among cases, compared to 56.3% of eyes in controls.

- Conversely, a normal TBUT was present in only 4.7% of case eyes, while 43.7% of control eyes showed normal tear film stability.

The difference between groups was statistically significant (Chi-square test, $P < 0.001$), indicating that cases had a significantly higher prevalence of tear film instability than controls.

These findings strongly support the association between the condition under study and disruption of tear film stability, as measured by TBUT.

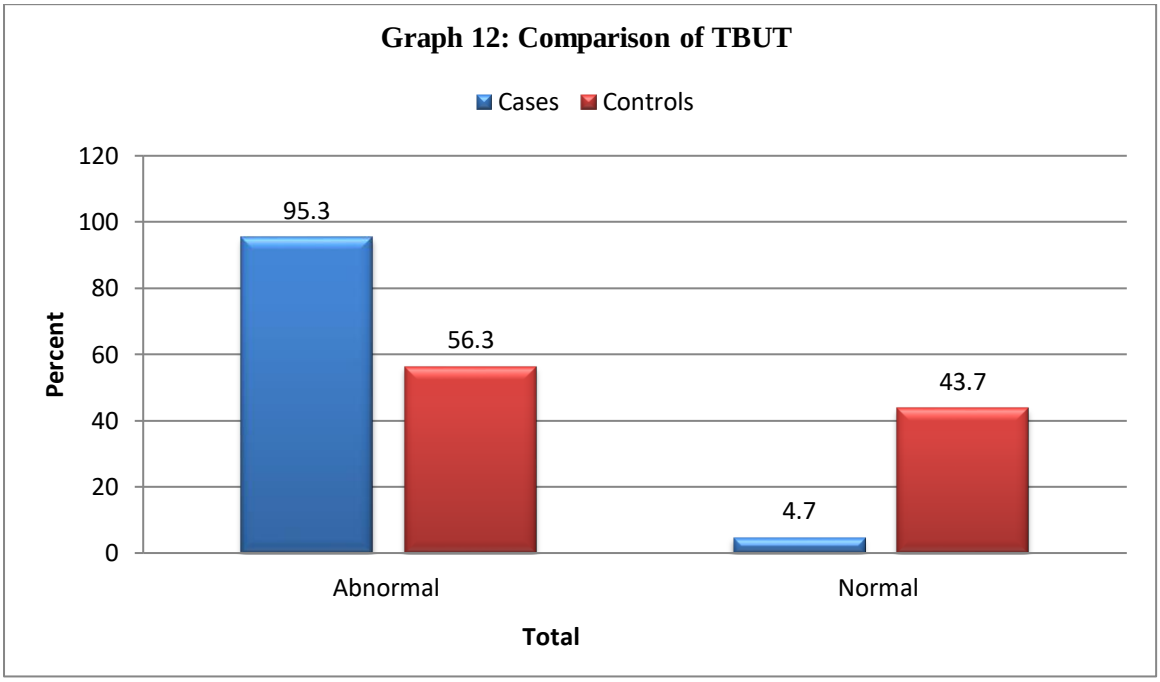


Table 16: CDK Grade (Both eyes) and Schirmers Test I

mm	CDK Grade			
	Grade 0 n (%)	**Grade 1 n (%)**	**Grade 2 n (%)**	**Grade 3 n (%)**
0-5	-	-	-	-
6-10		2 (9.1)	1 (6.3)	-
11-15	1 (16.7)	6 (27.3)	2 (12.5)	3 (15.0)
>15	5 (83.3)	14 (63.6)	13 (81.3)	17 (85.0)
Chi-Square Test, P Value = 0.635, Not Significant				

Tear secretion assessed by Schirmer's I Test was compared across various grades of CDK using categorical tear production levels.

- The majority of eyes across all grades exhibited normal tear secretion (>15 mm), with:
  - 83.3% in Grade 0
  - 63.6% in Grade 1
  - 81.3% in Grade 2
  - 85.0% in Grade 3
- Tear production in the 11–15 mm range was more commonly observed in Grade 1 (27.3%), and occurred less frequently in Grade 3 (15.0%) and Grade 2 (12.5%).
- Low tear secretion (6–10 mm) was minimally present, reported only in 2 cases (9.1%) in Grade 1 and 1 case (6.3%) in Grade 2. Notably, no eyes in any group showed severe dryness (0–5 mm).

The Chi-square test yielded a P value of 0.635, indicating no statistically significant association between Schirmer's I Test results and CDK grade.

These results suggest that while tear secretion patterns were generally preserved across CDK grades, Schirmer's I Test did not significantly correlate with disease severity.

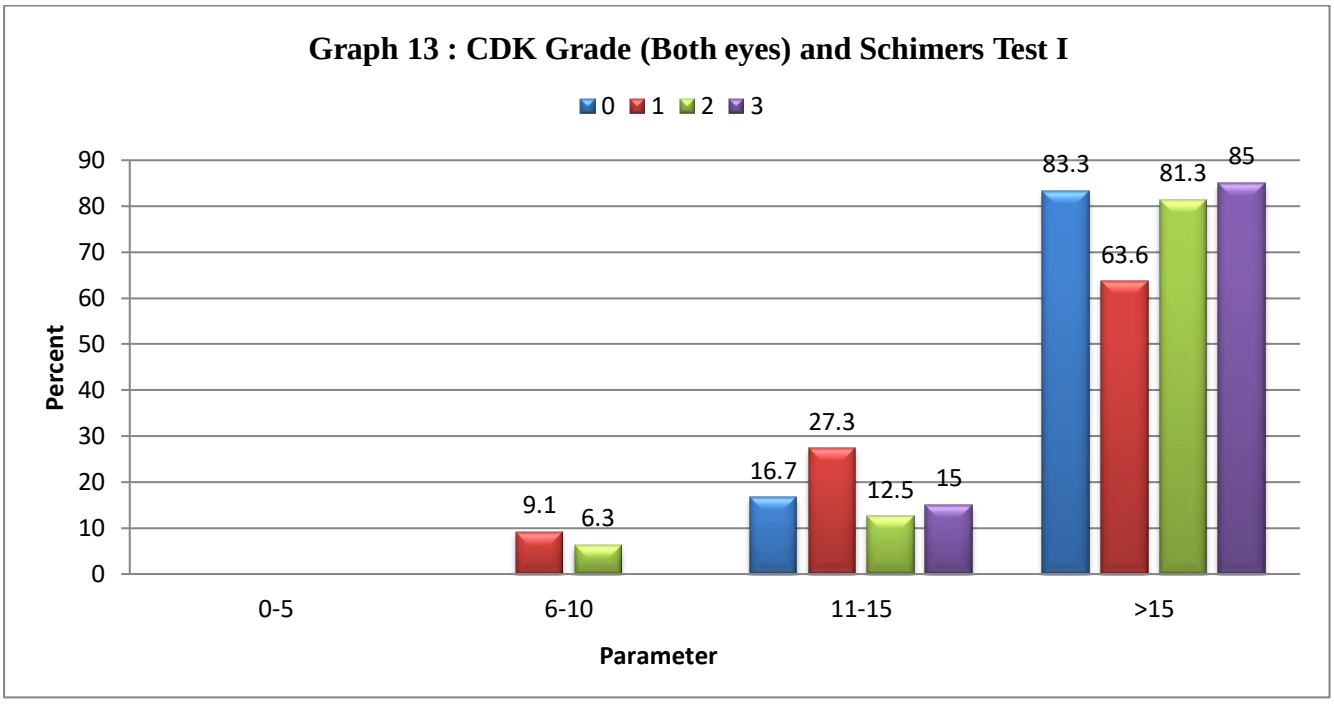


Table 17: CDK Grade (BOTH EYES) and Schirmers Test II

mm	CDK Grade			
	Grade 0 n (%)	**Grade 1 n (%)**	**Grade 2 n (%)**	**Grade 3 n (%)**
0-5	-	2 (9.1)	5 (31.3)	3 (15.0)
6-10	3 (50.0)	8 (36.4)	8 (50.0)	14 (70.0)
11-15	2 (33.3)	12 (54.5)	2 (12.5)	3 (15.0)
>15	1 (16.7)	-	1 (6.3)	-
Chi-Square Test, P Value = 0.022, Significant				

The Schirmer's II Test, measuring basal tear secretion, was analyzed across different CDK grades to assess its correlation with disease severity.

- A clear trend of reduced tear secretion was observed with increasing CDK severity:
  - Low values (6–10 mm) were most frequent across all grades, especially in Grade 3 (70.0%) and Grade 2 (50.0%).
  - Severe tear deficiency (0–5 mm) was absent in Grade 0, but increased progressively in Grade 1 (9.1%), Grade 2 (31.3%), and Grade 3 (15.0%).
- Higher tear secretion (11–15 mm) was more common in Grades 0 and 1 (33.3% and 54.5%, respectively), but declined sharply in Grades 2 and 3.
- Normal to high secretion (>15 mm) was found only in Grade 0 (16.7%) and Grade 2 (6.3%), with none observed in Grade 1 or Grade 3.

The Chi-square test yielded a P value of 0.022, indicating a statistically significant association between CDK grade and Schirmer's II Test values.These findings suggest that tear secretion significantly declines with increasing CDK severity.

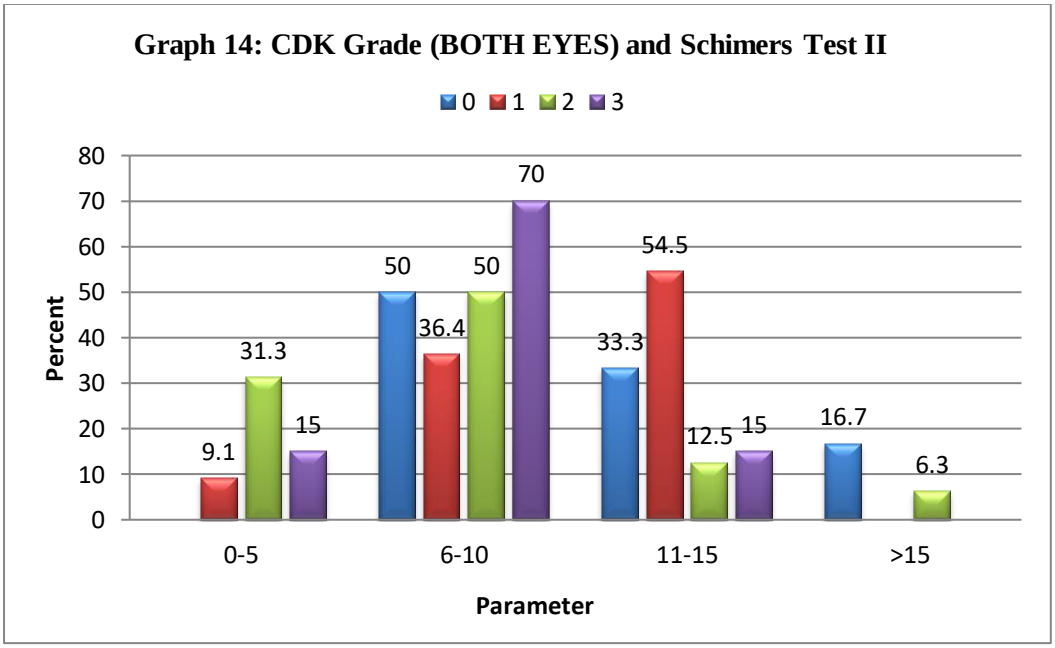


Table 18: Comparison of Schirmers Test between Cases and Controls (N=64)

Schirmers Test	Group		P Value
	Cases (n=32) Mean (SD)	Controls (n=32) Mean (SD)	
I	20.73 (6.53)	20.81 (6.54)	0.946
II	9.44 (4.08)	14.17 (5.71)	<0.001*
Unpaired t Test, P Value *Significant			

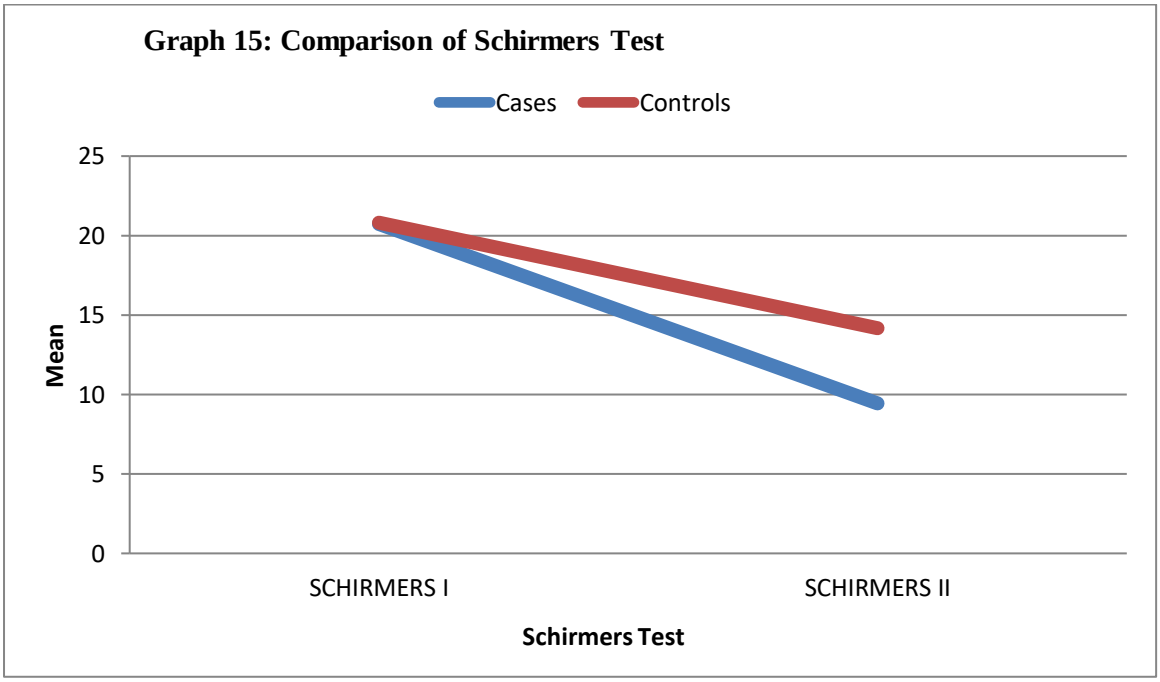


Table 19: CDK Grade (both eyes) and TBUT

T -BUT	CDK Grade			
	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)
Abnormal	4 (66.7)	21 (95.5)	16 (100.0)	20 (100.0)
Normal	2 (33.3)	1 (4.5)		
Chi-Square Test, P Value = 0.005, Significant				

Tear film stability, as measured by Tear Break-Up Time (TBUT), was compared across various grades of Climatic Droplet Keratopathy (CDK).

- A clear pattern of tear film instability was observed with increasing CDK severity:
    - Abnormal TBUT was seen in:
        - 66.7% of Grade 0
        - 95.5% of Grade 1
        - 100% of Grades 2 and 3
    - Normal TBUT was limited to Grade 0 (33.3%) and Grade 1 (4.5%), with no normal values observed in Grades 2 or 3.

The Chi-square test yielded a P value of 0.005, indicating a statistically significant association between TBUT and CDK grade.

These results strongly suggest that tear film instability worsens with increasing CDK severity, making TBUT a clinically relevant marker in assessing and monitoring the progression of ocular surface disease in CDK patients.

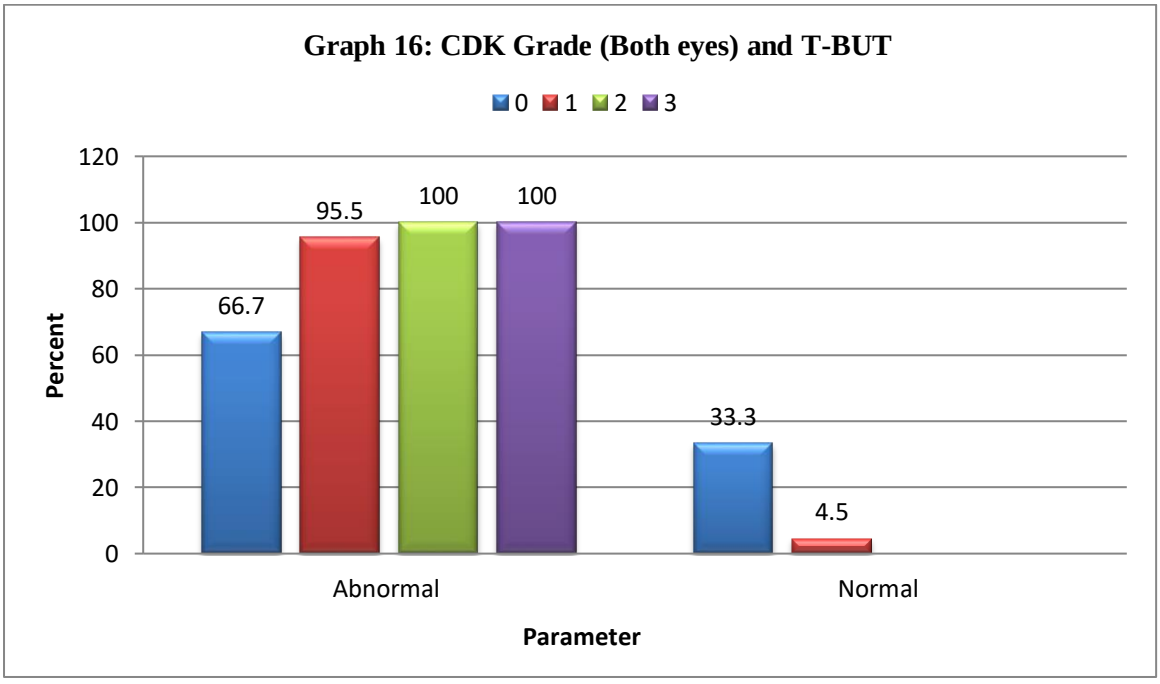


Table 20: Comparison of Protein between Cases and Controls (N=64)

Protein	Group	
	Cases (n=32) n (%)	**Controls (n=32) n (%)**
Low	4 (12.5)	5 (15.6)
Normal	27 (84.4)	27 (84.4)
Elevated	1 (3.1)	-
Chi-Square Test, P Value = 0.574, Not Significant		

Protein levels were categorized as low, normal, or elevated among both cases and controls.

- The majority of participants in both groups had normal protein levels: 84.4% in both cases and controls.
- Low protein levels were observed in 12.5% of cases and 15.6% of controls, indicating a slight but statistically insignificant variation.
- Elevated protein levels were reported in only one case (3.1%), and none among controls.

Statistical analysis using the Chi-square test showed no significant association between protein levels and case/control status (P = 0.574).

These findings suggest that protein level variations were minimal and did not significantly differ between the two groups.

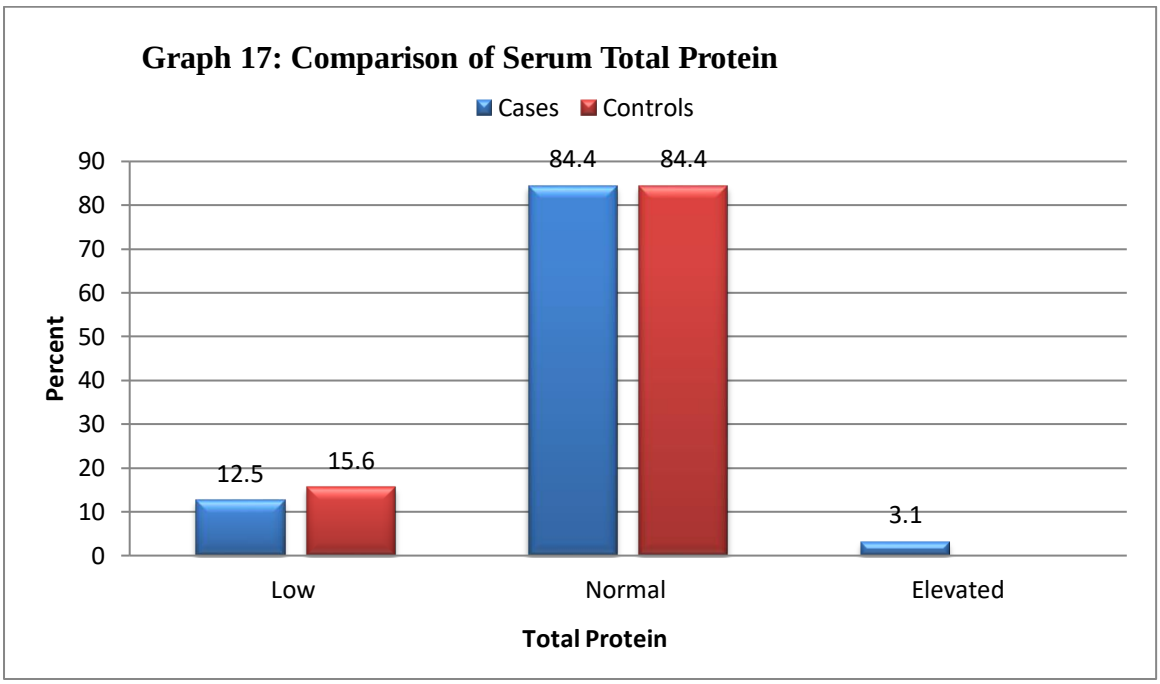


Table 21: Comparison of Albumin between Cases and Controls (N=64)

Albumin	Group	
	Cases (n=32) n (%)	Controls (n=32) n (%)
Low	12 (37.5)	6 (18.8)
Normal	19 (59.4)	26 (81.3)
Elevated	1 (3.1)	-
Chi-Square Test, P Value = 0.129, Not Significant		

Serum albumin levels were assessed and categorized as low, normal, or elevated among the 32 cases and 32 controls.

- Normal albumin levels were more common among controls (81.3%) compared to cases (59.4%).
- Low albumin was observed in a higher proportion of cases (37.5%) than controls (18.8%), suggesting a trend toward hypoalbuminemia in the case group.
- Elevated albumin was rare, seen in only 1 case (3.1%), and not observed in any control participants.

Despite these apparent differences, the Chi-square test revealed no statistically significant association between albumin levels and group status (P = 0.129).

These findings indicate that although low albumin was more frequent in cases, the difference did not reach statistical significance but may still warrant further exploration in larger studies.

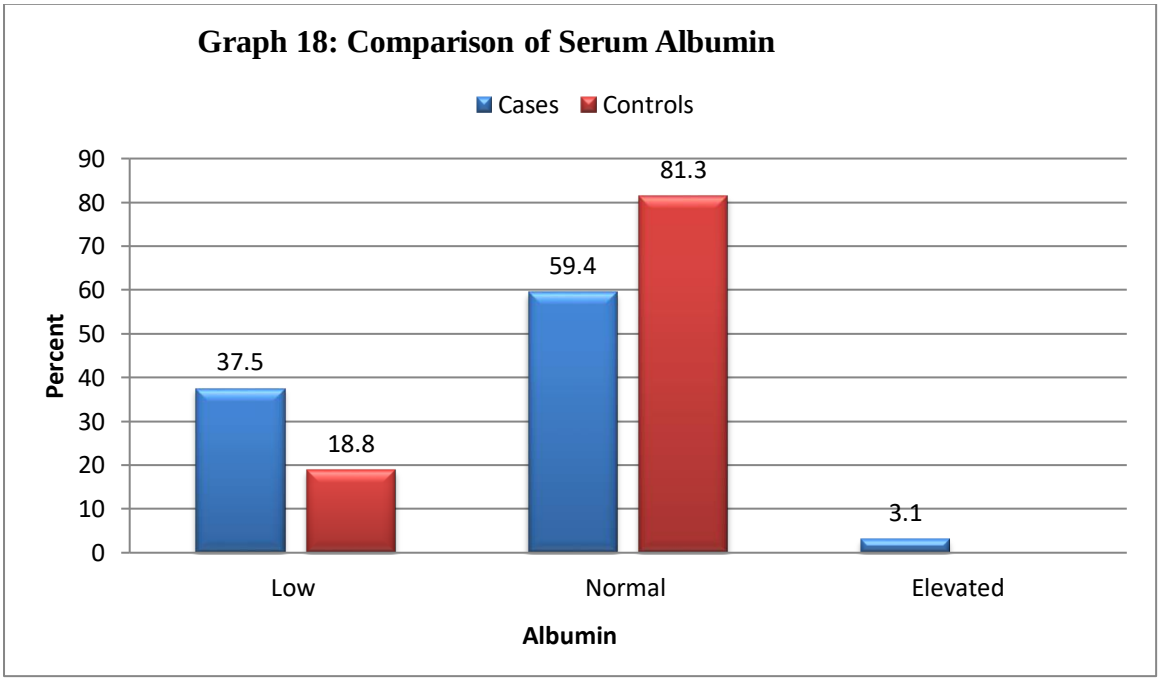


Table 22: Comparison of A/G Ratio between Cases and Controls (N=64)

AG Ratio	Group	
	Cases (n=32) n (%)	Controls (n=32) n (%)
Low	12 (37.5)	6 (18.8)
Normal	19 (59.4)	26 (81.3)
Elevated	1 (3.1)	-
Chi-Square Test, P Value = 0.129, Not Significant		

The A/G ratio, an important marker of protein balance, was categorized as low, normal, or elevated in both groups.

- Normal A/G ratios were more prevalent among controls (81.3%) compared to cases (59.4%).
- Low A/G ratio was found in 37.5% of cases, nearly double the 18.8% observed in controls, suggesting a relative imbalance in serum proteins among cases.
- Elevated A/G ratio was noted in only 1 case (3.1%), and was not seen in any control participants.

Although these trends hint at altered protein metabolism in the case group, the Chi-square test showed no statistically significant difference between the groups (P = 0.129).

Overall, while low A/G ratio appeared more frequently in cases, the results did not reach statistical significance, aligning with trends seen in albumin levels.

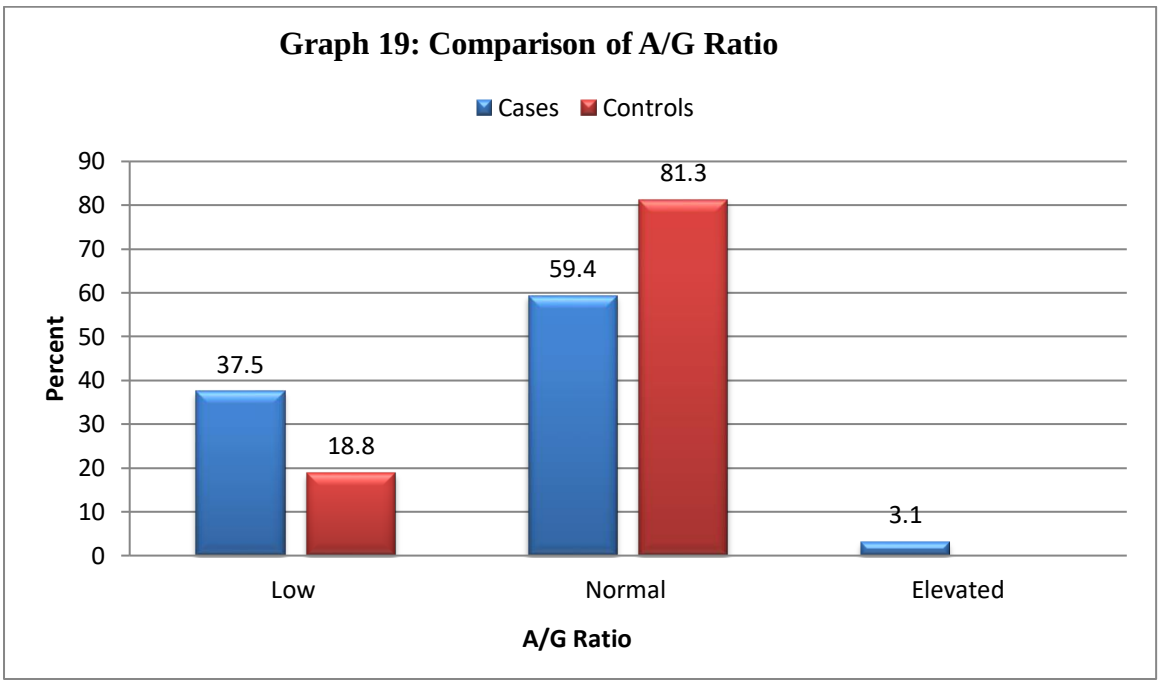


Table 23: Comparison of Calcium between Cases and Controls (N=64)

Calcium	Group	
	Cases (n=32) n (%)	Controls (n=32) n (%)
Low	7 (21.9)	4 (12.5)
Normal	25 (78.1)	27 (84.4)
Elevated	-	1 (3.1)
Chi-Square Test, P Value = 0.388, Not Significant		

Serum calcium levels were evaluated and categorized as low, normal, or elevated among cases and controls.

- Normal calcium levels were seen in the majority of participants in both groups—78.1% of cases and 84.4% of controls.
- Low calcium levels were more frequent in cases (21.9%) compared to controls (12.5%), indicating a modest difference.
- Elevated calcium was observed in 1 control participant (3.1%), but not in any of the cases.

Statistical analysis using the Chi-square test revealed that the differences in calcium distribution between the two groups were not statistically significant (P = 0.388).

These findings suggest that while hypocalcemia was slightly more prevalent among cases, overall calcium status did not differ significantly between the groups.

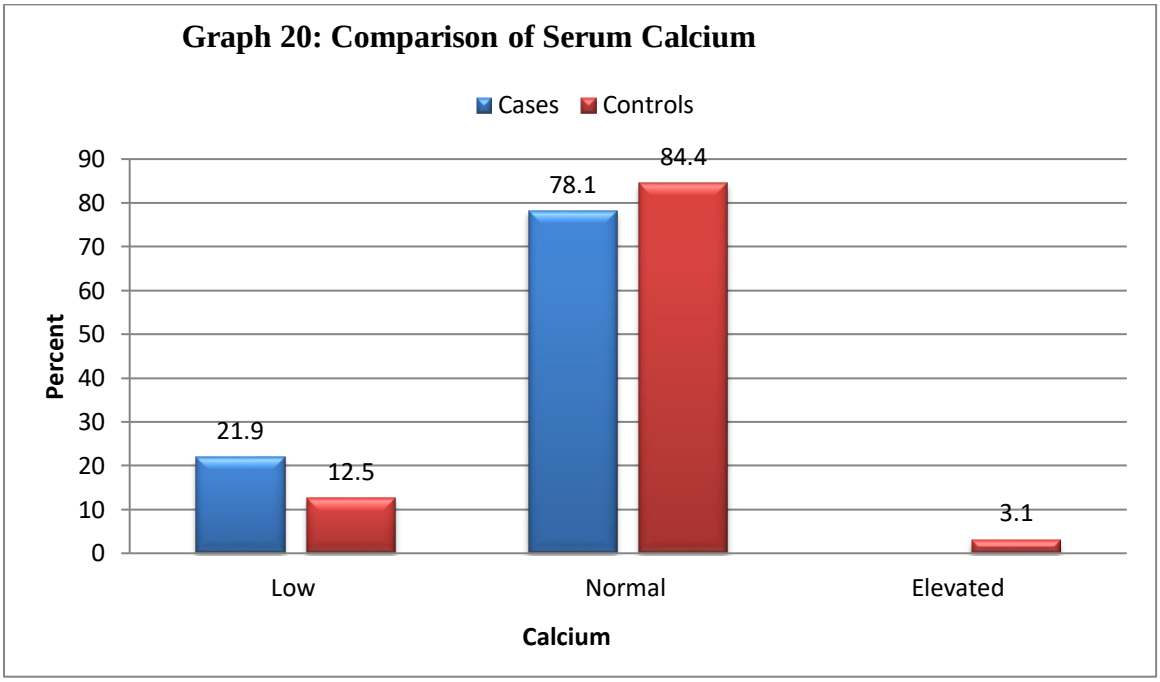


Table 24: Comparison of Cholesterol between Cases and Controls (N=64)

Cholesterol	Group	
	Cases (n=32) n (%)	Controls (n=32) n (%)
Normal	26 (81.3)	27 (84.4)
Elevated	6 (18.8)	5 (15.6)
Chi-Square Test, P Value = 0.740, Not Significant		

Cholesterol levels were categorized as normal or elevated in both the case and control groups.

- Normal cholesterol levels were observed in the majority of participants—81.3% of cases and 84.4% of controls.
- Elevated cholesterol was slightly more frequent among cases (18.8%) than controls (15.6%).

Despite this minor difference, statistical analysis via Chi-square test showed no significant association between cholesterol levels and group status (P = 0.740).

These findings suggest that cholesterol levels were comparable between cases and controls, with no meaningful difference in lipid profiles.

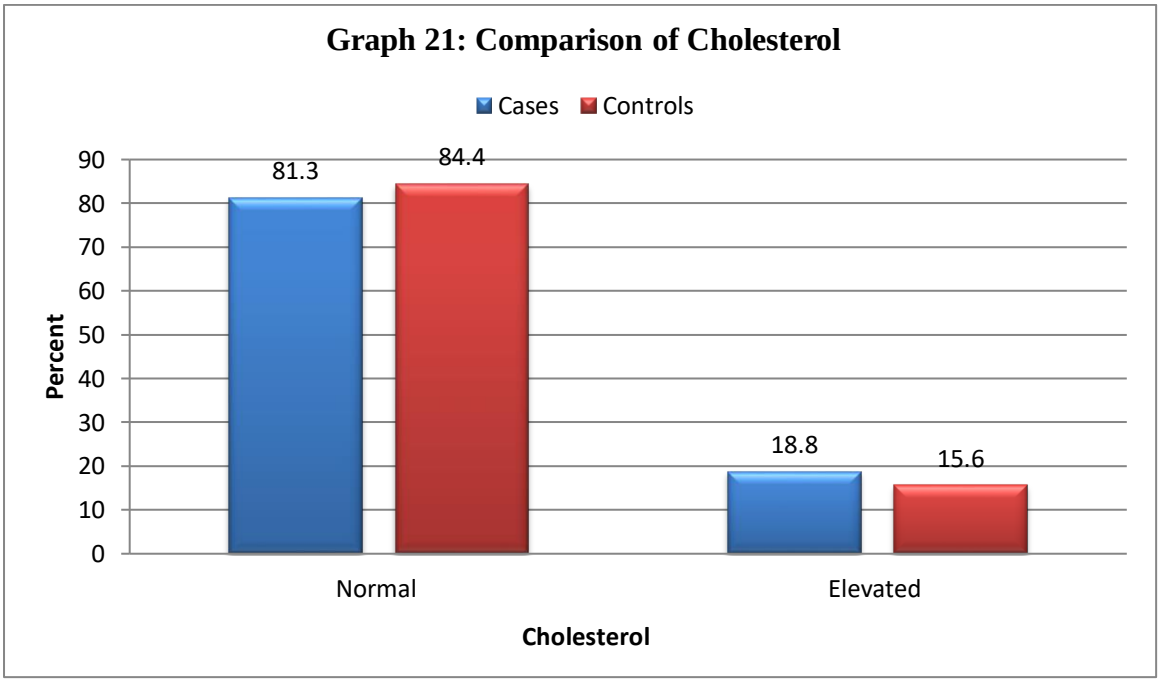


Table 25: Comparison of TG between Cases and Controls (N=64)

TG	Group	
	Cases (n=32) n (%)	Controls (n=32) n (%)
Normal	28 (87.5)	29 (90.6)
Elevated	4 (12.5)	3 (9.4)
Chi-Square Test, P Value = 0.689, Not Significant		

Triglyceride (TG) levels were assessed and categorized as normal or elevated across both study groups.

- Normal TG levels were seen in the vast majority of participants: 87.5% of cases and 90.6% of controls.
- Elevated TG levels were reported in 4 cases (12.5%) and 3 controls (9.4%).

The difference in TG distribution was not statistically significant, as indicated by the Chi-square test (P = 0.689).

These results suggest that triglyceride profiles were similar in both groups, with no meaningful difference in the prevalence of hypertriglyceridemia.

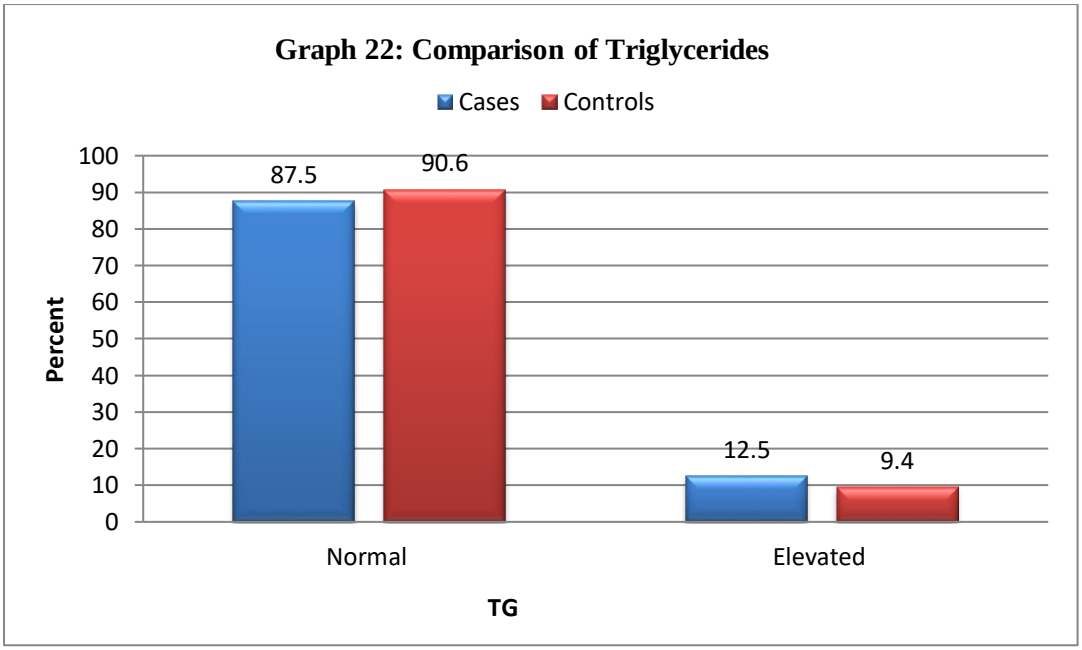


Table 26: Comparison of LDL between Cases and Controls (N=64)

LDL	Group	
	Cases (n=32) n (%)	Controls (n=32) n (%)
Normal	21 (65.6)	23 (71.9)
Elevated	11 (34.4)	9 (28.1)
Chi-Square Test, P Value = 0.590, Not Significant		

Low-Density Lipoprotein (LDL) cholesterol levels were compared between the two groups and categorized as normal or elevated.

- Normal LDL levels were observed in 65.6% of cases and 71.9% of controls.
- Elevated LDL was reported in 34.4% of cases and 28.1% of controls, showing a slightly higher occurrence among cases.

Despite this difference, the Chi-square test revealed no statistically significant association between LDL levels and group status (P = 0.590).

These findings indicate that LDL cholesterol distribution was similar across both groups, and elevated LDL was not significantly linked to case status in this study population.

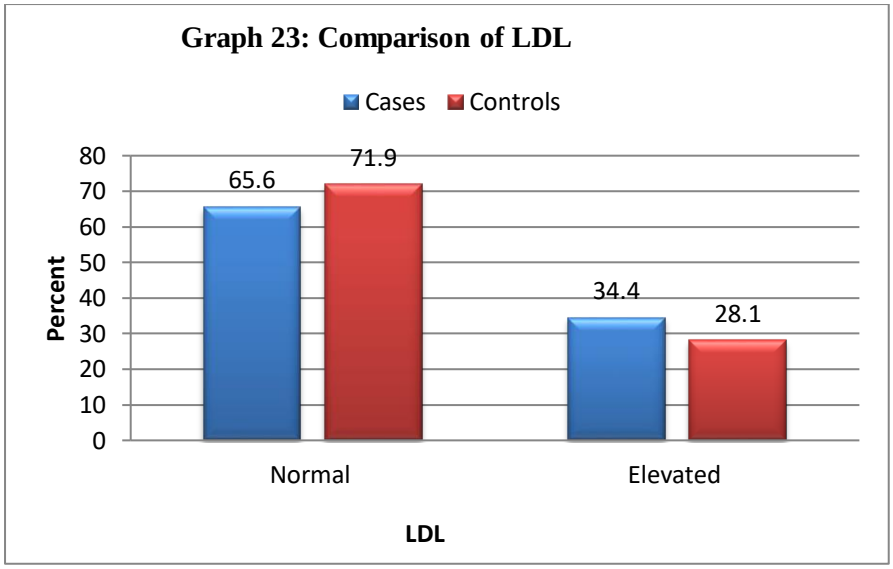


Table 27: Comparison of HDL between Cases and Controls (N=64)

HDL	Group	
	Cases (n=32) n (%)	**Controls (n=32) n (%)**
Low	22 (68.8)	8 (25.0)
Normal	10 (31.3)	24 (75.0)
Chi-Square Test, P Value <0.001, Significant		

High-Density Lipoprotein (HDL) levels were assessed and classified as low or normal across both study groups.

- A markedly higher proportion of cases (68.8%) had low HDL levels, compared to only 25.0% of controls.
- Conversely, normal HDL levels were found in 31.3% of cases and a significantly greater 75.0% of controls.

The difference in HDL distribution between groups was statistically significant, with the Chi-square test yielding a P value < 0.001.

These findings highlight a strong association between low HDL levels and case status, suggesting that reduced HDL may be a potential risk factor or associated biomarker in the study condition.

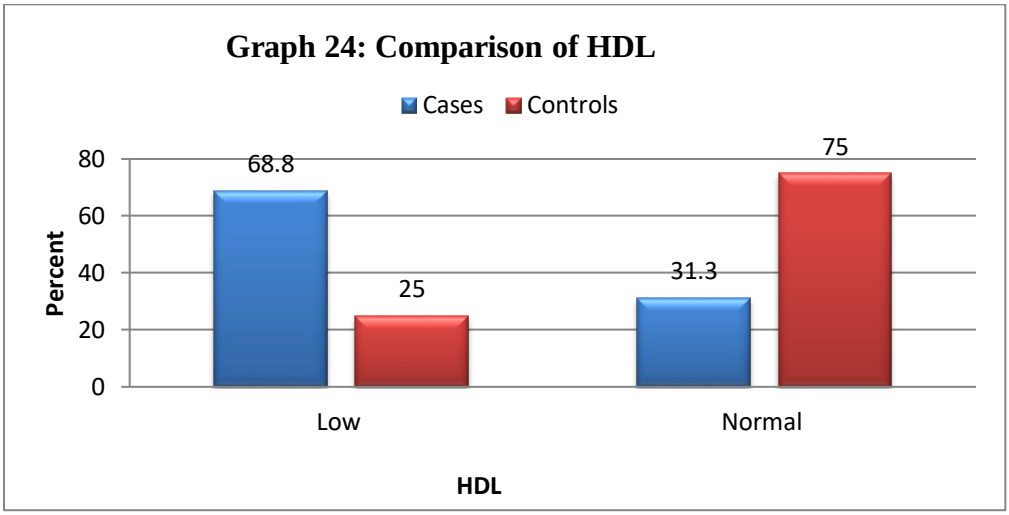


Table 28: Comparison of Cholesterol HDL Ratio between Cases and Controls (N=64)

Cholesterol HDL Ratio	Group	
	Cases (n=32) n (%)	Controls (n=32) n (%)
Normal	21 (65.6)	26 (81.3)
Elevated	11 (34.4)	6 (18.8)
Chi-Square Test, P Value = 0.157, Not Significant		

The cholesterol to HDL ratio, a key indicator of cardiovascular risk, was analyzed and categorized as normal or elevated.

- A normal ratio was observed in 65.6% of cases and 81.3% of controls.
- An elevated ratio was seen in 34.4% of cases, compared to 18.8% of controls, suggesting a higher proportion of dyslipidemia in the case group.

However, statistical analysis using the Chi-square test revealed no significant difference between the groups (P = 0.157).

These findings suggest that although a higher percentage of cases had an elevated cholesterol/HDL ratio, the difference was not statistically significant in this sample.

Graph 25: Comparison of Cholesterol /HDL Ratio

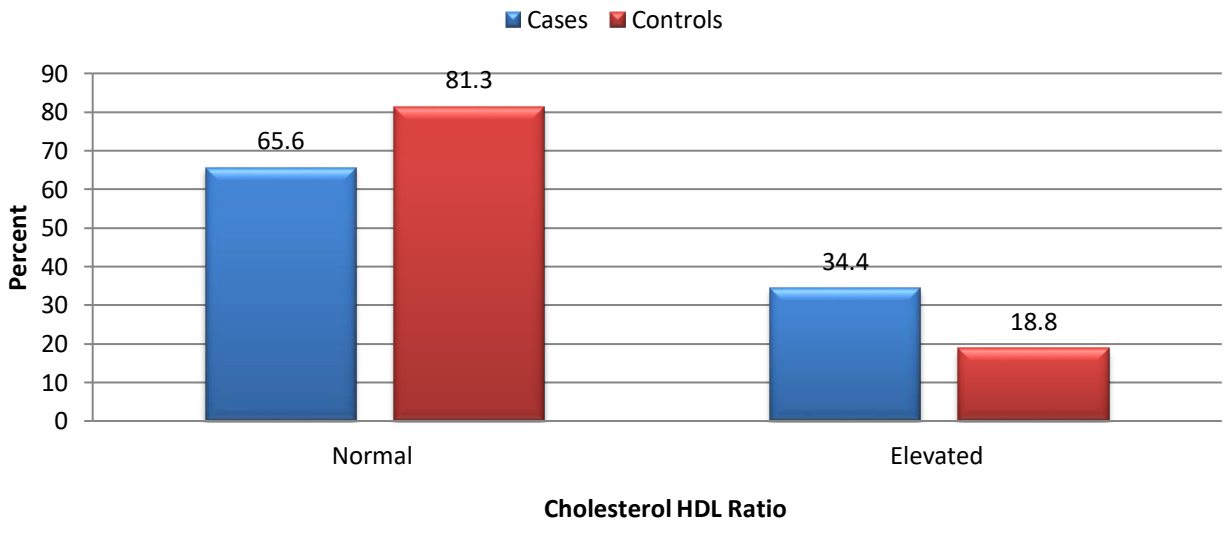


Table 29: CDK Grade (BOTH EYES) and Biochemical Parameters

Parameter	CDK Grade				P Value
	Grade 0 Mean (SD)	Grade 1 Mean (SD)	Grade 2 Mean (SD)	Grade 3 Mean (SD)	
Protein	6.633 (0.057)	7.064 (0.628)	6.867 (0.889)	6.475 (0.652)	0.221
Albumin	3.583 (0.376)	3.868 (0.812)	3.569 (0.656)	3.595 (0.476)	0.432
Globulin	2.933 (0.512)	2.968 (2.024)	3.119 (0.671)	2.705 (1.533)	0.874
A/G	1.228 (0.328)	1.120 (0.342)	1.271 (0.498)	1.635 (0.923)	0.062
Calcium	8.783 (0.204)	9.082 (0.449)	8.838 (0.424)	8.675 (0.358)	0.015*
ANOVA, P Value *Significant					

Biochemical parameters were evaluated across different grades of Climatic Droplet Keratopathy (CDK) to assess potential biochemical associations with disease severity. Mean values and standard deviations (SD) were compared across Grades 0 to 3, and statistical significance was determined using ANOVA

- Total protein levels varied slightly across grades, with the highest mean seen in Grade 1 (7.064 g/dL) and the lowest in Grade 3 (6.475 g/dL). However, this difference was not statistically significant (P = 0.221).
- Albumin levels also showed no significant trend, with values ranging from 3.569 g/dL in Grade 2 to 3.868 g/dL in Grade 1 (P = 0.432).
- Globulin levels remained relatively stable across grades, with the highest mean in Grade 2 (3.119 g/dL) and lowest in Grade 3 (2.705 g/dL), showing no significant association (P = 0.874).
- Albumin/Globulin (A/G) ratio increased progressively, reaching the highest mean in Grade 3 (1.635). While this trend approached significance, it did not reach the conventional threshold (P = 0.062).

- Serum calcium levels, however, showed a statistically significant difference across CDK grades (P = 0.015). The highest mean calcium was observed in Grade 1 (9.082 mg/dL), while the lowest was in Grade 3 (8.675 mg/dL), indicating a potential inverse relationship between calcium levels and disease severity.

These findings suggest that serum calcium may have a significant association with CDK severity, whereas protein, albumin, globulin, and A/G ratios do not show statistically significant trends, although the A/G ratio showed a borderline pattern worth further exploration.

Graph 26: CDK Grade Total and Biochemical Parameters

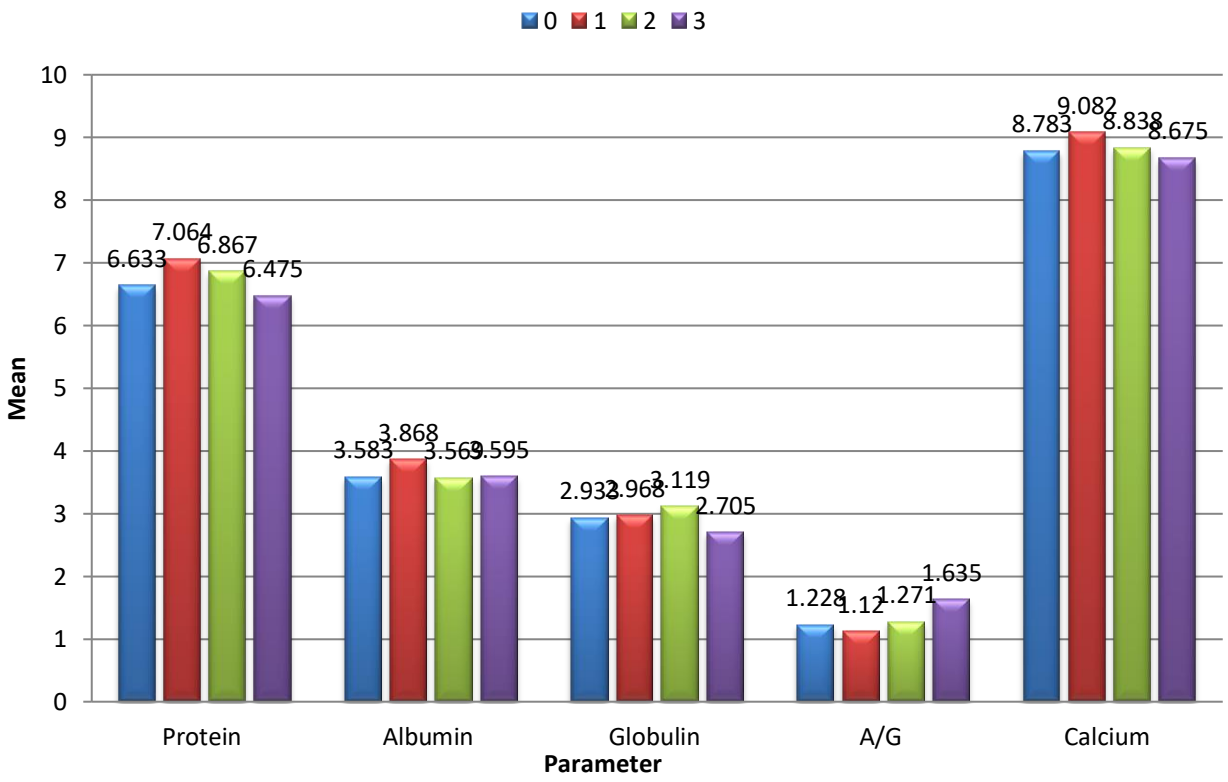


Table 30: CDK Grade (BOTH EYES) and Lipid Parameters

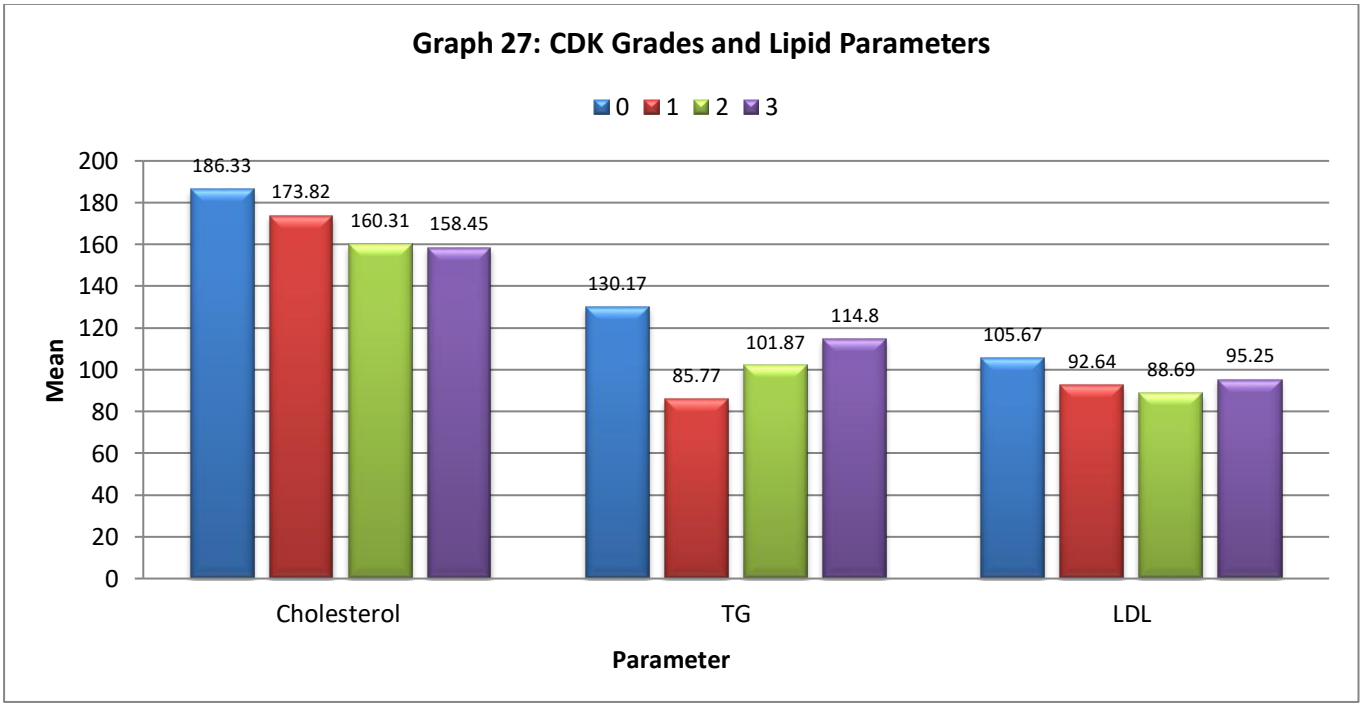
Parameter	CDK Grade				P Value
	Grade 0 Mean (SD)	Grade 1 Mean (SD)	Grade 2 Mean (SD)	Grade 3 Mean (SD)	
Cholesterol	186.33 (23.44)	173.82 (43.20)	160.31 (39.72)	158.45 (36.83)	0.321
TG	130.17 (39.78)	85.77 (33.77)	101.87 (61.56)	114.80 (57.50)	0.154
LDL	105.67 (28.47)	92.64 (24.14)	88.69 (20.02)	95.25 (20.65)	0.458
HDL	34.67 (12.40)	42.50 (12.11)	38.87 (11.60)	37.65 (11.10)	0.399
Cholesterol/HDL	4.96 (1.20)	4.25 (1.68)	4.11 (1.22)	4.43 (1.23)	0.620
VLDL	24.17 (4.35)	18.05 (3.64)	17.75 (4.21)	19.90 (4.88)	0.011*
ANOVA, P Value *Significant					

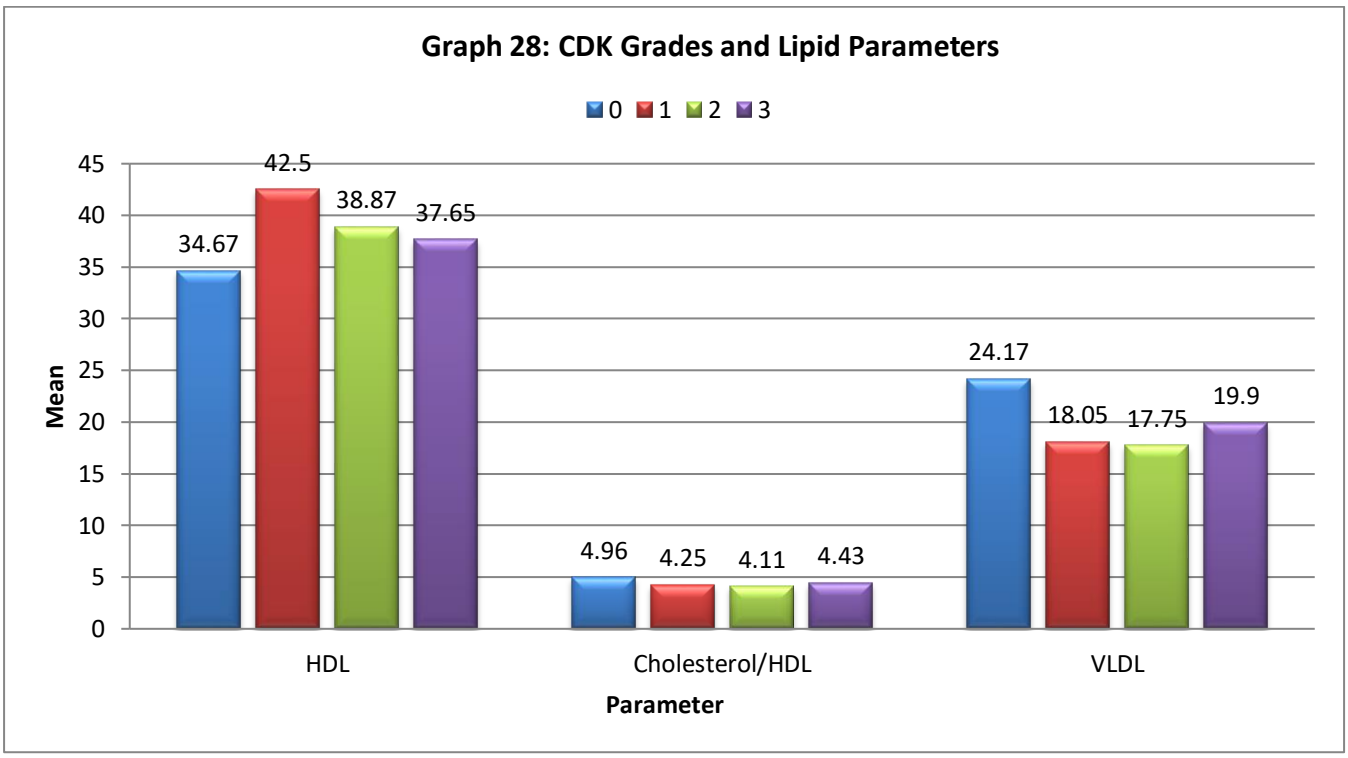
Lipid profiles were analyzed across different grades of Climatic Droplet keratopathy (CDK) to assess potential correlations between lipid metabolism and disease severity. Mean values and standard deviations were compared using ANOVA.

- Total cholesterol levels showed a decreasing trend from Grade 0 (186.33 mg/dL) to Grade 3 (158.45 mg/dL). However, this trend was not statistically significant (P = 0.321).
- Triglycerides (TG) were highest in Grade 0 (130.17 mg/dL) and lowest in Grade 1 (85.77 mg/dL), but again, this variation did not reach significance (P = 0.154).
- LDL cholesterol levels showed minimal fluctuation across grades, ranging from 105.67 mg/dL in Grade 0 to 88.69 mg/dL in Grade 2, with no significant association (P = 0.458).

- HDL cholesterol peaked in Grade 1 (42.50 mg/dL) and was lowest in Grade 0 (34.67 mg/dL). However, the differences were not statistically significant (P = 0.399).
- The Cholesterol/HDL ratio, an indicator of cardiovascular risk, showed a slight downward trend from Grade 0 (4.96) to Grade 2 (4.11), but increased again in Grade 3 (4.43). This variation was not significant (P = 0.620).
- Very Low-Density Lipoprotein (VLDL) levels exhibited a statistically significant difference across CDK grades (P = 0.011). VLDL was highest in Grade 0 (24.17 mg/dL) and lowest in Grade 1 (18.05 mg/dL), with a modest increase observed again in Grade 3 (19.90 mg/dL).

These results indicate that VLDL levels are significantly associated with CDK severity, potentially reflecting changes in lipid transport or metabolism in progressive stages of the disease. Other lipid parameters, while showing trends, did not demonstrate statistically significant associations.




Graph 28: CDK Grades and Lipid Parameters
0
1
2
3
45
40
35
30
25
20
15
10
5
0
Mean
34.67
42.5
38.87
37.65
4.96
4.25
4.11
4.43
24.17
18.05
17.75
19.9
HDL
Cholesterol/HDL
VLDL
Parameter

DISCUSSION

The distribution of CDK cases across demographic categories in this study underscores several sociobiological and behavioral predispositions. Although age did not demonstrate statistical significance ($p = 0.178$), the trend was unmistakable — individuals in the 61–80 age group showed the highest CDK prevalence. This aligns with the established notion that CDK is a cumulative degenerative disorder, exacerbated by long-term exposure to ultraviolet (UV) radiation and environmental insult over decades [61]. Taylor et al., in their Australian study, also found the highest incidence of CDK among older Aboriginal populations, directly attributing this to lifelong sunlight exposure without protective eyewear [62].

The study was conducted in the semi-arid zone of northern Karnataka, India.This region is characterized by intense solar radiation, low ambient humidity, and frequent dust-laden winds—conditions that collectively exacerbate ocular surface stress .During peak summer months, temperatures often soar to 44°C, accompanied by clear skies and a high ultraviolet (UV) index, increasing phototoxic risk to the corneal epithelium. In contrast, winters are marked by dry, gusty winds and minimal atmospheric moisture, which contribute to tear film instability and evaporative dry eye. These harsh environmental factors form a compelling backdrop for the development and progression of climatic droplet keratopathy (CDK).

The study revealed a statistically significant male predominance among CDK patients ($p = 0.006$). This sex-based disparity may be attributable to occupational patterns — where men are more likely to engage in farming, outdoor labor, and long-term exposure to harsh climates, all of which heighten susceptibility. In addition, androgenic regulation of ocular surface immunity and meibomian gland activity may also underlie differences in tear film stability between sexes [63].

No significant associations were observed with marital status, education level, or income. However, these sociodemographic indicators often correlate with occupational exposure and access to protective gear, and their subtle influences cannot be entirely dismissed. In a rural context, illiteracy and low income often limit awareness about ocular health, as echoed in similar CDK studies conducted in Argentina, region of red sea and Northern India [64,65,21].

The predominant symptoms among CDK patients were pricking (68.8%) and watering (65.6%), followed by photophobia and irritation, reflecting a pattern of ocular surface instability and inflammation. These symptoms align with earlier literature characterizing CDK as a tear-deficiency-driven inflammatory keratopathy, resulting in epithelial disruption and stromal droplet accumulation [6].

Laterality data showed 81.3% of cases were bilateral, suggesting that the disease is not merely focal but rather a symmetrical response to chronic environmental exposure. Similar bilateral presentations have been documented where cumulative environmental factors (UV, wind, dust) affect both eyes relatively evenly over time [67].

The grade-wise distribution, with the majority of patients in Grade 2 (46.9%), suggests that most patients seek care after moderate visual disruption, indicating a lack of awareness or access to early interventions. This delayed presentation pattern has been observed in multiple studies of rural ocular diseases [8].

One of the most striking findings in this study was the statistically significant reduction in Tear Break-Up Time (TBUT) ($p < 0.001$) and Schirmer's II test scores ($p < 0.001$) in CDK cases. These values reflect a dysfunctional tear film, central to the pathogenesis of CDK.

TBUT, which evaluates the stability of the tear film's lipid layer, was markedly decreased in affected individuals. Tear film instability facilitates ocular surface desiccation and oxidative stress, setting the stage for epithelial barrier breakdown and stromal infiltration of environmental proteins, hallmark features of CDK [66]. A 2024 study by Awargaonkar et al. emphasized TBUT's predictive value in early detection of ocular surface changes in keratopathy [68].

Schirmer's II test, which assesses basal aqueous secretion, was also significantly compromised. The low scores suggest UV-induced inflammation. Zhou and Beuerman identified basal secretion impairment as a critical event in environmentally driven dry eye and CDK [66].

Interestingly, Schirmer's I test (which includes reflex tearing) was not significantly different. This aligns with findings by Shimmura et al., who noted that reflex tearing can be misleading in chronic tear dysfunction conditions [69]. Basal secretory decline is more relevant in long-term ocular surface deterioration, as seen in CDK. The collective findings affirm that tear film homeostasis is severely disrupted in CDK, and both TBUT and Schirmer's II should be considered key diagnostic and monitoring tools.

Biochemical parameters measured in this study reveal key systemic alterations among CDK patients, potentially providing insight into the pathophysiological pathways that go beyond local ocular surface damage. A statistically significant inverse relationship was observed between serum calcium levels and CDK grade ($p = 0.015$), with lower calcium associated with more advanced disease. Calcium plays a vital role in epithelial tight junction integrity, wound healing, and cellular signaling. Chronic hypocalcemia impairs the renewal of corneal epithelium and compromises stromal structure, potentially enhancing susceptibility to environmental injury [70].

Experimental studies have shown that corneal epithelial cells rely on extracellular calcium gradients for migration and repair [71]. Furthermore, oxidative stress — a key driver of CDK — is exacerbated by calcium imbalance, which disrupts mitochondrial function and epithelial resistance to UV-induced apoptosis [61].

In rural populations with limited access to diverse nutrition, hypocalcemia may reflect underlying micronutrient deficiency, further compounding ocular surface vulnerability. While causality remains to be proven, serum calcium could serve as a biomarker for disease severity or predictive indicator in at-risk individuals.

The study reported a significantly lower level of HDL among CDK cases ($p < 0.001$) and a significant correlation between VLDL levels and CDK grade ($p = 0.011$). HDL cholesterol possesses potent antioxidant and anti-inflammatory properties that are protective across multiple tissues, including the ocular surface [66].

Low HDL may lead to increased lipid peroxidation in corneal epithelial membranes, compromising barrier function. A study among Korean women has linked dyslipidemia to dry eye and inflammatory cytokine expression in patients with ocular surface disease, suggesting a systemic-lipid influence on local ocular immunity [72]. Studies have shown that individuals with lower HDL levels tend to have higher levels of inflammatory markers, such as C-reactive protein (CRP), which is implicated in the pathogenesis of dry eye disease[73,74].

Another study by Rathnakumar K et al demonstrated low HDL – C values in patients with dry eye disease which coincides with the findings of our study[75].HDL also regulates nitric oxide pathways and suppresses reactive oxygen species — both critical in maintaining corneal homeostasis.

VLDL, on the other hand, is a pro-inflammatory lipid associated with vascular dysfunction. While its direct role in corneal pathology is less clear, elevated VLDL may reflect a broader metabolic-inflammatory state that predisposes to ocular surface degeneration [17]. Triglycerides did not show statistical significance, yet their borderline elevation among CDK cases may still hold clinical relevance, especially in populations with dietary dysregulation.

Although not statistically significant, albumin, total protein, and A/G ratio were marginally lower in CDK cases. Albumin is the primary carrier of antioxidants like zinc and copper and plays a role in maintaining oncotic pressure and tissue repair. Hypoalbuminemia may signal chronic inflammation, protein loss, or malnutrition, all of which impair the eye's ability to respond to environmental insult [76].

Reduced total protein levels in CDK patients, though not conclusive in this cohort, warrant attention — especially in settings with high prevalence of nutritional deficiency. Prior studies in ocular surface disorders like xerophthalmia and trachoma have linked low serum protein states to delayed corneal epithelial healing and increased susceptibility to keratinization [77].

Though not statistically significant in this dataset, occupational exposure (59.4% farmers among cases) suggests a pivotal environmental contribution. Farming involves prolonged UV exposure, wind, dust, and desiccating environments — all established triggers for ocular surface stress, inflammation, and CDK onset [78].

The literature strongly supports a link between CDK and environmental extremes, particularly in regions like the Atacama Desert (Chile), Northern India, and parts of Africa [69,74]. In these areas, CDK correlates with solar radiation intensity, atmospheric particulates, and humidity variation, regardless of genetic background.

The lack of statistical significance in this study may be due to small sample size or occupational homogeneity in the region. However, clinically and epidemiologically, farming remains a key modifiable risk factor.

When CDK grades were cross-tabulated with systemic markers, HDL, serum calcium, and VLDL showed statistically significant associations with disease severity. Specifically-Lower HDL and calcium levels correlated with higher CDK grades, reinforcing the idea that systemic oxidative burden and nutritional deficiency accelerate disease progression. Higher VLDL levels were also associated with more advanced grades, supporting a role for metabolic inflammation in CDK pathophysiology.

This suggests that CDK grading could potentially be enriched by biochemical profiling. These associations are consistent with growing models that position CDK not just as a local epithelial disease, but as a systemic–environmental interaction disorder .

The findings from this study support and expand existing models of Climatic Droplet Keratopathy (CDK) as a multifactorial degenerative disorder resulting from cumulative ocular surface stress, tear film dysfunction, and systemic metabolic imbalance.

The classical model of CDK centers on the accumulation of proteinaceous and lipid droplets in the Bowman's layer, secondary to chronic exposure to UV radiation, wind, and dryness. This environmental stress triggers oxidative damage, resulting in epithelial compromise and subsequent corneal remodeling [61,62].

Our study adds critical nuance to this model:Tear film instability, evidenced by reduced TBUT and Schirmer's II, compromises epithelial defense and hydration, allowing UV-induced peroxidation to accelerate droplet formation. Low HDL levels remove an antioxidant defense mechanism, permitting unchecked lipid peroxidation within the corneal stroma. HDL also modulates inflammation and endothelial protection—its deficiency implicates chronic inflammation in CDK progression [72].Serum calcium deficiency suggests that epithelial healing, nerve integrity, and stromal resistance are impaired systemically, not just locally [80].

These factors intersect in a vicious cycle: tear film dysfunction facilitates oxidative damage, systemic deficiency slows repair, and chronic environmental insult sustains the degenerative process. Figure models from Holopainen et al. and Zhou et al. depict this multidimensional etiology clearly [47,20].

The integration of ocular, biochemical, and demographic risk factors has clear implications for both clinical practice and public health interventions in endemic regions. TBUT and Schirmer's test should be standard in evaluating rural patients presenting with ocular discomfort, especially in sun-exposed occupations. Screening of serum calcium and HDL levels in at-risk populations may help stratify severity and inform targeted supplementation. CDK grades could be enhanced with a biochemical risk index, combining TBUT, HDL, and calcium into a composite severity score.

Public health measures can be undertaken like Implementing UV-blocking strategies for outdoor workers, such as distribution of polarized eyewear and educational campaigns. Initiating nutrition programs with calcium and vitamin A supplementation in endemic areas can also be implemented.

Given that CDK is often under-recognized until moderate to severe stages, early community-level interventions could significantly reduce the burden of irreversible corneal damage.

Study Limitations and Scope for Future Work

Despite strong findings, several limitations merit discussion:

With 64 subjects, subgroup analysis (especially by occupation and education) may be underpowered. A larger cohort would allow multivariate regression and interaction analysis.Temporal relationships cannot be confirmed due to its cross-sectional design. Future longitudinal studies could assess causality—especially the predictive value of HDL and calcium on disease progression. Environmental factors like local UV index, humidity, and wind exposure levels were not quantified. Integrating satellite-derived UV data and climatic indices could strengthen environmental associations . Serum calcium and protein levels suggest systemic undernutrition, but dietary histories and micronutrient panels were not evaluated.

Future Directions

Tear proteomics and metabolomics can be used to identify early biomarkers in preclinical CDK [81]. Randomized trials of nutritional supplementation and antioxidant therapy need to be evaluated to delay or prevent disease progression. Integration with machine learning models can be incorporated to predict CDK risk using ocular and systemic variables [82].

Summary

This case-control study investigated clinical, biochemical, and demographic correlates of Climatic Droplet Keratopathy (CDK) in a cohort of 64 individuals (32 CDK cases and 32 controls). The analysis revealed a statistically significant male predominance among CDK patients ($p = 0.006$), with a majority engaged in agricultural occupations, implicating chronic environmental exposure as a key risk factor. Although age distribution was not statistically significant, a higher prevalence was observed in individuals aged 61–80 years, consistent with the cumulative nature of UV-related corneal damage.

Clinically, CDK presented bilaterally in 81.3% of cases, with pricking and watering as the most common symptoms. Most patients were classified under Grade 2 severity, indicating moderate disease at presentation.

Tear film parameters were significantly impaired in CDK cases. Both Tear Break-Up Time (TBUT) and Schirmer's II test were markedly reduced ($p < 0.001$), suggesting a dual deficiency in tear film stability and basal aqueous production, key contributors to CDK pathogenesis.

Biochemically, CDK patients exhibited significantly lower serum calcium levels ($p = 0.015$), with values inversely correlated to disease grade, highlighting impaired epithelial recovery mechanisms. High-density lipoprotein (HDL)levels were significantly reduced ($p < 0.001$), while Very Low-Density Lipoprotein (VLDL) levels increased with disease severity ($p = 0.011$), supporting the role of lipid dysregulation and systemic inflammation in disease progression.

CONCLUSION

Climatic Droplet Keratopathy is a chronic, degenerative ocular surface disorder strongly influenced by environmental exposure, male sex, tear film dysfunction, and systemic metabolic imbalance. This study reinforces the pathogenic importance of tear film instability (low TBUT) and basal tear deficiency (low Schirmer's II), alongside systemic deficiencies in serum calcium and HDL cholesterol.

These findings advocate for a comprehensive, integrative approach to CDK risk assessment and management, including:

- Routine tear function testing in at-risk individuals
- Biochemical screening for calcium and lipid abnormalities
- Preventive strategies such as UV protection and nutritional supplementation in high-exposure populations

Early detection of tear and systemic alterations may enable timely interventions and potentially halt or slow the progression of this vision-threatening yet preventable disease.

Appendix I

Consent form

STUDY SUBJECT CONSENT FORM

I confirm that Dr VIVEA NAGDEV has explained the purpose of the research, the study procedure, the benefits, and the possible discomfort that I may experience in the language best understood by me. Therefore, I agree to participate as a subject in this research project and willfully consent.

(Participant) (Date)

(Witness to above signature) (Date)

ಅಧ್ಯಯನವಿಷಯಮಾಹಿತಿಪತ್ರ

ಡಾ. ,ನನಗೆ ಸಂಶೋಧನೆಯ ಉದ್ದೇಶ, ಅಧ್ಯಯನದ ವಿಧಾನ ಮತ್ತು ಸಂಭವನೀಯ ಅನುಕೂಲತೆಗಳು ಮತ್ತು ನನ್ನ ಸ್ವಂತಭಾಷೆಯಲ್ಲಿ ನಾನು ಅನುಭವಿಸಬಹುದಾದ ಪ್ರಯೋಜನಗಳನ್ನು ವಿವರಿಸಿದ್ದೀರಿ ಎಂದು ನಾನು ಖಚಿತ ಪಡಿಸುತ್ತೇನೆ. ಮೇಲಿನ ಎಲ್ಲಾ ವಿಷಯಗಳನ್ನು ನನ್ನ ಸ್ವಂತ ಭಾಷೆಯಲ್ಲಿ ವಿವರವಾಗಿ ವಿವರಿಸಲಾಗಿದೆ ಮತ್ತು ನಾನು ಅದನ್ನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ. ಆದ್ದರಿಂದ, ಈ ಸಂಶೋಧನಾಯೋಜನೆಯಲ್ಲಿ ವಿಷಯವಾಗಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪಿಗೆ ನೀಡಲು ನಾನು ಒಪ್ಪುತ್ತೇನೆ

(ಭಾಗವಹಿಸುವವರು) (ದಿನಾಂಕ)

Appendix II

Institutional Ethical Clearance

BLDE

(DEEMED TO BE UNIVERSITY)

Declared as Deemed to be University u/s 3 of UGC Act, 1956

Accredited with 'A' Grade by NAAC (Cycle-2)

The Constituent College

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA

BLDE (DU)/IEC/ 902/2023-24 10/4/2023

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this University met on **Saturday, 18th March, 2023 at 11.30 a.m. in the CAL Laboratory, Dept. of Pharmacology,** scrutinizes the Synopsis/ Research Projects of Post Graduate Student / Under Graduate Student /Faculty members of this University /Ph.D. Student College from ethical clearance point of view. After scrutiny, the following original/ corrected and revised version synopsis of the thesis/ research projects has been accorded ethical clearance.

TITLE: "A CROSS-SECTIONAL STUDY OF CORRELATION OF CLIMATIC DROPLET KERATOPATHY WITH DRY EYE, SERUM PROTEINS, SERUM CALCIUM AND LIPID PROFILE".

NAME OF THE STUDENT/PRINCIPAL INVESTIGATOR: DR.VIVEA NAGDEV

NAME OF THE GUIDE: DR. VALLABHA K., PROFESSOR, DEPT. OF OPHTHALMOLOGY.

Dr. Santoshkumar Jeevangi
Chairperson
IEC, BLDE (DU),
VIJAYAPURA
Chairman,
Institutional Ethical Committee,
BLDE (Deemed to be University)
Vijayapura

Dr.Akram A. Naikwadi
Member Secretary
IEC, BLDE (DU),
VIJAYAPURA
MEMBER SECRETARY
Institutional Ethics Committee
BLDE (Deemed to be University)
Vijayapura-586103. Karnataka

Following documents were placed before Ethical Committee for Scrutinization.

- Copy of Synopsis/Research Projects
- Copy of inform consent form
- Any other relevant document

Smt. Bangaramma Sajjan Campus, B. M. Patil Road (Sholapur Road), Vijayapura - 586103, Karnataka, India.
BLDE (DU): Phone: +918352-262770, Fax: +918352-263303, Website: www.bldedu.ac.in, E-mail:office@bldedu.ac.in
College: Phone: +918352-262770, Fax: +918352-263019, E-mail: bmpmc.principal@bldedu.ac.in

Appendix III [Case proforma]

Appendix X

DEPARTMENT OF OPHTHALMOLOGY
B.L.D.E UNIVERSITY'S SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA-586103

CASE PROFORMA

Case No: ☐☐☐

Name : ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Age: ☐☐ years Sex: ☐ (1-Male 2-Female) IP no: ☐☐☐☐☐☐☐

Address: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐
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Contact no: ☐☐☐☐☐☐☐☐☐☐ / ☐☐☐☐☐☐☐☐☐☐

Date of admission: ☐☐☐☐☐☐☐☐ Date of Discharge ☐☐☐☐☐☐☐☐

Is the patient eligible for study? (1-Yes, 2-No): ☐

Has informed consent been given? (1-Yes, 2-No): ☐

Chief Complaints:

1. Diminution of vision: Right Eye ☐ Duration: ☐☐ days/months/years

   Left Eye ☐ Duration: ☐☐ days/months/years

2. Others (if any):

☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

History of Present Illness:

1. Diminution of vision: Insidious (1) or Sudden (2): ☐
   Progressive (1) or Non-progressive (2): ☐
   Painless (1) or Painful (2): ☐
   For distance (1) or For near (2): ☐
2. Diplopia / Polyopia: Present (1) or Absent (2): ☐
3. Coloured halos: Present (1) or Absent (2): ☐
4. Black spots / non seeing area before eye
   Present (1) or Absent (2): ☐
5. Redness: Present (1) or Absent (2): ☐
6. Watering: Present (1) or Absent (2): ☐
7. Discharge: Present (1) or Absent (2): ☐
8. Pain in eyes: Present (1) or Absent (2): ☐
9. Headache: Present (1) or Absent (2): ☐
10. H/O present trauma: Present (1) or Absent (2): ☐
11. H/O wearing glasses: Present (1) or Absent (2): ☐
    Near (1) or Far (2) or Both (3): ☐
    Duration: ☐

Past history:

1. H/O past trauma to eye: Present (1) or Absent (2): ☐
2. Ocular surgery: Present (1) or Absent (2): ☐
   Type of surgery:……
   When performed ? : ……..
3. Diabetes: Present (1) or Absent (2): ☐
   Duration:……..
   Medication:……..
4. Hypertension: Present (1) or Absent (2): ☐
   Duration:……..

Medication:……..

5. CAD: Present (1) or Absent (2): ☐

Duration:……..

Medication:……..

6. Any other medical disorder:……

Personal History:

1. Smoking: Present (1) or Absent (2): ☐

Duration:……..

2. Alcohol intake: Present (1) or Absent (2): ☐

Duration:……..

3. Diet: Vegetarian(1) or Non Vegetarian (2) or Mixed (3): ☐

General Physical Examination:

1. Built: ☐

(Well built – 1, Moderately built – 2, Poorly built – 3, Emaciated – 4)

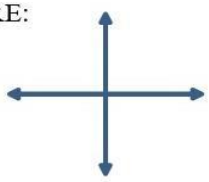
2. Pallor: Present (1) or Absent (2): ☐
3. Icterus: Present (1) or Absent (2): ☐
4. Clubbing: Present (1) or Absent (2): ☐
5. Koilonychia: Present (1) or Absent (2): ☐
6. Cyanosis: Present (1) or Absent (2): ☐
7. Lymphadenopathy: Present (1) or Absent (2): ☐
8. Edema: Present (1) or Absent (2): ☐
9. Pulse: ☐ /minute
10. Temperature: ☐ degree Fahrenheit
11. Blood pressure: ……../……mmHg
12. Respiratory rate: ☐ cycles per minute

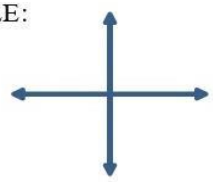
Systemic Examination:

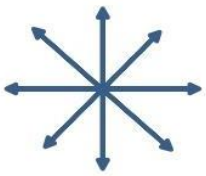
1. CVS: ☐ Normal – 1, Abnormal – 2
   If 2, specify:.....
2. CNS: ☐ Normal – 1, Abnormal – 2
   If 2, specify:.....
3. Respiratory System ☐ Normal – 1, Abnormal – 2
   If 2, specify:.....
4. Per abdomen: ☐ Normal – 1, Abnormal – 2
   If 2, specify:.....

Ocular Examination:

- Head posture: 1 – Erect, 2 – Tilted ☐
- Visual axis: 1 – Parallel, 2 – Deviated ☐
- Facial Symmetry: 1 – Symmetrical 2 – Asymmetrical ☐
- Ocular motility: 1 – Normal (N) , 2 – Restricted (R) ☐

RE: 

LE: 

BINOCULAR: 

- Visual Acuity:

	RE	LE
DISTANT		
PINHOLE		
NEAR		
AIDED		

- Refraction:

Prescription	Spherical	Cylindrical	Axis	BCVA
RE				
LE				

• **Adnexa:** 1- Normal 2- Abnormal	☐	☐
• **Sclera:** 1- Normal 2- Congested	☐	☐
• **Conjunctiva** 1- Normal 2- Conjunctival Congestion 3- Ciliary congestion 4- Chemosis	☐	☐

• **Cornea** **Climatic droplet keratopathy** **0- Grade 0** 1- Grade 1 2- Grade 2 3- Grade 3	☐	☐
• **Anterior Chamber** 1- Normal depth 2- Shallow 3- Deep	☐	☐
• **Iris** 1- Normal colour and pattern 2- Abnormal	☐	☐
• **Pupil** **Shape:** 1-Round and regular; 2- Irregular **Reaction:** Direct: 1-Present; 2-Absent Indirect: 1-Present; 2-Absent Near reflex: 1-Present; 2-Absent	**Size** .....mm ☐ ☐ ☐	**Size** .....mm ☐ ☐ ☐

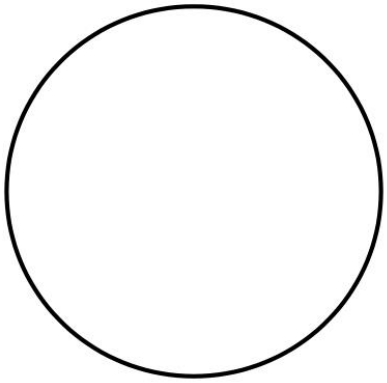
• **Lens** **Clarity:** 1-Clear; 2-Opaque 1- Cataract; 2- PCIOL If cataract present: 1- Immature 2- Mature 3- Hyper mature **A) Cortical cataract** (1-Present;2-Absent) **B) Nuclear sclerosis** (1-Present; 2-Absent)If present: GRADE: 1- Grade 1 2- Grade 2 3- Grade 3 4- Grade 4 C) **Posterior Sub capsular cataract** (1-Present 2-absent)		
• **Lacrimal duct patency** **(**1-Patent, 2-Regurgitation, 2A-Clear fluid; 2B-Mucopurulent; 2C- Blocked)		

Right eye	Left eye

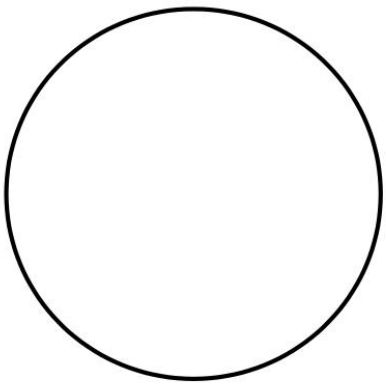
	

FUNDUS EXAMINATION:

Fundus	**Right eye**	**Left eye**
Glow		
Media		
Disc		
CD ratio		
Blood vessels		
Background		
Macula		



RIGHT EYE



LEFT EYE

DIAGNOSIS:

INVESTIGATIONS:

Investigations	Obtained value	Reference value
Tear film break up time		>10 seconds
Schirmers test		>5 seconds
Serum total protein		6-8 g/dl
Serum albumin		3.4-5.4 g/dl
A/G ratio		18.5-10.2
Serum calcium		8.5-10.2 mg/dl
Cholesterol(mg/dl)		< 200 mg/dl
Triglyceride(mg/dl)		<150 mg/dl
LDL(mg/dl)		< 100 mg/dl
HDL (mg/dl)		< 60 mg/dl

Dr. Vivea Nagdev

Candidate
PG Student
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Dr. Vallabha K

Thesis guide
Professor
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Appendix IV

Colour plates

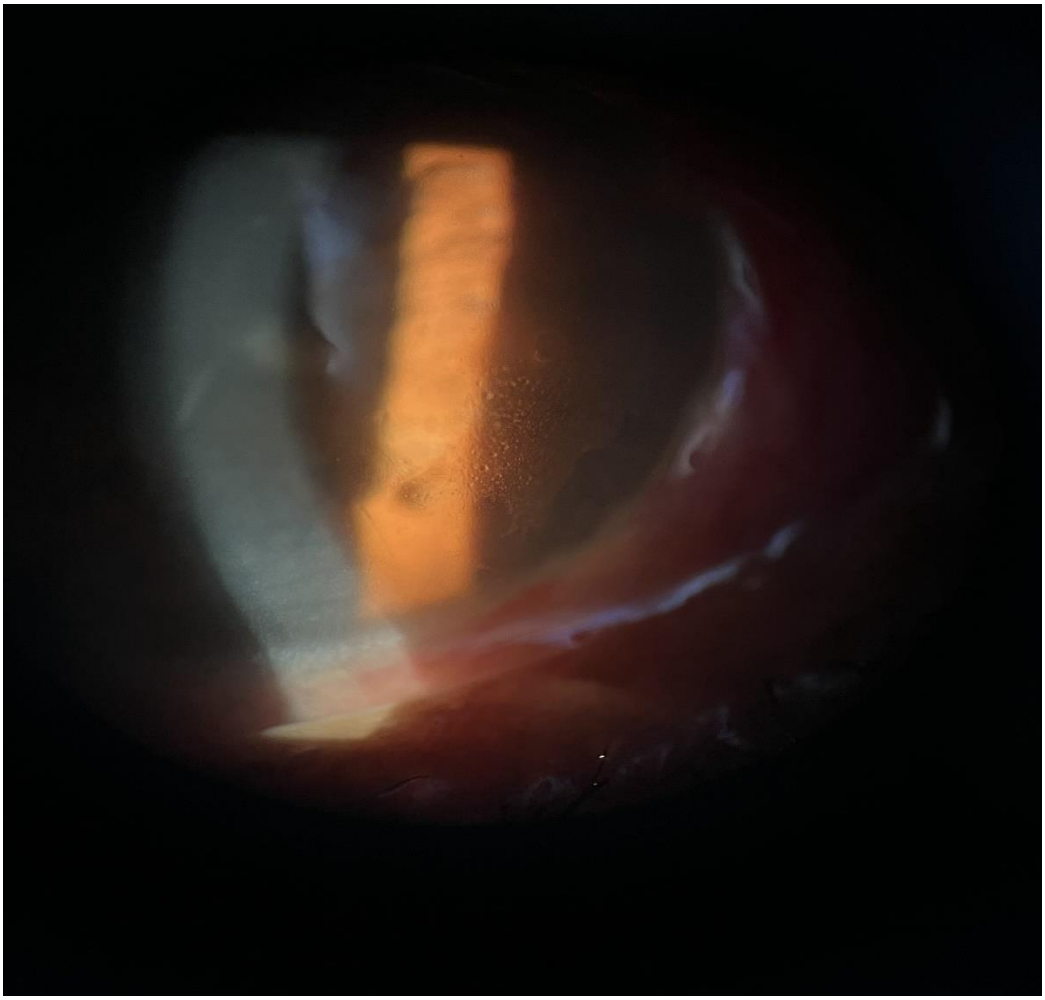

Figure 10 : Grade 1 Climatic Droplet Keratopathy.

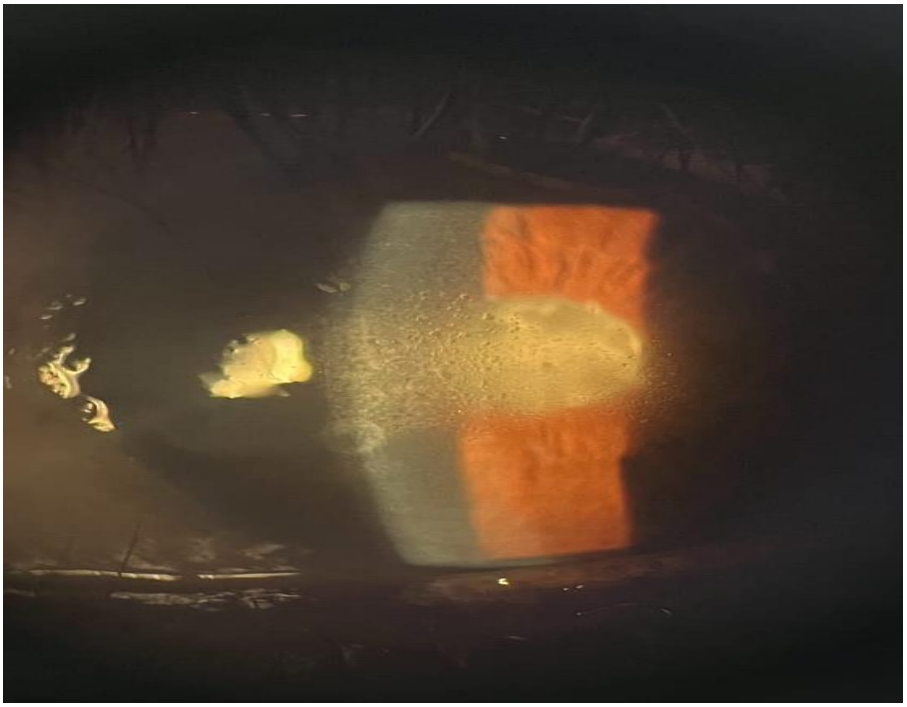

Figure 11 : Grade 2 Climatic Droplet Keratopathy.

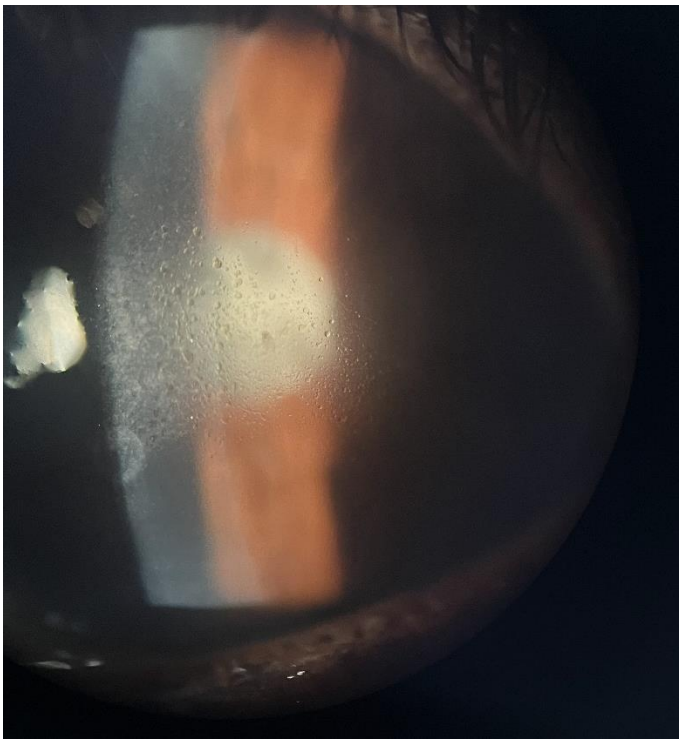

Figure 12: High magnification picture of Grade 2 Climatic Droplet Keratopathy.

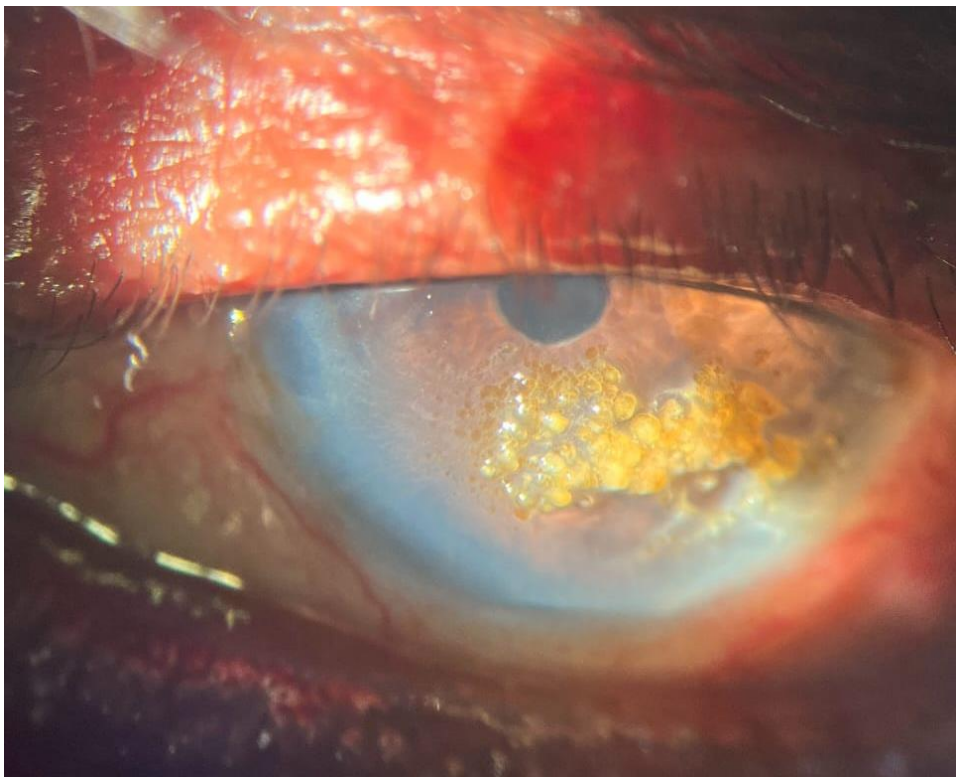

Figure 13 : Grade 3 Climatic Droplet Keratopathy.

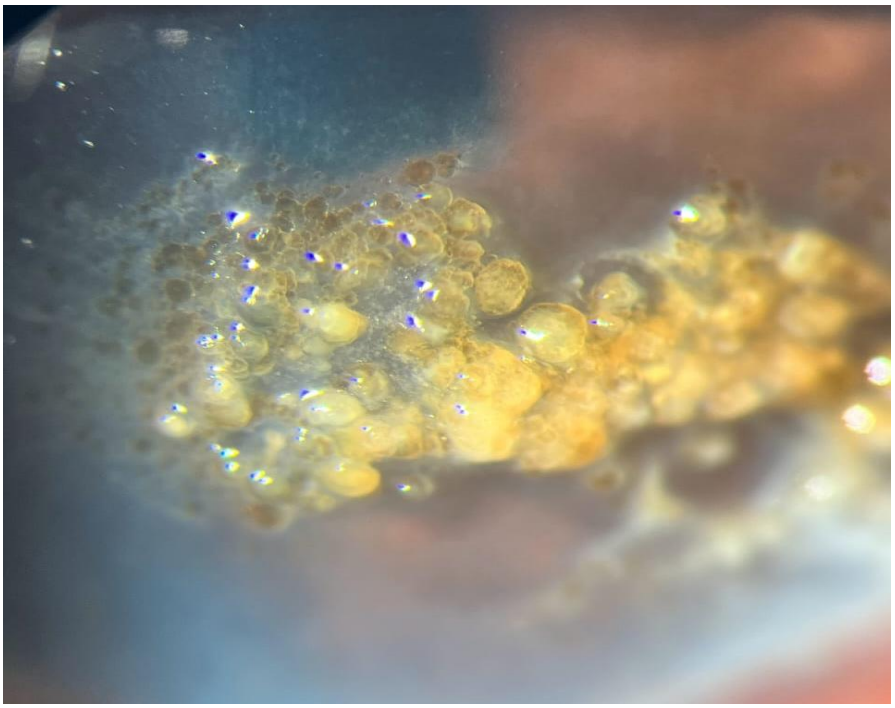

Figure 14: High magnification picture of Grade 3 Climatic Droplet Keratopathy.

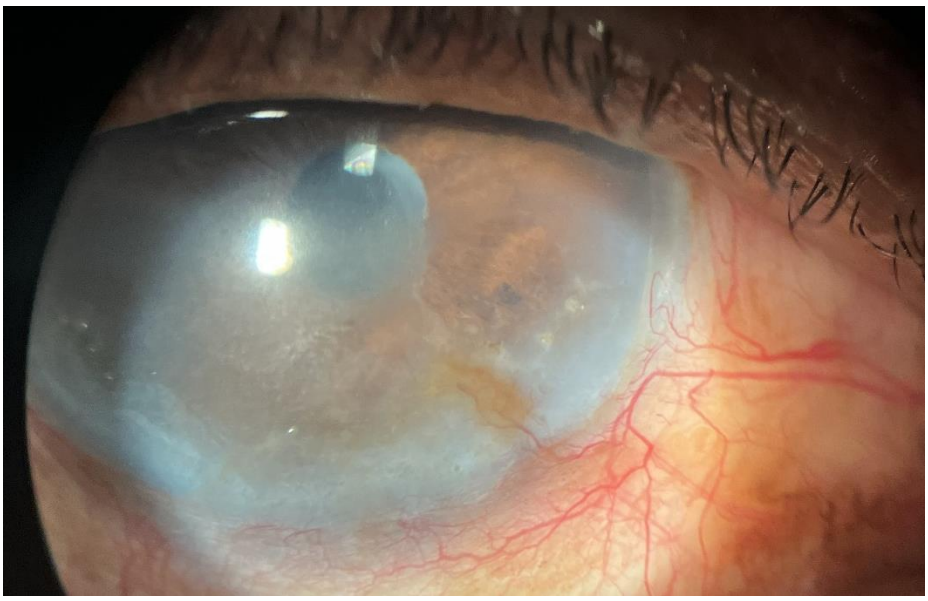

Figure 15: Superficial vascularization at 4 o'clock position in Climatic Droplet Keratopathy

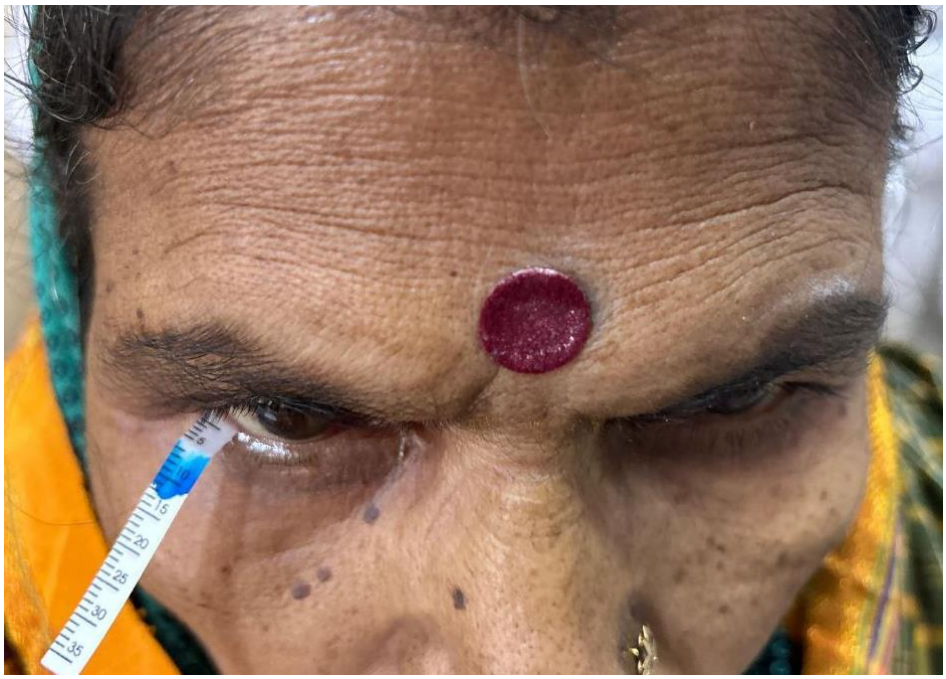

Figure 16: Picture demonstrating Schirmer's test

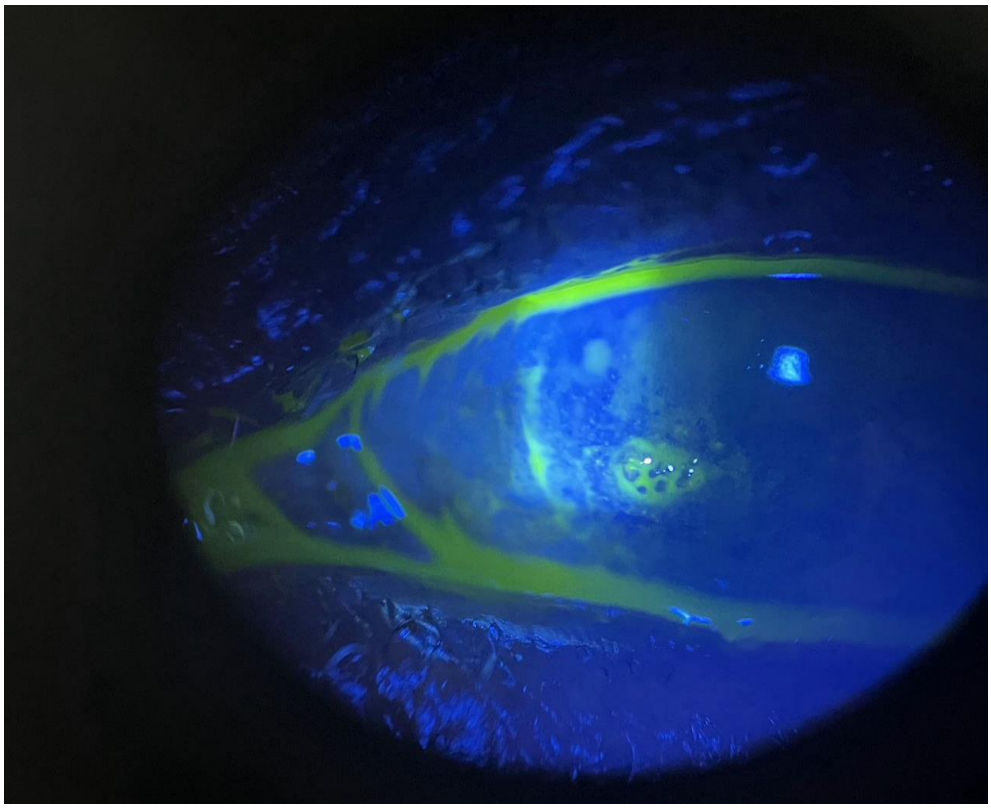

Figure 17: Fluorescein stained cornea with CDK

Appendix V

Master Chart

Key for Master Chart:

Abbreviations	Full expansion
RE	Right eye
LE	Left eye
CDK	Climatic droplet keratopathy
Chol	cholesterol
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
VLDL	Very low-density lipoprotein
TG	Triglycerides
T-BUT	Tear film Break-up Time
A/G Ratio	Albumin/Globulin Ratio
DM 0 1	Diabetes Mellitus Absent Present
HTN 0 1	Hypertension Absent Present
Symptoms 0 1	 Absent Present

CASES

SR NO	AGE	SEX	ADDRESS	OCCUPATION	Eye involved	PRICKING	WATERING	Comorbidities	ADDICTION	CDK GRADE RE	CDK GRADE LE	RE LENS Status	LE LENS Status
1	70	M	Muddebihal	FARMER	1	1	1	-	TOBACCO	3	0	1	1
2	70	M	Nimbal	FARMER	2	0	1	-	SMOKING	1	3	1	1
3	75	F	Shivanagi	HOUSEWIFE	2	1	0	-	-	3	2	1	1
4	45	F	Vijayapura	FARMER	2	1	1	-	-	3	2	1	3
5	81	M	Vijayapura	FARMER	2	1	1	-	SMOKING	3	2	1	1
6	70	M	Bagewadi	FARMER	2	1	1	DM, HTN	-	2	3	1	1
7	65	F	Yadagiri	HOUSEWIFE	1	1	0	-	TOBACCO	3	0	1	1
8	60	M	Indi	SHOPKEEPER	1	1	0	HTN	-	3	0	1	1
9	63	M	Yadagiri	FARMER	2	0	0	-	SMOKING	1	1	1	1
10	75	M	Vijayapura	UNEMPLOYED	2	1	1	-	-	2	3	2	1
11	70	F	Indi	HOUSEWIFE	2	1	0	-	-	3	2	1	1
12	48	M	Indi	FARMER	2	1	1	DM	-	3	3	1	1
13	70	F	Budihal	FARMER	2	0	0	-	-	1	1	1	1
14	80	M	Indi	FARMER	2	0	1	-	TOBACCO	1	2	1	1
15	70	F	Sindagi	HOUSEWIFE	2	1	1	HTN	-	3	3	1	1
16	76	F	Bagewadi	VENDOR	2	1	0	HTN	SMOKING	1	3	1	1
17	78	M	Yadagiri	FARMER	2	0	0	-	-	2	1	1	1
18	63	M	Indi	DRIVER	2	1	1	DM, HTN	-	1	1	2	1
19	73	M	Indi	FARMER	2	0	1	-	-	2	1	1	2
20	73	M	Indi	FARMER	2	0	1	-	ALCOHOL	1	1	1	1
21	56	M	Chadchan	SHOPKEEPER	2	1	1	-	-	2	2	1	1
22	74	F	Hebbal	UNEMPLOYED	1	1	1	DM, HTN	-	0	2	3	1
23	65	M	Jigaji Vanagi	FARMER	2	1	1	-	-	3	3	2	2
24	81	M	Kannur	FARMER	2	1	1	-	-	3	2	2	1
25	75	M	Devara Hipparagi	FARMER	2	0	0	-	-	2	3	1	1
26	61	M	Arjunagi	FARMER	1	1	1	DM	TOBACCO	0	2	1	1
27	85	M	Sindagi	UNEMPLOYED	2	0	0	-	-	1	1	1	1
28	77	M	Indi	UNEMPLOYED	2	1	1	-	-	1	1	2	1
29	84	M	Sindagi	UNEMPLOYED	2	1	0	-	-	1	1	1	1
30	57	F	Kaggod	FARMER	2	1	1	-	-	1	1	1	1
31	61	M	Nidagundi	FARMER	2	1	1	HTN	-	3	2	1	2
32	70	M	Bommanahalli	FARMER	1	0	1	HTN	SMOKING	0	1	1	1

CASES

SR NO	AGE	SEX	LE LENS Status	SCHIRMERS I Test RE (mm)	SCHIRMERS II Test RE (mm)	T BUT RE (Seconds)	SCHIRMERS I Test LE (mm)	SCHIRMERS I Test LE (mm)	T BUT LE (Seconds)	PROTEIN	ALBUMIN	GLOBULIN	A/G	CALCIUM	CHOLESTEROL	Triglycerides	LDL	HDL	Cholesterol/HDL	VLDL
1	70	M	1	26	9	3	35	28	8	7	4	3	1.3	8.8	190	127	129	36	5	25
2	70	M	1	23	15	5	35	7	2	7.5	3.7	3.8	0.9	8.7	142	72	96	32	4	22
3	75	F	1	12	9	4	11	9	6	7.1	3.8	3.3	1.15	8.9	194	67	114	67	3	13
4	45	F	3	19	13	3	23	18	4	7	3.9	3.1	1.25	9.1	107	73	114	38	4	15
5	81	M	1	28	11	5	23	14	7	6.4	3.9	2.5	1.56	8.8	154	115	87	44	4	23
6	70	M	1	21	4	4	20	9	4	7.2	3.7	3.5	1.05	8.9	167	108	98	47	4	22
7	65	F	1	24	9	2	20	14	9	6.1	3.9	2.2	1.7	8.8	206	155	122	53	4	31
8	60	M	1	25	9	5	15	9	11	6.1	3.6	2.5	1.44	8.6	172	102	112	40	4	24
9	63	M	1	15	13	8	10	9	6	6.4	3.6	2.8	0.8	9	134	81	72	46	3	21
10	75	M	1	23	8	3	26	9	3	5.8	3.1	2.7	1.14	8.5	94	51	55	29	3	19
11	70	F	1	12	6	4	13	9	5	5.3	3.8	1.5	2.5	8.5	121	292	121	39	6	22
12	48	M	1	26	9	3	27	8	2	6.3	4	2.3	1.7	8.8	151	116	79	49	3	18
13	70	F	1	19	12	8	12	15	12	7.1	4.6	2.5	1.84	9.2	170	58	95	63	3	20
14	80	M	1	26	8	8	18	12	8	7.7	3.2	4.5	0.71	9.8	227	127	98	38	5.97	21
15	70	F	1	31	7	3	21	6	2	6.9	3.1	3.8	0.81	9.2	187	146	77	28	6.67	23
16	76	F	1	16	12	6	25	5	3	7.1	3	4.1	0.7	8.4	189	214	115	29	6.4	16
17	78	M	1	6	5	4	7	5	4	8.4	5.2	3.2	1.62	9.6	142	84	85	40	4	17
18	63	M	1	18	13	9	18	14	10	7.6	3.3	4.3	0.76	8.6	119	68	40	65	2	14
19	73	M	2	25	7	3	11	9	8	6.9	3.1	3.8	0.81	8.7	180	101	113	37	3	19
20	73	M	1	18	9	9	15	11	9	8	3.6	5.6	1	9.5	144	73	95	34	4	23
21	56	M	1	22	4	4	20	5	5	6.5	3.1	3.4	0.91	8.8	141	66	78	50	3	13
22	74	F	1	23	15	11	20	9	7	6.6	3.3	3.3	0.9	8.5	148	77	67	15	4	20
23	65	M	2	26	4	2	11	7	7	6.9	3.2	3.7	4	8	110	92	96	24	5	18
24	81	M	1	21	4	3	18	6	3	7.2	4.7	2.5	1.8	8.7	129	85	83	29	4	23
25	75	M	1	21	7	8	26	11	10	6.4	3.5	2.9	1.2	8.8	196	80	94	36	5	16
26	61	M	1	23	10	9	30	7	5	6.6	3	3.6	0.83	9	212	191	73	31	6.8	19
27	85	M	1	15	12	8	15	11	9	6	3.3	2.7	1.2	8.4	269	74	102	32	7.8	15
28	77	M	1	21	7	8	23	9	9	6.9	3.7	3.2	1.15	9.6	196	72	130	52	4	14
29	84	M	1	19	14	8	18	15	9	6.3	3.7	2.6	1.4	9	142	75	84	33	3	15
30	57	F	1	30	7	5	28	5	6	7.1	5.8	1.3	1.2	9.5	203	79	82	38	5.34	16
31	61	M	2	30	6	3	33	4	3	5.4	2.7	2.7	2	8	212	47	61	32	3	9
32	70	M	1	17	9	8	19	8	9	6.7	3.7	3	1.2	9	190	129	131	33	6	26

CONTROLS

SR NO	AGE	SEX	ADDRESS	OCCUPATION	Comorbidity	ADDICTION	RE LENS Status	LE LENS Status	SCHIRMERS I Test RE (mm)	SCHIRMERS II Test RE (mm)	T BUT RE (Seconds)	SCHIRMERS I Test LE (mm)	SCHIRMERS I Test LE (mm)	T BUT LE (Seconds)	PROTEIN	ALBUMIN	GLOBULIN	A/G	CALCIUM	CHOLESTEROL	Triglycerides	LDL	HDL	Cholesterol/HDL	VLDL
1	66	F	YADAGARI	HOUSEWIFE	-	-	SIMC	SIMC	15	6	9	15	9	6	6.7	4	2.6	1.57	9.3	239	323	140	35	7	26
2	75	M	KATIJAPUR	UNEMPLOYED	-	Tobacco	SIMC	SIMC	10	3	3	14	4	4	6	3.5	2.5	1.4	9	161	85	104	40	4	18
3	60	F	BABLESHWAR	FARMER	-	-	SMC	SIMC	18	15	12	22	16	13	6.4	3.7	2.7	1.37	8.9	194	52	138	56	4	10
4	45	F	SINDAGI	HOUSEWIFE	-	-	SMC	SIMC	35	25	13	31	16	14	7	4.1	2.9	1.4	9.4	146	85	95	44	3.32	16
5	66	F	HAVERI	HOUSEWIFE	-	-	SIMC	SIMC	12	6	6	12	8	7	4.8	2.5	2.3	1.08	8.1	153	75	89	49	3	18
6	65	M	BAGEWADI	FARMER	-	SMOKING	SIMC	SIMC	11	6	3	12	6	3	6.6	4.3	2.3	1.86	6	9.1	103	154	63	4	11
7	87	M	VIJAYAPURA	UNEMPLOYED	Hypertension	-	SIMC	SMC	32	15	10	27	16	10	5.1	3.5	1.6	2.18	9	154	73	93	46	3	15
8	75	F	VIJAYAPURA	FARMER	-	Tobacco	SIMC	SIMC	31	15	9	30	13	10	6.7	3.9	2.8	1.39	9.3	187	149	94	46	4	28
9	65	F	SINDAGI	HOUSEWIFE	Diabetes	-	SIMC	SIMC	26	21	10	27	22	11	6.4	4	2.4	1.6	9.4	191	108	96	53	4	22
10	66	M	BAGEWADI	FARMER	-	-	SIMC	SIMC	18	8	7	21	10	9	7.1	4.6	2.5	1.84	8.9	223	167	93	31	7.19	29
11	76	M	BALAGANUR	UNEMPLOYED	Hypertension	-	SIMC	SIMC	11	8	10	13	10	12	5.6	3.1	2.5	1.24	8.9	136	44	92	35	3.8	9
12	55	M	VIJAYAPURA	BUSINESSMAN	-	-	SIMC	SIMC	13	9	10	11	8	9	6.2	3.7	2.5	1.48	9	122	127	63	34	4	25
13	63	F	SINDAGI	FARMER	-	-	SIMC	SIMC	15	10	8	13	10	7	6.7	4	2.7	1.48	9.3	265	129	186	41	5	16
14	65	F	BAGEWADI	FARMER	-	Alcohol	SIMC	SIMC	31	26	13	28	25	13	6.3	3.6	2.7	1.9	9.4	186	124	94	46	4.04	25
15	53	F	SINDAGI	HOUSEWIFE	-	-	SIMC	SIMC	21	14	10	24	12	11	6.4	3.4	3	0.8	9.3	236	156	157	48	5	31
16	81	F	CHADCHAN	UNEMPLOYED	Diabetes, Hypertension	-	SIMC	SIMC	27	18	12	26	17	13	6.8	3.5	3.3	1.06	9	167	123	78	51	3.27	22

CONTROLS

SR NO	AGE	SEX	ADDRESS	OCCUPATION	Comorbidity	ADDICTION	RE LENS Status	LE LENS Status	SCHIRMERS I Test RE (mm)	SCHIRMERS II Test RE (mm)	T BUT RE (Seconds)	SCHIRMERS I Test LE (mm)	SCHIRMERS I Test LE (mm)	T BUT LE (Seconds)	PROTEIN	ALBUMIN	GLOBULIN	A/G	CALCIUM	CHOLESTEROL	Triglycerides	LDL	HDL	Cholesterol/HDL	VLDL
17	62	M	TALIKOTI	DRIVER	-	-	SMC	SIMC	21	17	11	18	16	10	6.4	3.2	3.2	1	8.3	138	46	87	42	3	9
18	45	M	TALIKOTI	FARMER	-	-	SIMC	SIMC	17	12	9	15	12	9	6.4	3.5	2.9	1.2	8.7	169	61	97	60	3	12
19	60	M	MUDDEBIHAL	FARMER	-	-	SMC	SMC	30	25	13	29	24	13	6.2	3.8	2.4	1.9	8.6	192	148	90	62	3	24
20	74	F	GEDDALAMRI	HOUSEWIFE	Hypertension	-	SIMC	SIMC	13	7	7	16	8	6	5.9	3.3	2.6	1.2	9.2	141	101	80	41	3	20
21	50	F	GEDDALAMRI	FARMER	Diabetes	-	SIMC	SMC	17	14	10	19	13	11	6.8	3.8	3	1.26	10	187	80	86	65	2	16
22	47	F	JAMALPUR	FARMER	-	-	SIMC	SIMC	24	17	11	21	14	14	6.4	3.8	2.6	1.2	8.6	192	126	90	68	3	22
23	43	F	VIJAYAPURA	TAILOR	-	-	SIMC	SMC	16	12	8	18	11	9	7.1	4	3.1	1.29	10	188	53	137	40	5	11
24	50	M	HUNASANGI	FARMER	Diabetes, Hypertension	SMOKING	SIMC	SIMC	22	16	11	25	17	12	6.9	3.9	3	1.3	8.6	148	126	90	48	3	19
25	66	M	VIJAYAPURA	FARMER	-	-	SIMC	SIMC	30	21	11	28	23	13	6.8	3.6	3.2	1.125	8.9	148	126	86	48	3	21
26	68	F	VIJAYAPURA	HOUSEWIFE	-	-	SIMC	SIMC	26	18	11	25	16	10	7.6	4.5	3.1	1.45	908	182	82	108	58	3.8	16
27	61	F	MUDDEBIHAL	HOUSEWIFE	-	Tobacco	SMC	SIMC	13	7	7	12	7	9	7.2	4.1	3.1	1.32	9.2	246	107	179	46	5	21
28	70	M	MUDDEBIHAL	UNEMPLOYED	Diabetes	-	SIMC	SMC	25	21	9	26	19	11	6.8	4.3	2.5	1.72	9	158	115	99	36	4	23
29	68	F	VIJAYAPURA	UNEMPLOYED	-	-	SIMC	SIMC	20	14	9	19	12	8	6.9	3	3.9	0.76	8.5	150	133	87	36	4	27
30	65	F	INDI	UNEMPLOYED	-	-	SMC	SIMC	24	19	13	22	18	12	7.8	3.8	4	0.95	10	146	121	89	48	3.04	12
31	62	F	VIJAYAPURA	UNEMPLOYED	-	-	SIMC	SIMC	21	17	10	22	18	12	6.8	4	2.8	1.43	9.2	152	110	84	42	3.62	13
32	48	F	VIJAYAPURA	FARMER	-	-	SIMC	SIMC	22	18	11	24	17	11	6.7	4.2	2.5	1.68	8.7	149	115	90	51	2.92	23

Appendix VI

Plagiarism report

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