COMPARISON OF SEVERITY OF DRY EYE AND MEIBOMIAN GLAND DYSFUNCTION IN DIABETICS AND NON- DIABETICS – ONE YEAR CROSS SECTIONAL STUDY IN A TERTIARY CARE CENTER

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ABBREVIATIONS

A1C: Hemoglobin A1C

DED: Dry Eye Disease

DEWS: Dry Eye Workshop

DM: Diabetes Mellitus

GDM: Gestational Diabetes Mellitus

GLUT-2: Glucose Transporter Type 2

GLP-1: Glucagon-Like Peptide-1

GIP: Gastric Inhibitory Polypeptide

IFG: Impaired Fasting Glucose

IDF: International Diabetes Federation

IGT: Impaired Glucose Tolerance

KCS: Keratoconjunctivitis Sicca

LLT: Lipid Layer Thickness

LFU: Lost to Follow-Up

MG: Meibomian Gland

MGD: Meibomian Gland Dysfunction

MODY: Maturity-Onset Diabetes of the Young

NIBUT: Non-Invasive Break-Up Time

NIDDM: Non-Insulin Dependent Diabetes Mellitus

NSAIDs: Nonsteroidal Anti-Inflammatory Drugs

ODI: Ocular Surface Disease Index

OSDI: Ocular Surface Disease Index

OGTT: Oral Glucose Tolerance Test

SIT: Schirmer's Test

TBUT: Tear Break-Up Time

T2D: Type 2 Diabetes

T2DM: Type 2 Diabetes Mellitus

TFOS: Tear Film and Ocular Surface Society

VEGF: Vascular Endothelial Growth Factor

ABSTRACT

Background: Diabetes mellitus is a chronic metabolic disorder caused by deficiencies in either insulin action or synthesis, or both, has been linked to various complications, including those affecting the eyes. With the global rise in diabetes prevalence, understanding its impact on ocular health is crucial. This study aims to assess and compare the severity of dry eye and meibomian gland dysfunction (MGD) in diabetic and non-diabetic individuals.

Material and Methods: A one-year cross-sectional study was conducted at a tertiary care center. The sample included 140 subjects aged above 40, divided equally into diabetic and non-diabetic groups. Data collection involved routine eye examinations, Schirmer's test, tear film breakup time (TBUT), blink interval, meibum expressibility, and quality assessments. Statistical analyses were performed using R version 4.2.0 and Microsoft Excel.

Results: The study found significant differences between diabetic and non-diabetic groups. Diabetic patients had a higher incidence of vision blurring (68.6% vs. 48.6%) and pain (42.9% vs. 11.4%). The mean Ocular Surface Disease Index (OSDI) score and Schirmer's test results were significantly worse in diabetics. However, no significant differences were observed in TBUT, blink interval, Oxford staining score, meibum expressibility, and quality scores. Diabetics exhibited more severe dry eye grades and advanced stages of MGD.

Conclusion: Diabetic individuals experience more severe dry eye and MGD than non-diabetics. This underscores the need for thorough ocular assessments and targeted

management strategies in diabetic patients to mitigate discomfort and prevent visual deterioration.

Keywords: Diabetes mellitus, tear film, dry eye, ocular surface meibomian gland dysfunction, , hyperglycemia

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INTRODUCTION

"Diabetes mellitus is a chronic metabolic disease that can be avoided with the right preventive actions."[1,2]. “This is a class of metabolic illnesses distinguished by hyperglycemia caused by abnormalities in insulin production, insulin action, or both.” It is divided into two categories: Type 1 and Type 2. Insulin deficit is total or almost complete in type 1 diabetes. Type-2 diabetes mellitus is associated with decreased ability of the insulin to act on the peripheral tissues, which is called insulin resistance. During the early stages of insulin resistance, pancreatic β cells produce enough insulin to regulate blood glucose. However, over production of insulin can cause failure of β cells, resulting in type-2 diabetes. “Chronic hyperglycemia is associated with dysfunction and failure of different organs such as kidneys, eyes, nerves and heart.”[3]

“In recent years, the incidence of diabetes has been on the rise, leading to a notable increase in diabetes-related eye complications. India stands out as the global epicenter of diabetes, with an estimated 41 million individuals affected by the condition. Projections indicate a steady growth in diabetes prevalence, from 2.8 percent in 2000 to an anticipated 4.4 percent by 2030 across all ages. According to estimates from the International Diabetes Federation in 2017, the projected prevalence rates for diabetes in 2017 and 2045 are 8.8% and 11.4% respectively. This upward trend underscores the growing concern of diabetic eye disease.

Numerous studies conducted over the years have highlighted that type 2 diabetes mellitus patients are more prone to experience disruptions in the stability of the tear film. The tear film consists of mucins, water, and lipids, where lipids and proteins secreted by the meibomian glands serving as crucial components. These secretions play a pivotal role in

maintaining the tear film's stability. However, irregularities in insulin secretion can impede the functioning of sterols and lipid receptors within the meibomian glands. Consequently, dysfunction of these glands can lead to tear film instability, resulting in accelerated tear evaporation and elevated tear osmolarity, ultimately leading to ocular surface disorders, notably dry eye. **“**Meibomian gland dysfunction is a significant contributor to dry eye, yet it often goes unnoticed. While various systemic and environmental factors have been proposed as the underlying causes of dry eyes, diabetes stands out as a particularly significant factor. Therefore, it is crucial to comprehend the interconnection between diabetes mellitus, meibomian gland dysfunction and dry eyes. This study aims to evaluate and compare the severity of dry eye and meibomian gland dysfunction between individuals with diabetes and those without the condition.”

REVIEW OF LITERATURE

"Type 2 diabetes mellitus is a disease with a massive worldwide impact that is already causing epidemics in both developed and developing nations. According to the International Diabetes Federation, over 463 million persons have diabetes."[4]

Diabetes mellitus - an overview

"Diabetes prevalence has risen worldwide as a result of changing lifestyles and growing obesity. Diabetes has a global prevalence of 425 million people in 2017. In 2015, approximately 10 percent of the American population was reported to have diabetes, as per the International Diabetes Federation (IDF). 7 million of these individuals went undiagnosed. Diabetes is more common in older age group. Diabetes affects over 25% of those over the age of 65."[6]

"With 41 million diabetics in the country, India is the world's diabetes capital. Diabetes prevalence for all age groups was expected to be 2.8percent in 2000 and 4.4percent in 2030.[7,8] According to the IDF (2017), the prevalence of diabetes in 2017 and 2045 is expected to be 8.8 and 11.4 percent, respectively. Hence Diabetic eye disease is also getting more prevalent.[9] According to the most recent epidemiological estimates from 2019, 77 million people in India have diabetes, which is anticipated to reach nearly 134 million by 2045. India ranks second in global diabetes prevalence, with 77 million individuals diagnosed with the condition. Among them, 12.1 million are aged 65 and above, and this figure is projected to escalate to 27.5 million by 2045. Additionally, around 57% of diabetes cases in India, roughly 43.9 million people, remain undiagnosed."[10]

Criteria for the diagnosis of Diabetes Mellitus[5]

1) "Symptoms associated with > 200 mg/dl plasma glucose concentration

2) Fasting blood sugar of ≥126 mg/dl

3) OGTT: ≥ 200 mg/dl at 2 hours plasma glucose"

CLASSIFICATION OF DIABETES MELLITUS

"There are four types of diabetes mellitus as per the new classification.[11]

Type 1,

Type 2,

Other specific types

Gestational diabetes.

Type 1: autoimmune β-cell destruction leading to absolute insulin deficiency.

Type 2: (NIDDM / Adult onset) is presents with insulin resistance in peripheral tissues and an insulin secretary defect of the β cells.

Other Specific Types: dysfunction of αβ-cell function (MODY or Maturity onset Diabetes Mellitus) or with defects of insulin action. Persons with diseases of exocrine pancreas, dysfunction associated with endocrinopathies.

SECONDARY

- Pancreatic disease
- Genetic diseases
- Hormonal abnormalities
- Ingestion of certain drugs or chemical compounds.

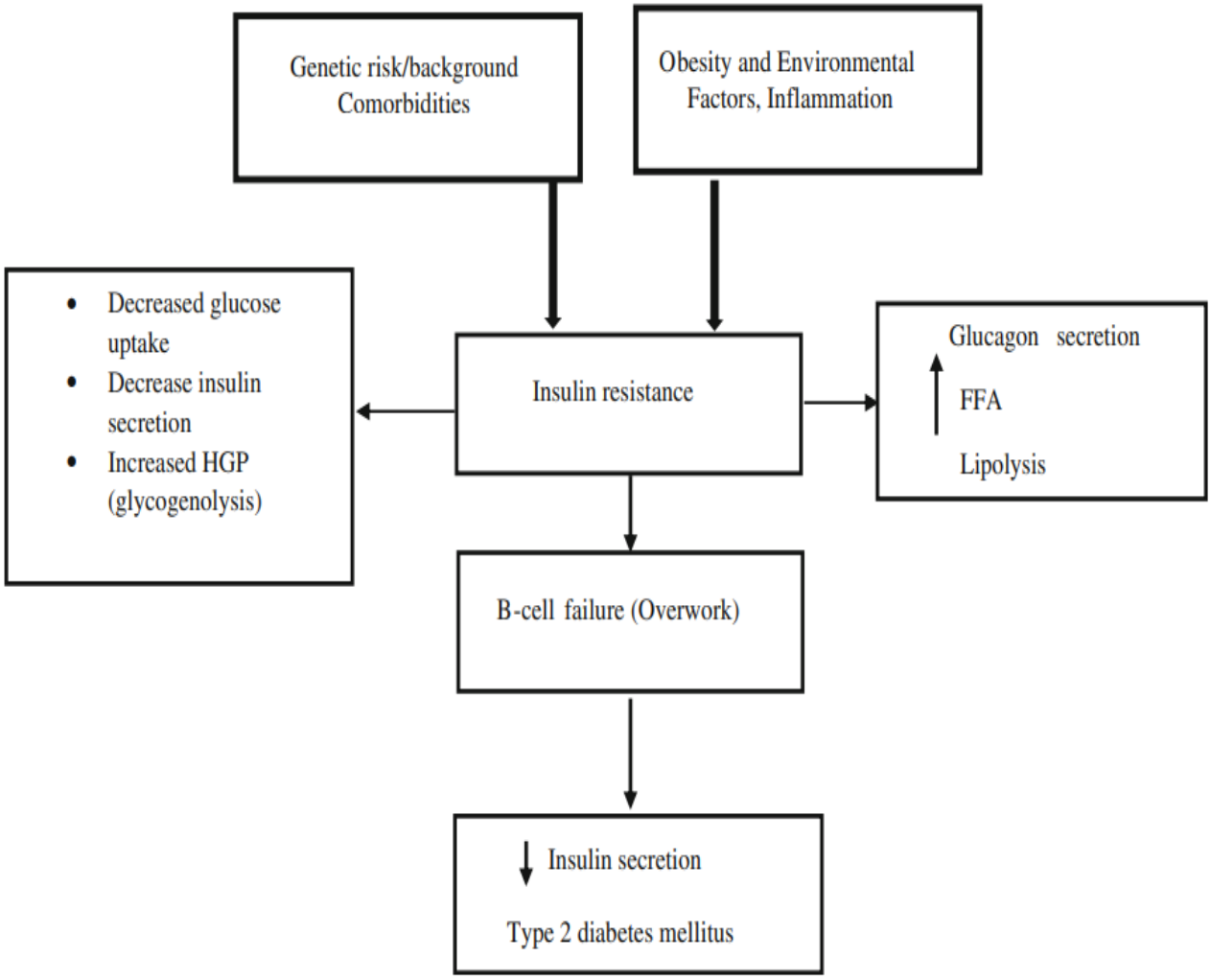


Figure 1: Mechanism of genetic predisposition and obesity induced insulin resistance and T2DM

T2DM is characterised by

- "Reduced glucose uptake due to muscle insulin resistance
- Increased glucose production due to hepatic insulin resistance
- Increase in plasma free fatty acids due to adipocyte insulin resistance
- Increase in hepatic sensitivity to glucagon
- Progressive beta-cell failure
- Increased insulin resistance resulting in increased adipocytokine release
- Hyperglucagonemia
- Impaired incretin - (GLP-1 and GIP) action
- Increased reabsorption of renal glucose "

Ocular manifestations of type 2 Diabetes Mellitus

"Diabetes complications are progressive and are most likely the outcome of long-term exposure to high blood sugar levels caused by changes in the metabolism of insulin and biological macromolecules such as carbs, lipids, proteins, and nucleic acids.[12] Diabetes and its consequences is a quickly becoming the world's leading cause of morbidity and death.[13,14] The diabetes epidemic has spread rapidly in both industrialised and poor nations. Diabetes can cause a variety of visual issues, including diabetic retinopathy, diabetic papillopathy, glaucoma, cataracts, and ocular surface disorders.[15] Diabetes-related ocular consequences are a widespread public health issue, thus we intend to focus on the frequency, pathophysiology, and therapy of these ocular problems."

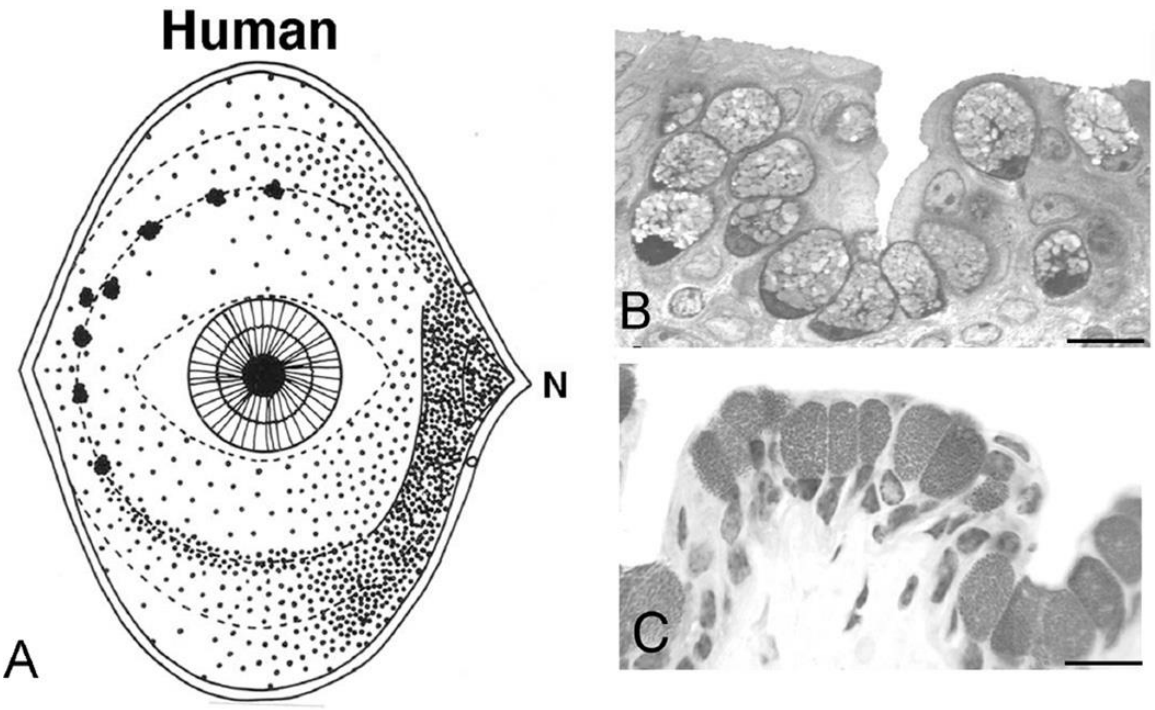
Anatomy of the Ocular Surface

It has been hypothesised that the ocular surface consist of the cornea, conjunctiva, lacrimal gland, and eyelid all working together. The anatomical surface of the eye consists of the mucosa surrounding the eyeball , the corneal edge, the corneal epithelium, and the tear film.[16]

"These constituents are interconnected through a continuous epithelium, as well as the vascular, nervous, immune and endocrine systems."

- **Conjunctiva:**

  "The conjunctiva is a thin, transparent tissue that borders the interior of the upper and lower eyelids. At the edge of the eyelid, it connects with the eyelid epithelium and the corneal epithelium.[17] The conjunctival epithelium is stratified nonkeratinizing epithelium with 5 layers. It is composed of cuboidal and cylindrical cells mixed with mucin-producing goblet cells. The placement of goblet cells in the epithelium differs between species. Humans have the maximum goblet cells in their nasal part of conjuctiva."[18]

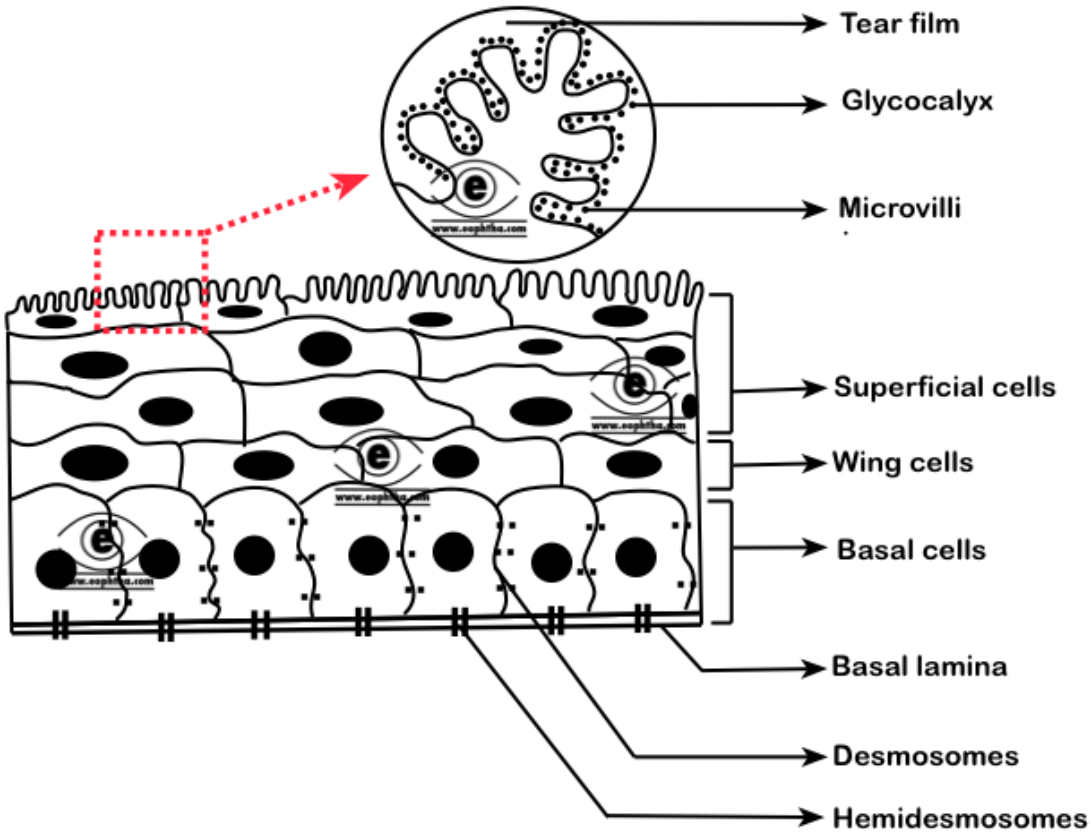


Goblet cells are spherical cells with surface mucin granules. MUCs, which are anchored mucus-associated membranes, enclose mucus granules. This connected mucus helps with barrier function. The major function of goblet cells is to secrete mucus onto the surface of the eyeball. As a result, goblet cells have specific duties like lubrication, tear film maintenance on the ocular surface, and barrier function.[18]

Reduction of goblet cells has been demonstrated in severe drying and cicatricial conditions of the ocular surface.

Cornea:

Epithelium, Bowmans membrane, Stroma, Descemet anterior membrane (Dua layer), Descemet membrane and Endothelium are the six layers that make up the cornea. The corneal epithelium accounts for about 10percent of the total thickness of the cornea.[16] It is stratified non-keratinizing squamous epithelium with stroma that connects neighbouring cells to the basement membrane ith the help of Hemidesmosomes. The surface of the corneal epithelium is covered in microvilli and microfolds. These cells generate glycocalyx which is necessary for the tear film's adherence and stability.[19]



+Figure 2: Cornea

“The glycocalyx on the microplicae are large glycoproteins that cover the surface of the epithelium. They are composed of membrane-associated mucins, specifically MUC1 and MUC16, which are concentrated around the tip of the microplicae. These transmembrane mucins have three main purposes:

1. Surface protection against friction.
2. Increasing the wettability of epithelium by glycosylating the hydrophobic plasma membrane into a hydrophilic one.
3. Mucin glycosylation is changed in eyes with ocular surface diseases. Contact lens wearers, DED patients, and glaucoma patients using beta-blockers have lower levels of sialylated mucin chains. This change results in the development of shorter and fewer mucin glycans, generating a vicious cycle.”[19]

Lacrimal Functional Unit:

The lacrimal gland functional unit (LFU) comprises of a sophisticated mechanism involving the lacrimal glands, ocular surface,eyelids, and the sensory and motor neurons connecting these elements. Its primary function is to maintain the tear film layers and facilitate the equilibrium of the ocular surface.[20] LFU modulates tear film shape and reacts to environmental, endocrinal, and cerebral cues. It mostly serves to protect the following:

1. “Health of the ocular surface.
2. Tear film integrity.
3. The quality of the image projected onto the retina.”

The afferent component of the LFU is amplified by ocular surface and trigeminal nociceptors, which synapses with autonomic and motor (efferent) neurons in the brainstem. Autonomic nerves innervate the lacrimal glands,conjunctival goblet cells and meibomian glands.[21]

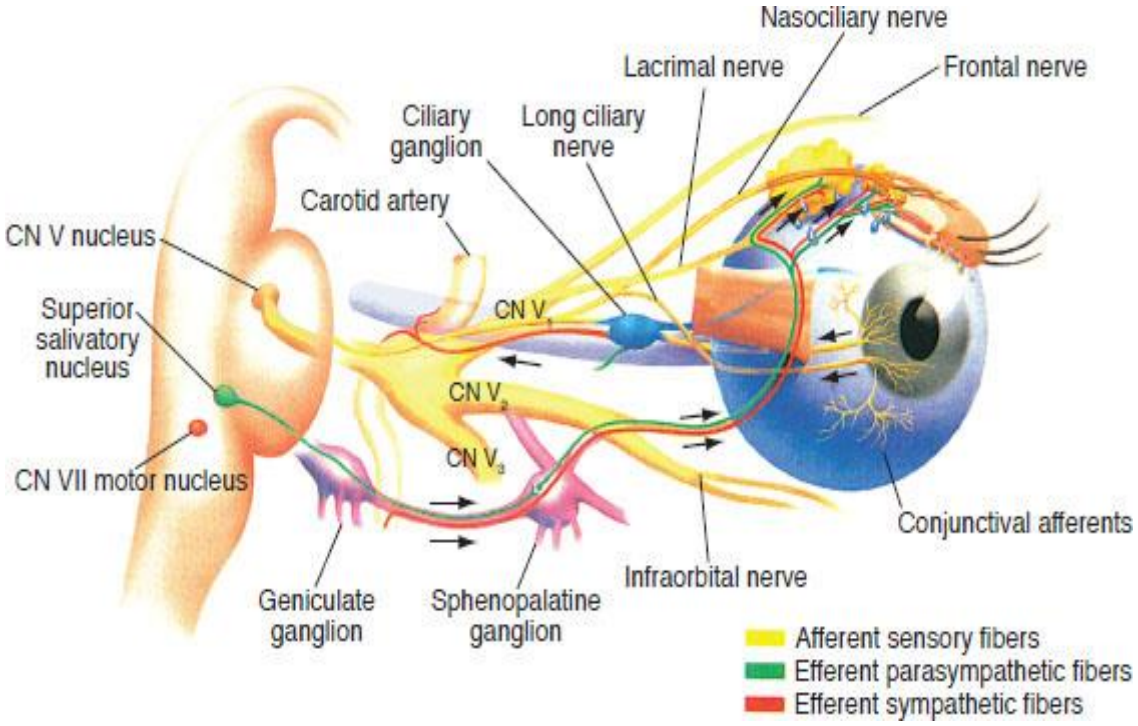


Figure 3: Lacrimal Functional Unit

Tear film formation[22]

"The tear film protects the ocular surface by lubricating it, maintaining a smooth surface for ideal light refraction, and protecting the conjunctiva and avascular cornea. Its usual volume ranges from 3 µL to 10 µL, its thickness is approximately 3 µm, and its average secretion rate is 1 µL to 2 µL/min.[23,24] The pH of tears is 7.45, with variations occurring throughout the day and seasons. Prolonged lid closure causes carbon dioxide accumulation,

reducing the pH. It is theoretically divided into three primary layers: inner mucin layer , middle aqueous layer , and outside lipid layer. Goblet cells in the conjunctiva and accessory lacrimal glands produce minute amounts of the aqueous tear layer, but the primary lacrimal glands produce the majority of it. After then, the tears evaporate or drain via the lacrimal puncta."[23]

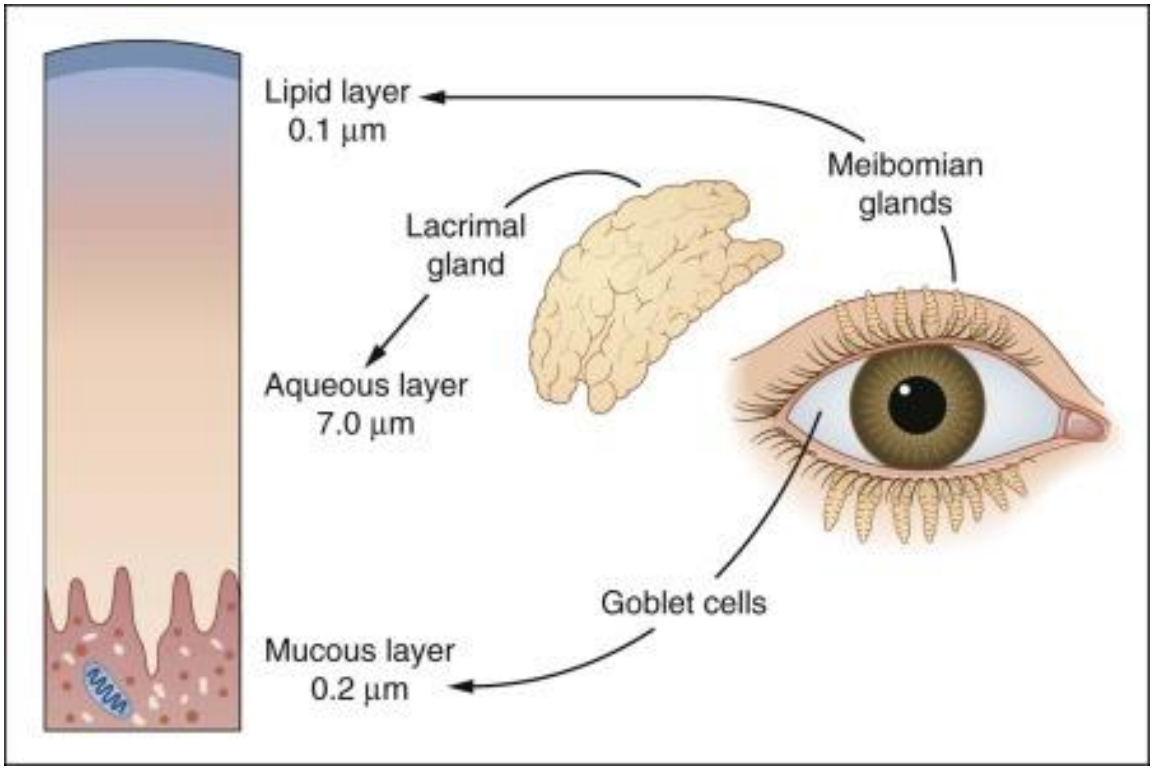


Figure 4: Tear film formation

"There are three types of tears, and each has a unique biochemistry. On the surface of the eye, basal tears are commonly seen. They provide nutrients, preserve eye comfort, and remove dirt from the surface. Tears that are generated in response to irritants and foreign objects are known as reflex tears. Reflex tears help remove irritants from the surface of the eyes and are produced in larger quantities than basal tears. The tears that lubricate the eyes as you sleep are called closed eye tears.

The Mucin Layer:

"The mucosa, which is 1.0 μm thick and is made up of water, electrolytes, and mucus generated by the conjunctival goblet cells, is the deepest layer of the tear film. This important defence system was created by goblet cells. The mucus on the surface of the eyeball is produced by the goblet cells, the apical cells of the conjunctiva, and the acinar cells of the lacrimal gland. Mucus is a glycoprotein consisting of a backbone protein with the addition of a long-chain carbohydrate compound. There are 20 different types of mucus in the human body and 7 of them are found on the surface of the eyeball. Mucus molecules can be membrane anchored or dissolved. Membrane-bound mucins including MUC1, MUC4, and MUC16 are produced by the apical cells of the conjunctiva and cornea.[18] These mucins are responsible for the formation of the glycocalyx that essentially protects the ocular surface. Soluble mucin is derived from 2 cell types, conjunctival goblet cells and lacrimal acinar cells.[19] Goblet cells produce MUC5AC, known as mucus-producing gel cells, and lacrimal acinar cells produce MUC7. The MUC5AC form binds to mucous membranes. Other soluble mucilages dissolve in the water layer and act as lubricants.[25]

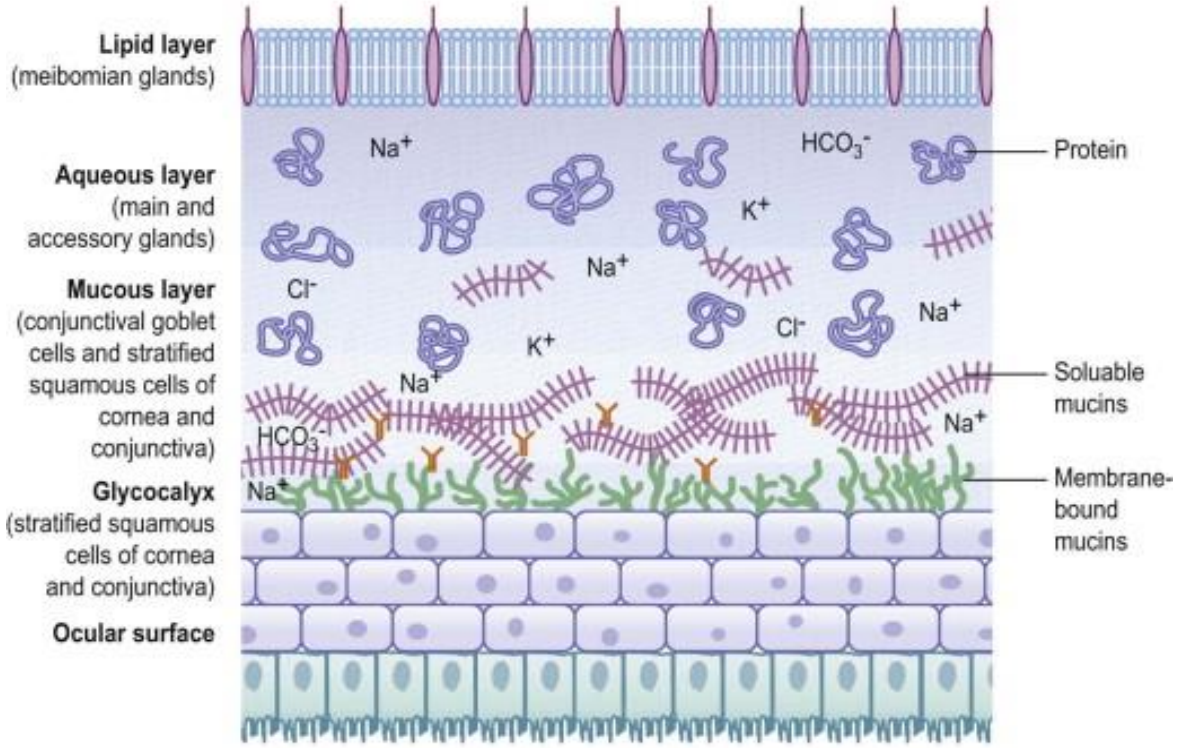


Figure 5: Tear film layers

The mucus layer also has a high carbohydrate content which makes it hydrophilic. This provides a way for nutrients and gases to pass through. Many studies have shown that mucus also serves as a reporter of tissue damage and serves as a tear film sensor that helps cells respond to changes in tear osmolarity.[26]

The Aqueous Layer:

"Most prominent layer of the tear film is the aqueous layer, which is approximately 7 µm thick. The primary lacrimal gland, which also makes proteins and electrolytes, is the source of aqueous layer.

It serves as a protective layer as well as a source of oxygen for the corneal epithelium. The additional elements of the aqueous layer include sodium, potassium, chloride, bicarbonates, calcium, amino acids, and Vascular endothelial growth factors (VEGF).[26] Lysozymes, lactoferrin, betalysin, and immunoglobulins are bactericidal proteins found in the aqueous layer." Plasma cells of the main and auxillary lacrimal glands produce immunoglobulins, primarily IgA.[27,28]

The secretion of the aqueous layer is mostly a reflex action. The fifth cranial nerve, the Trigeminal Nerve, forms the afferent route in the reflex arc, and its activation causes secretion. The efferent arc is more intricate. The parasympathetic fibres travel from the 7th cranial nerve - Facial nerve to the sphenopalatine ganglion through the Greater petrosal nerve.[29] Before accessing the lacrimal gland, the lacrimal secretory fibres go to the Zygomaticotemporal nerve of maxillary division of Trigeminal nerve and join with the lacrimal section of the ophthalmic division of the Trigeminal nerve. [30]

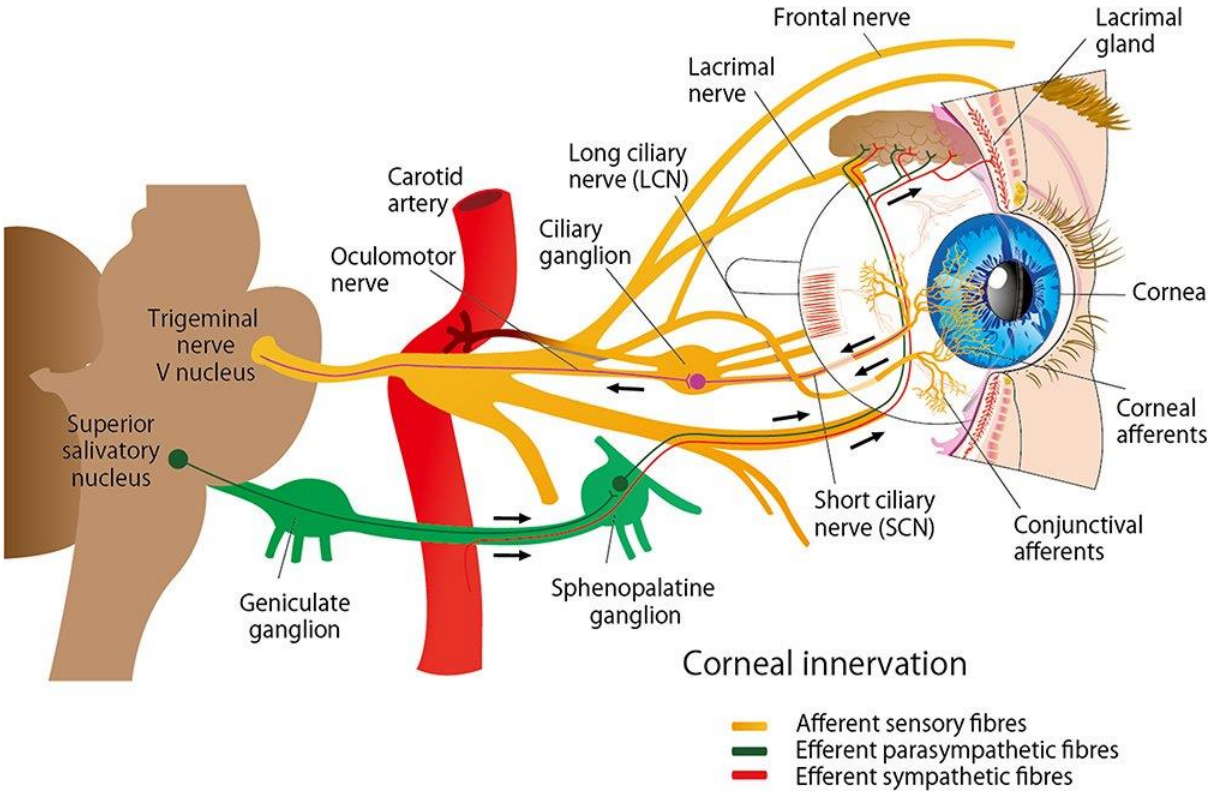


Figure 6: Tear formation

The lacrimal gland also receives hormonal input. Androgens are crucial for the lacrimal gland's aqueous secretion. It not only stimulates the secretion of certain proteins but also controls the structure and morphology of the lacrimal tissue.

The Lipid Layer:

The outermost layer of the tear film at the air-tear interface is called the lipid layer. It is mostly made up of meibomian lipid, which is generated from the lid's marginal glands. It produces a continuous strip anteriorly that extends from the upper to lower lids. It is a relatively thin layer, 0.015 to 0.160 μm thick. [31]

Meibomian glands are tubulacinar glands and are about 20 to 30 in number and are located inside the ankle plates. With each blink, meibomian secretions are released into marginal reservoirs, where they are distributed over the anterior tear layer of the cornea. [32]

“Cholesterol esters and waxes, together with diesters, fatty acids, cholesterol and triacylglycerols, make up the lipid layer. Because of its complexity, the lipid layer of the tear film has a multilayered structure. The interface between the lipid layer and the underlying water layer is made up of a thin layer of polar amphoteric lipids, primarily glycolipids and phospholipids.

The lipid layer is composed of 80% non-polar hydrophobic lipids, such as cholesterol, wax esters, and cholesterol, which are larger than other lipids.” [33]

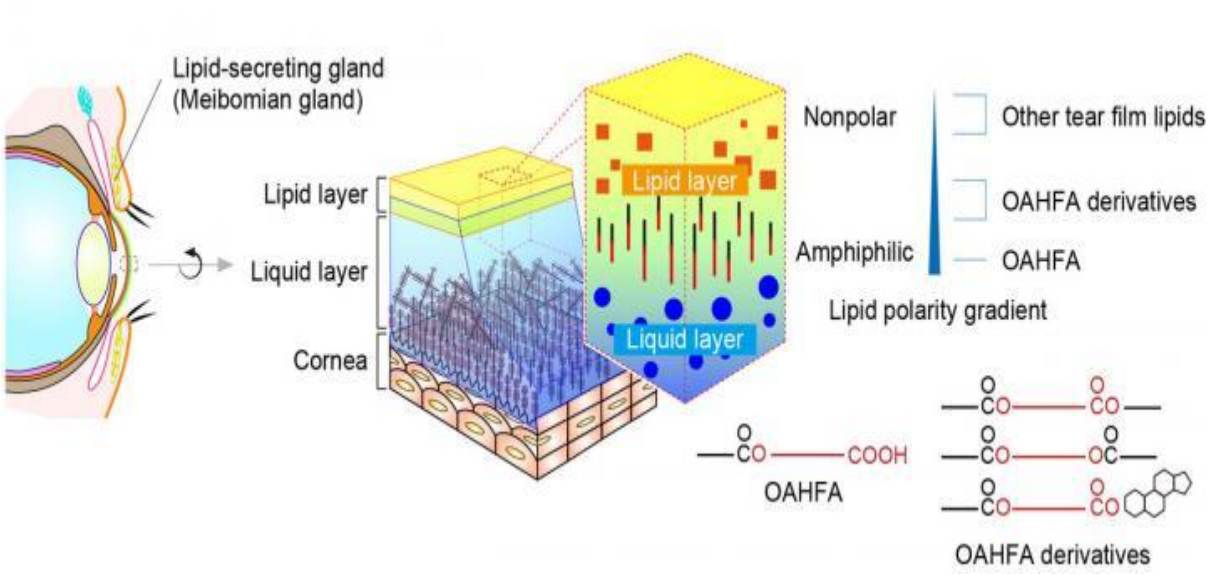


Figure 7: Lipid layer

“The lipid layer's primary function is to decrease the tear film's surface tension. The stabilization of the tear film is achieved by reducing the surface tension to about two thirds of that of water. It also smoothens the surface, retards the evaporation of water and also demonstrates antimicrobial function.[34] Each blink's up-phase involves the movement of the lipid layer to the tear film. The top lid takes oil from the marginal reservoirs when the lids are apposed. The lipid coating spreads across the aqueous surface as the top lid rises.[35]”

Function of tears

“The ocular surface and eyelids are lubricated by the tear film, which also serves as an antibacterial barrier, surface for refraction, and a source of nutrition and oxygen for the avascular corneal epithelium. “

“The tear film possesses antibacterial properties and shields the surface of the eyes from the outside world. In the aqueous layer of the tear film, important antimicrobial agents include ceruloplasmin, complement, glycoprotein, lactoferrin, anti-proteinase, transferrin, IgG, IgA, and IgE.”

Bacteriolytic lysozyme hydrolyzes bacterial peptidoglycan cell walls. When compared to other physiological fluids, tears have the highest concentration of it. “Iron is chelated by lactoferrin, which inhibits bacteria from consuming it for growth and metabolism. Immunoglobulins are crucial for maintaining immunity against bacterial, viral, and parasitic infections.

IgA levels rise in infectious or inflammatory conditions such corneal transplant response, blepharoconjunctivitis, acute bacterial conjunctivitis, acute keratoconjunctivitis,

keratomalacia, and blepharoconjunctivitis. Another antibacterial component identified in tears is alpha-lysin, which promotes cell rupture."[36,37]

Goblet cells also secrete mucins and glycoproteins, which serve as bacterial decoy receptors, prevent bacteria from adhering to ocular tissue, and trap foreign objects or germs. These mechanisms augment ocular defence. Additionally, they concentrate IgA close to the mucosal surface, which might harbour bacteria..[37]

Mechanism of tear production:

Controlling the production of tears requires sensory innervation. Mechanoreceptors, polymodal receptors and cold receptors are the mechanisms in which trigeminal nerve (V-1) afferent neurons in the cornea and eyelids receive sensory inputs in response to temperature changes and painful stimuli. Thus they set off somatic and autonomic reflexes, leading to enhanced blinking and tear production. [38]

The lacrimal and meibomian glands, which produce the aqueous and lipid layers of the tear film, are innervated by the sympathetic and parasympathetic nervous systems, respectively. They constitute a neural circuit that controls tear secretion. When the parasympathetic nervous system is activated in reaction to pain, discomfort, or cold, it produces more aqueous and mucin, as well as tears. Conjunctival epithelial cells secrete more when they get sympathetic input.[38]

Tear Film Dynamics – Role of blinking

The flashing cycle is divided into four parts. Downswing occurs when the upper eyelid moves down and stops.[31] The tear film is forced to move rapidly during the downward

swipe and subsequent upward pull, creating ripples. The downward action of the upper eyelid stops at the point of rotation and the direction is adjusted to initiate the upward action. The ascent begins after the turn, at about half the speed of the descent. The tear film effectively covers the surface in this step. Even when the upper eyelid stops moving, the tear film continues to move higher due to the surface activity of the lipids. This process is known as "upward drift" because the kinetic energy defies gravity. The interstitial interval indicates the time when tear outflow is minimised and, as a result, evaporation takes over.[35]

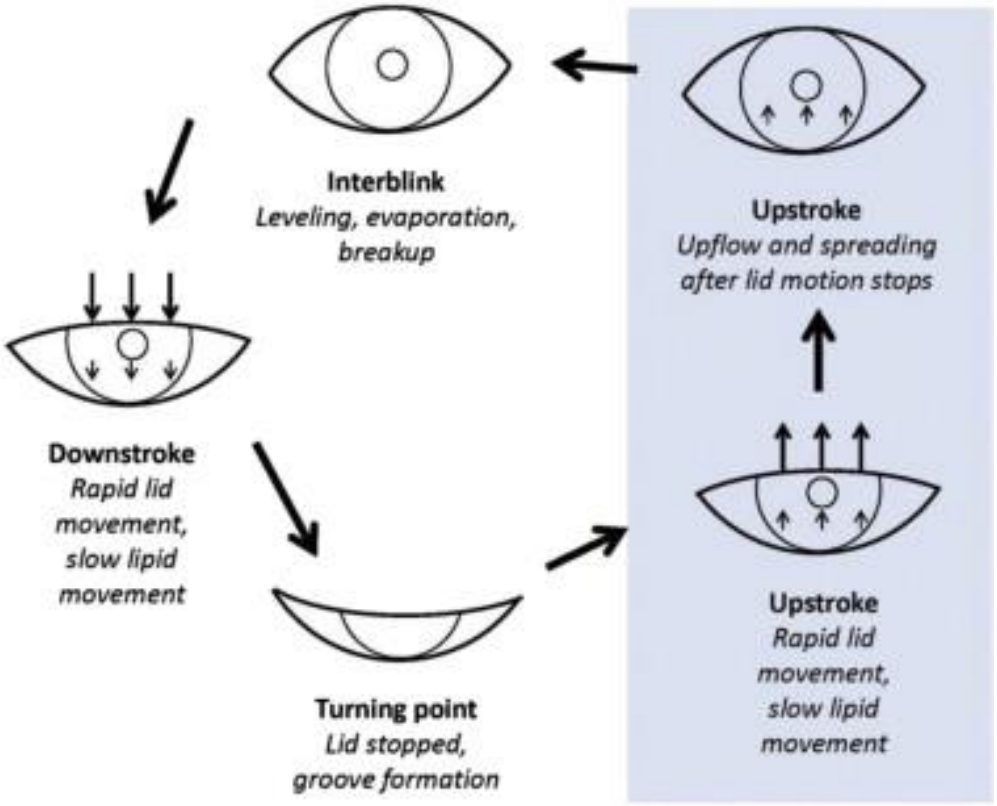


Figure 8: Tear film dynamics

DRY EYE[22]

Keratoconjunctivitis sicca (KCS), commonly called dry eyes or dry eye syndrome, is a common disorder of the eyes and is characterized by a loss of lubrication and moisture on the surface of the eyes.Tears are essential for preserving the comfort and well-being of the eyes. They include vital substances including oils, mucus, and antibodies that shield the eyes from infections in addition to providing moisture.

According to multiple clinical studies on DED conducted by the: National Eye Institute, the first widely recognised definition of Dry Eye Disease (DED) was published in 1995. "Dry eye is a condition of the tear film caused by tear deficit or excessive evaporation, which causes damage to the interpalpebral ocular surface and is linked with feelings of ocular discomfort," according to the paper.[39]

The simple idea that DED is merely a tear fluid illness has developed into a more nuanced understanding as a disruption in the intricate interplay of ocular surface, lacrimal apparatus and the tear film. The following significant advancement was presented in the report of the Tear Film and Ocular Surface Society (TFOS) of the International Dry Eye Workshop (DEWS) in 2007. This study broadened the scope of DED and refocused research on numerous ocular surface disorders.[40]

This definition recognised loss of tear film homeostasis as an important key factor for the characteristic features of DED and neurosensory anomalies as a contributing etiology for DED. The adaptation of this definition indicates that DED is a part of a larger spectrum of disorders of the ocular surface.[40]

There are three main components to the tear film, which covers the cornea and is 2 to 5 m thick.[41–43] The terms "layers" to describe these components (lipid, aqueous, and mucin) may be oversimplifying the environment of the tear film.[40] The lipid layer, which is the uppermost layer and lowers the amount of tears that evaporate, is produced by the meibomian glands in the eyelids.

The conjunctival accessory lacrimal glands (Glands of Krause and Wolfring) and orbital lacrimal glands produce the middle aqueous layer, which is the thickest part of the tear film.

Dry Eye disease prevalence

The prevalence of dry eye disease (DED) ranges from 5 to 50percent in various population-based studies conducted around the world. This large disparity in existing prevalence statistics is related to two main factors: (a) differences in demographic variables and (b) selection of diagnostic tools and criteria used to identify dry eye disease.[4] The prevalence pattern of DED in India is also quite different. Hospital studies are a great way to determine the prevalence of the disease. Extrapolation from hospital study data is often wrong when applied to the general population.[44]

Hospital-based research in north India found a prevalence of 32%, with patients classified as having moderate or severe DED. Another research from south India found a 1.46% incidence rate. In contrast to these, some research from India's eastern areas have indicated a lower prevalence rate. Rege et al. reported a 15.4% prevalence rate, whereas Sahai et al. reported a 18.4% prevalence rate.[45]

Etiology:

"DED may arise from a multitude of plausible aetiologies, many of which may be complicated. These include, among other things, iatrogenic causes (drugs or surgeries), sociodemographic factors, environmental factors, systemic illnesses, and local ocular variables."[46,47]

Factors associated with DED

"Systemic medications such as antihypertensives, anxiolytics, antihistamines, NSAIDS, isotretinoin etc.,

Topical medications like glaucoma drops

Skin diseases around eyelids like eczema or rosacea.

"Meibomian gland dysfunction is frequently associated with thickness and erythema of the eyelids as well as insufficient or changed meibomian gland secretions.

Ocular allergies

Ophthalmic surgeries like cataract surgery, keratoplasty etc

Chemical or thermal burns that scar the conjunctiva

Digital screen use like computer or mobile phones for longer duration

Graft versus host disease

Environmental factors such as exposure to cigarette smoke, chemical fumes, low humidity and pollution."

Pathophysiology:

DED is generally divided into two types: "aqueous deficient and evaporative.[48,49] These two groups, however, are not exclusive of one another, and many individuals combine elements of the two DED processes. The hallmark of aqueous tear insufficiency is inadequate tear production, and the most prevalent reasons include systemic medications, lacrimal gland blockage, infections, inflammation, and/or malfunction of the lacrimal gland (primary or secondary). Evaporative dry eye is characterized by increased tear film evaporation due to lipid deficiency in the tear film.The number of tears generated in this scenario is normal; nevertheless, the quality of tears causes excessive evaporation. The most common cause for this alteration is malfunction of the meibomian gland."

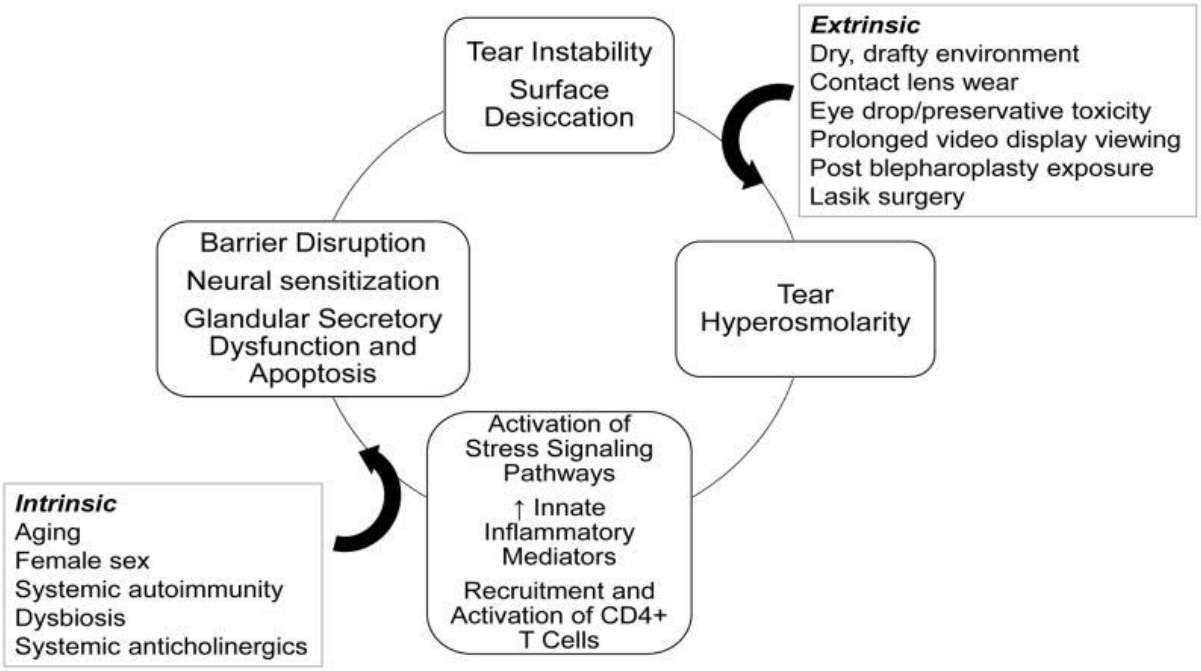


Figure 9: Numerous mechanism for dry eye

“Meibomian glands line the eyelid edges and release oils that form the lipid layer of the tear film, preventing tears from evaporating. Inadequate secretion owing to atrophy, gland drop out, or blockage of gland orifices can all induce meibomian gland dysfunction. Poor blinking (low rate, partial lid closure), abnormalities of the lid aperture, contact lens use, vitamin A deficiency, and environmental conditions (high airflow, low humidity) are all key causes of excessive tear evaporation.”

“DED is distinguished by hyperosmolarity of the tear film, which can directly or indirectly harm the ocular surface by inducing inflammation.[50] The typical osmolarity of the tear film is less than 300 mOsm/L, but in individuals with DED, it has been found to be as high as 360 mOsm/L.[51] The release of inflammatory mediators and damage to the ocular surface is caused by hyperosmolarity of the tear film. This may further reduce the stability of the tear film and lead to the self-perpetuation of the disease in a "vicious circle." In addition to hyperosmolarity, other factors that might initiate this pathologic cycle include topical preservative toxicity and ocular surface inflammation caused by conditions including allergic eye disease.”[52,53]

Risk factors

The most common risk factors include;

- Female gender (post menopausal women on estrogen therapy)
- Older age
- Antihistaminics
- Connective tissue disorders
- Deficiency of Vitamin A

- Laser refractive surgeries
- Contact lens use
- Environmental conditions
- Autoimmune disorders or inflammatory disorders.

Classification of Dry eye disease:

"International Dry Eye Workshop (DEWS) 2007, is the most widely used categorization of dry eye which split dry eye into evaporative and aqueous deficient"[54,55]

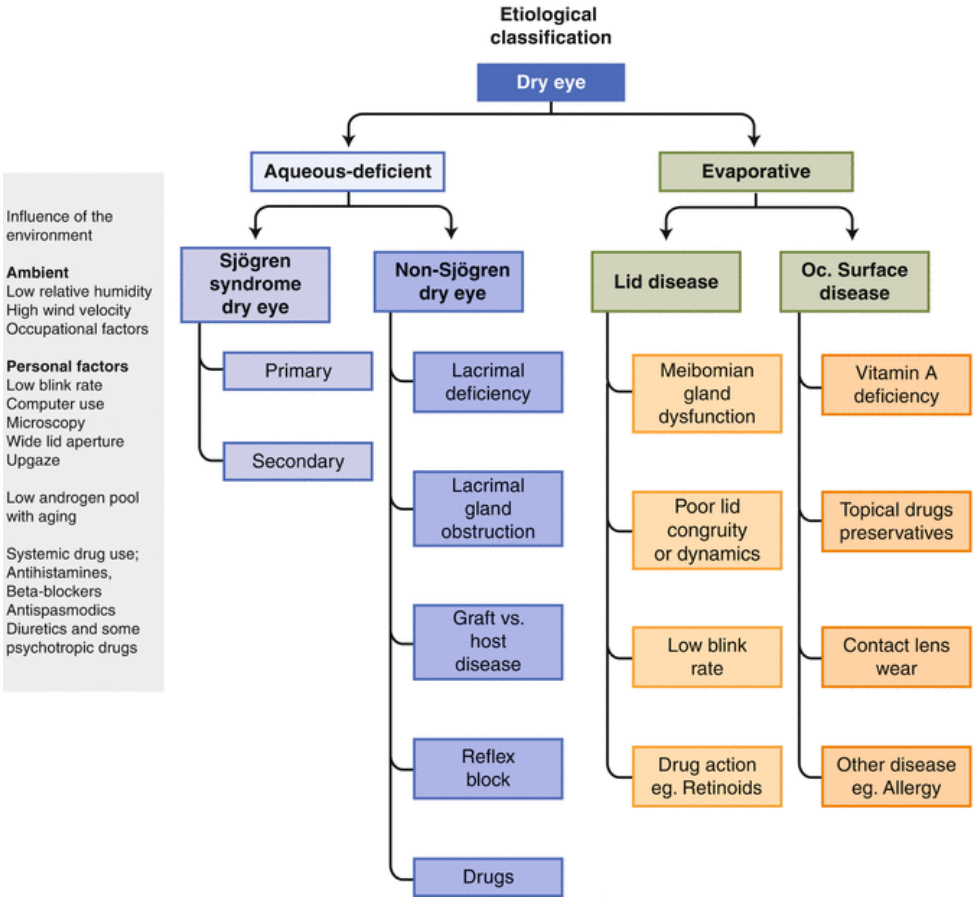


Figure 10: Classification of Dry eye

Common symptoms of dry eyes include:

- Dryness and irritation: The eyes may feel gritty, scratchy, or as if there's a foreign object present.
- Redness: The eyes may appear red.
- Burning or stinging: The eyes may feel a burning or stinging sensation.
- Watery eyes: Paradoxically, dry eyes can sometimes trigger excessive tearing as the compensation for the lack of moisture.
- Increased sensitivity to light: Dry eyes can increase sensitivity to bright lights.
- Blurred vision: Vision may become temporarily blurred, especially during prolonged periods of reading or computer use.

Complications

- Blepharitis and conjunctivitis
- Corneal vascularization
- Sterile stromal ulcer
- Band shaped keratopathy

Factors which contribute to the development of dry eyes:

- “Age: Dry eye is more common in older individuals, as tear production tends to decrease with age.

- Environmental factors: Exposure to windy or dry climates, air conditioning, and heating systems might contribute to dry eyes.
- Screen time: Extended periods of staring at screens (computers, smartphones, etc.) can reduce blinking, leading to dry eyes.
- Contact lens wearers: Contact lenses can disrupt the tear film, causing dryness.
- Medical conditions: Conditions like diabetes, sjögren's syndrome, rheumatoid arthritis and thyroid disorders can be associated with dry eyes.
- Medications: Certain medications, such as antihistamines, decongestants, and antidepressants, may decrease tear production.
- Hormonal changes: Hormonal fluctuations, such as those that occur during pregnancy or menopause, can affect tear production."

Diagnostic methodology

Despite the fact that different signs and symptoms have been listed in the literature over the years, there is a weak association between the symptoms valued by patients and the indicators present in DED. Around the world, there are several dry eye societies, for example European consensus group, ocular dryness and disease severity (ODISSEY), Japan dry eye society and Asia dry eye society. The following test are used to conclusive diagnosis.[56,57]

Standard patients evaluation of eye dryness questionnaire (SPEED): this gives scores from 0 to 28 with 8 items assessing the frequency and symptoms severity. The questionnaire assess the grittiness, dryness, irritation, watering, burning, scratchiness, eye fatigue and

soreness. Also it includes parameters like tolerable, bothersome, problematic, uncomfortable and intolerable to assess disease severity. [56]

"Ocular surface disease index questionnaire (OSDI): questionnaire with 12 items to assess dry eye symptoms and effect on visual function. The questionnaire includes the three subdomain which consists of ocular symptoms, environmental triggers and vision related symptoms. The response are recorded from 0 to 4 with 0 corresponding to none of the time and 4 corresponding to the all of the time. The final score is in ranges from 0 to 100. The interpretation is greater than 33 is considered severe dry eye disease, 23 to 32 as moderate dry eye disease, 13-22 as mild dry eye disease and 0 to 12 as normal."[56]

"McMonnies questionnaire: it include fourteen questions which assess the risk factors associated with dry eye, Which includes the gender, use of contact lens, age, symptoms of dry eye, secondary symptoms, any medical conditions associated like dryness of mucous membrane, medication and previous history of treatment." [56]

Diagnostic testing

- Test to assess tear film stability:
    - Fluorescence breakup time
    - Non invasive break up time
- Test for tear volume assessment:
    - Schirmer's test
    - Tear meniscus assessment
- Tear osmolarity
- Matrix metalloproteinase-9 test

- Interferometry
- Lactoferrin test
- Meibography
- The Sjo test
- Conjunctival impression cytology

Meibomian Gland disease

" It is the chronic diffuse abnormality of the meibomian glands, characterised by obstruction of the terminal duct along with qualitative or quantitative changes in glandular secretion" is the definition of meibomian gland dysfunction (MGD) given by the international workshop on the subject. The meibum is viscous and the duct epithelium is hyperkeratinized, the terminal duct becomes clogged. These may result in the meibomian glands atrophying and dropping out, which would reduce output. Tear film abnormalities, inflammation, ocular surface illness, and irritation are among the side effects of MGD.[58,59]

These eyelid-based meibomian glands are a kind of sebaceous gland. These bear the name Heinrich Meibom in honour of the German physician and anatomist. These glands are arranged in a single row parallel to the tarsal plates of the upper and lower lids.

The proximal edges of the tarsal plates are where the meibomian glands stop. The excretory duct near the distal end of the tarsus receives the secretion, or meibum, and deposits it into the lid border. It is believed that the bottom lid has 40–50 glands, whereas the top lid contains 20–30 different glands.[58,59]

Meibomian glands create lipids, which make up the majority of the lipid layer covering the tear film's surface.It is widely known that this lipid layer prevents the tear film's aqueous layer from over-evaporating. By lowering surface tension, it also helps to stabilise the tear film. It functions as an external barrier to keep bacteria out of the tear film and as a lubricant during blinking. The term "posterior blepharitis" describes anomalies in function brought on by malfunctioning meibomian glands, which alter secretions from the glands. Based on when it first manifests, MGD is divided into two categories: congenital and malignant. Its duration determines whether it is considered acute or chronic.[60]

Depending on Etiology, they can be divided into

High delivery

Low delivery

Poor delivery may be obstructive (cicatricial or non-cicatricial) or hyposecretory (meibomian sicca). Meibomian gland atrophy or medication adverse effects are the causes of meibomian sicca. The amount of meibomian glands that are active decreases due to MG atrophy. The most common kind of MGD is obstructive. Keratinization and ductal epithelial hypertrophy are the causes of this. This is separated between situations that are cicatricial and those that are not. Excessive lipid secretion is the reason of high delivery type, sometimes referred to as hypersecretory (meibomian seborrhea). Meibomian seborrhea arises secondary to underlying systemic illnesses such as acne rosacea and seborrhoeic or atopic dermatitis.[61,62]

Pathophysiology[63]

The type of MGD that is most common is obstructive MGD. The pressure inside the meibomian glands rises as a result of the continuous synthesis of meibum. Ductal dilatation, duct dropouts, acinar degeneration, and ultimately meibocyte development are brought on by this elevated pressure.[60]

Stagnation of meibomian secretions causes changes such as higher melting points, loss of clarity, and bacterial colonisation. Bacteria generate lipolytic enzymes and release inflammatory mediators, most notably Staphylococcus epidermidis, Staphylococcus aureus, and Propionibacterium acnes.[63,64] The lipolytic enzymes produced act on the lipids in the tear film, causing lipolysis and loss of tear film integrity.

Various studies associating the dry eye and meibomian gland among patients with diabetes mellitus;

Patients with type 2 diabetes mellitus showed more unstable tear films, severe complaints of dry eyes, considerable morphological and cytological alterations, and dysfunction in the meibomian glands when compared to non-diabetic patients, according to a study conducted in China by Tao V et al. (2016). The study was limited by the absence of evaluation of meibomian gland expressibility and eyelids, as well as the omission of assessment of other variables such blood sugar level and the severity of diabetic retinopathy.[65]

Dyslipidemia and the advancement of dry eye disease are strongly correlated, especially in women, according to a study by Rathnakumar K et al. (2018), on the prevalence of dry eye disease and its link with dyslipidemia. The study was limited by its small sample size, and further research is required to validate the underlying process.[66]

According to a study conducted by Chan TCY et al., (2019) on update about the correlation between meibomian gland dysfunction and dry eye illness it was determined that the aetiology of dry eye illness is complex and that it is a prevalent ophthalmic ailment. One important cause of dry eye illness is malfunction of the meibomian glands. The study explains a number of additional illness aetiologies as well as a step-by-step diagnostic and therapy process. The lack of direct patient engagement in the study is one of its limitations.[67]

In a prospective study by Johanna S et al., (2019) we establish the relation between type 2 diabetes, meibomian glands dysfunction and dry eye. The average age was 59 ±8 years, and 71% of individuals had MGD (76% diabetics and 67% controls). The diabetic group

had considerably greater OSDI (p = 0.01). In Meibomian Gland Dysfunction (MGD), there was a notable correlation between blood sugar levels and symptoms (p = 0.0005), along with a significant relationship between Hb1Ac and Ocular Surface Disease Index (OSDI) scores. Compared to the control group, the diabetes group had a higher Non-Invasive Break-Up Time (NIBUT) and a strong negative association (52.22%) with Meibomian Gland (MG) inflammation. MGD tends to be more severe in patients with type 2 diabetes compared to those without diabetes. Prolonged duration of diabetes correlates with more severe symptoms in MG. The diabetic group exhibited notable alterations in eyelid and tear function, contributing to evaporative dry eye and showing a robust association with MG inflammation.[68]

In a prospective study by Manjula TR et al., (2019) that was done to assess the and dry eye and meibomian gland dysfunction in patients with type 2 diabetes mellitus. Of the 100 diabetics, 56 (56%) had dry eye disease; 24 of them also had MGD, with 56 cases with dry eyes, or 42% of all cases, MGD is the cause. Six of the 100 non-diabetics with dry eye disease also had MGD, making up 15% of the group. Diabetes can change both the qualitative and quantitative characteristics of the ocular surface. Diabetic people are more likely to have dry eye problems than the general population. Compared to the non-diabetic population, the prevalence of MGD among diabetics is significantly greater. The frequency and intensity of MGD increases with the duration of DM.[69]

According to a study conducted by Xiao J et al., (2020) on Meibomian gland morphological and functional assessment in determining the subtype and severity of meibomian gland dysfunction it was shown that patients with low-delivery MGD had poorer dry eye metrics and ocular symptoms when compared to patients with high meibum

delivery. This suggests that meibum secretion plays a crucial role in maintaining the health of the ocular surface and should be the focus of therapy for meibomian gland dysfunction. Conventional dry eye tests are unable to identify nonobvious meibomian gland failure, and morphologic evaluation of meibography pictures is necessary to confirm meibomian gland loss. The study lack of a control group made it difficult to compare the results.[70]

In a study conducted by Mussi N et al., (2021) to assess the association between risk factors for MS and MGD in a dry eye patients. MGD did not correlate with BMI, smoking, type 2 diabetes, hypertension, or hyperlipidemia in the group of individuals with dry eyes. MGD has been associated with ageing and male sex. Blood lipid levels were unrelated to MGD, while ageing was associated with decreased levels of non-high density lipoprotein cholesterol and low-density lipoprotein cholesterol. Crucially, the study found no apparent correlation between risk factors for metabolic syndrome and an increase in MGD, as compared to people without MGD who also have dry eyes. Although there is a connection between dry eye disease and metabolic syndrome risk factors, these factors most likely indicate a chronic low-grade systemic inflammation that affects the function of the meibomian and lacrimal glands.[71]

In a study conducted by Abu E et al., (2022) They studied dry eye disease (DED) and meibomian gland dysfunction (MGD) in diabetic individuals. Results showed DED in 72.3% and MGD in 55.3% of participants. Symptomatic dry eye, as indicated by OSDI scores, correlated significantly with diabetes duration and conjunctival abnormalities. MGD was identified as a risk factor for DED, while ocular surface damage was the best predictor of MGD. Correlation between OSDI scores and corneal lesions was not observed,

possibly due to reduced corneal sensitivity. These findings underscore the importance of dry eye screening as part of routine care for type 2 diabetic patients. [72]

In a study conducted by Wu H et al., (2022) the purpose of the study was to assess Meibomian gland and tear film findings in patients with type 2 diabetes. In the diabetic group, HbA1c levels were associated with various parameters including OSDI, BUT, FL, LLT, and MGD characteristics ($p < 0.001$). Interestingly, patients with low HbA1c, normal SIT value, and low OSDI exhibited higher MGD values when compared to the non-diabetic group ($p < 0.05$). Diabetes duration was positively correlated with MGD characteristics ($p < 0.001$). Asymptomatic MGD may serve as an early indicator of type 2 diabetes-associated dry eye and ocular pain. Overall, MGD characteristics were found to be linked to HbA1c levels and diabetes duration.[73]

In a cohort study by Pan L et al., (2022) to assess the dry eye disease in patients with type 2 diabetes mellitus. The study found that the initial and average glycated hemoglobin levels, as well as the prevalence of diabetic neuropathy and retinopathy, were significantly higher in the group with dry eye disease (DED).

Advanced age emerged as a risk factor. After adjusting for gender, age, and diabetes duration, average glycated hemoglobin levels, diabetic neuropathy, retinopathy, nephropathy with eGFR 30-59, and specific ocular procedures such intravitreal injection, vitrectomy, pan-retinal photocoagulation, and cataract surgery were among the factors that contributed to DED. Protective factors against DED, compared to metformin alone, included DPP4 inhibitors, SGLT2 inhibitors, GLP-1 agonists, and insulin monotherapy, as well as combination therapies involving any two of these treatments. SGLT2 inhibitors had the lowest odds ratio in the monotherapy group, followed by GLP-1 agonists, DPP4

inhibitors, and insulin. According to the study's conclusions, microvascular problems, advanced age, female sex, inadequate diabetes management, and prior ocular treatments are all associated with diabetic patients' DED. In preventing diabetes-related DED, GLP-1 agonists, SGLT-2 inhibitors, DPP4 inhibitors, and insulin were found to be more efficacious than metformin alone.74

In a study conducted by Yang Q et al., (2023) to assess the evaluation of meibomian gland dysfunction in type 2 diabetes with dry eye disease. The DM-DED group had a considerably greater proportion of MG dropout in the upper and lower lids than the DED group ($P < 0.01$). Other MG characteristics, however, did not change significantly between these two groups. In contrast when comparing the DM group to normal controls, significant differences were observed in all MG parameters with the exception of MG dropout in the lower lids ($P<0.05$). There were not significant variations in any tear metrics between the DM-DED and DED groups, although SIT values did drop in the former group ($P<0.05$).

Compared to patients with only DED, those with T2DM also had a higher prevalence and severity of MGD. [75]

AIMS & OBJECTIVES

To compare the severity of dry eye disease and meibomian gland dysfunction in diabetics and non- diabetics, one-year cross sectional study in a tertiary care centre.

MATERIAL & METHOD

Source of Data: Subjects aged above 40 years of either sex attending at ophthalmology outpatient department at KLES DR. Prabhakar Kore hospital and medical research centre, Belagavi

Study Design: Cross sectional study.

Study Period: August 2022 to July 2023

Sample Size: Formula used for sample size calculation:

$$n = (SD_1^2 + SD_2^2)\frac{\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)^2}{(\bar{x}_1 - \bar{x}_2)^2}$$

where n is the sample size required, SD_1 is the standard deviation for the first group and SD_2 is the standard deviation for the second group.

$\bar{x}_1$ and $\bar{x}_2$ are the means of first and second group, respectively. Taking 95% Confidence level and 95% Power.

Among type 2 diabetic patients 76% patients had MGD. Considering this at 95% confidence level and 10% of maximum error, the sample size is given by,

$$n = ((7.93)^2 + (10.60)^2)\frac{(1.96 + 1.645)^2}{(22.2 - 16.2)^2}$$

$$n = 63.1$$

Sample size at 10% attrition = 63.1 x 1.1= 69.4

sample size required is 70 in each group.

Hence the total sample size is 140

As sample size increases, accuracy of result also increases

Sampling technique: Convenient sampling.

Inclusion Criteria: Patients of either sex, aged above 40 years

Exclusion Criteria:

- Patients who have previously used systemic or topical eye medications, such as lubricants, beta blockers, diuretics, anticholinergics, antihistamines, or antidepressants, in recent past or present.
- Individuals who have experienced recent ocular surgery or trauma, blepharitis, an active ocular infection, lid deformities, active systemic autoimmune diseases known to affect the ocular surface, cranial nerve injury, or any other disease known to affect the tear film, as well as those who have a history or clinical evidence of these conditions.
- Smokers, those who have had LASIK surgery, and people who wear contact lenses.

Study protocol: Hospital based cross sectional study

Data collection procedure: Subjects attending ophthalmology outpatient department aged above 40 years. Subjects of the above age meeting the inclusion and exclusion criteria underwent routine eye examination and relevant investigations and were enrolled in the study.

Investigations or interventions to be conducted on patients

1. Schirmer's I test, using Schirmer's test strips.
2. Measurement of tear film breakup time (TBUT) using Fluorescein strips and topical anaesthesia, 1% proparacaine drops

3. Blink interval
4. Meibum expressibility
5. Meibum quality

Ethical clearance was obtained from the institutional ethical committee. Informed/written consent was taken after explaining in detail about the methods and procedures involved in the study in patients own vernacular language.

Upon the initial visit, demographic parameters such age, sex, occupation, and address were recorded on a pre-made proforma by the investigator.

A detailed clinical history including the history of diabetes, drug history for systemic illnesses and use of contact lenses was taken from the patients.

The patients eligible for the study were divided into two groups:

Group 1: Non-Diabetic individuals

Group 2: Diabetic individuals

To assess the symptoms of dry eye disease and meibomian gland dysfunction, Ocular surface disease index (OSDI) Questionnaire was used.

The OSDI Questionnaire has 3 subscales , ocular symptoms, vision related function and environmental triggers which assessed the following symptoms:

- Sensitivity to light
- Dryness/Grittiness

- Pain/sore eyes
- Blurring of vision
- Poor vision
- Limitation of performing daily activities
- Feeling uncomfortable in windy/low humidity/ air conditioned areas

Patients then rate their responses based on the frequency of the occurrence of symptoms over the last week from zero to four, with zero indicating “none of the time” and four indicating “all of the time”.

The OSDI produces a quantifiable score between 0 and 100, with higher numbers suggesting more severe disease.

Ocular examination:

- Best corrected visual acuity was noted using Snellen’s visual acuity chart.
- Anterior segment examination was done using slit lamp biomicroscope was which included examination of eyelids and adnexa, conjunctiva, cornea, anterior chamber, iris, pupils and lens.
- Posterior segment evaluation was done using indirect ophthalmoscopy.
- Nasolacrimal duct patency was judged by performing lacrimal sac syringing.

Following this, diagnostic tests, namely Schirmer’s test and Tear film break-up time (TBUT), Blink interval, ocular surface staining score(OSS) was done for evaluation of dry eye disease.

Schirmer’s Test:

Whatman No. 41 paper strips, measuring 5 x 35 mm, were used to carry out Schirmer's 1 test. The patient was made to sit with the fan turned off in a room. To avoid contamination from skin oils, the terminal end of the Schirmer's strip was folded at the designated region at a 90° angle without coming into direct contact with the paper. The lower eyelids were retracted, and the patient was instructed to look upward, the folded paper was placed at the junction of lower eyelid's medial two thirds and lateral one thirds . The patient was instructed to gently close their eyes in order to prevent the tear film from evaporating and to prevent reflex tear production, which can be brought on by blinking.

The amount of wetting was measured from the bent end till the wetted strip area in millimetres (mm).

Interpretation:

Measurement of more than 15 mm of wetting was considered to be normal.

10 mm – 15 mm : Mild dry eye

5 mm – 10 mm: Moderate dry eye

0 mm – 5 mm: Severe dry eye (krachmer)

Tear Film Break-up Time (TBUT)

When assessing the stability of the tear film and the rate of evaporation in evaporative dry eye illness, TBUT is a quantitative method that can be used. It is defined as the interval, measured in seconds, between the last blink and the onset of the first dry spot on the cornea's surface.

Under a slit lamp, the patient was seated. After taking a sterile fluoresceine strip, a drop of antibiotic solution was applied to the strip. After that, the lower palpebral conjunctiva was exposed to the moist fluoresceine portion of the strip, allowing the dye to stain the lower cul de sac. After removing the strip from the eye, the patient was instructed to blink in order to distribute the dye uniformly across the tear film. After instructing the patient to maintain a straight line of sight without blinking, the tear film was examined through the cobalt blue filter to identify the initial disruption in its continuity. This was shown by a black spot on the green background of the tear film. The tear film break up time was defined as the amount of time in seconds that passed between the last blink and the emergence of the first black spot.

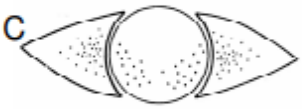
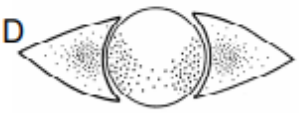
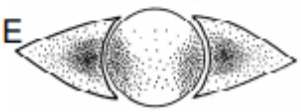
TBUT > 10 seconds = Normal tear film stability.

5 – 10 seconds = Marginal tear film stability.

< 5 seconds = Low tear film stability.

Oxford staining score-

Grading Scheme: On a set of panels (A-E), staining is depicted by punctate dots. Each panel's staining runs from 0 to 5, while the entire exposed cornea and inter-palpebral conjunctiva ranges from 0 to 15. A log scale is used to arrange the dots.

PANEL	GRADE	CRITERIA
A 	0	Equal to or less than panel A
B 	I	Equal to or less than panel B, greater than A
C 	II	Equal to or less than panel C, greater than B
D 	III	Equal to or less than panel D, greater than C
E 	IV	Equal to or less than panel E, greater than D
>E	V	Greater than panel E

Grading of dry eye: The final grading of DED was done taking into consideration of the Schirmer's I test results, TBUT results ,ocular surface staining score (OSSS) and the DEWS II report.

- Normal eyes was defined as patients who had Schirmer's I test value > 15mm and TBUT > 10 seconds, none to mild conjunctival and corneal staining (ocular surface staining score <2).
- Mild dry eye was defined as patients who had Schirmer I test value between 10 – 15 mm of wetting and TBUT of 10 seconds, mild to moderate conjunctival and corneal staining (ocular surface staining score less than or equal to 2).
- Moderate dry eye was defined as patients who had Schirmer I test value of 5 – 10 mm of wetting and TBUT of 5 – 10 seconds, moderate to severe conjunctival and corneal staining (ocular surface staining score 2-3).
- Severe dry eye was defined as patients who had Schirmer I test value of < 5 mm of wetting and TBUT of < 5 seconds. severe conjunctival and corneal staining (ocular surface staining score 3-4).

Meibum quality and expressibility, lid margin characteristics, conjunctival and corneal staining(oxford staining score), and meibum expressibility were all taken into account in the final grading of meibomian gland dysfunction.

Meibum Expressibility is assessed on a scale of 0 to 3 in five glands in the lower or upper lid, according to the number of glands expressible:

Scale 0 -all glands expressible,

Scale- 1 three to four glands expressible,

Scale-2 one to two glands expressible,

Scale-3 no glands expressible.

Meibum quality is assessed in each of eight glands of the central third of the lower lid on a scale of 0 to 3 for each gland:

Score 0-clear,

Score 1-cloudy,

Score 2- cloudy with debris (granular),

score 3- thick, like toothpaste,

(total score range, 0 –24).

Stage 1- No symptoms of ocular discomfort, itching, or photophobia,

Meibum quality: grade more than or equal to 2–4 expression

Expressibility: 1

No ocular surface staining

Stage 2 Minimal to mild symptoms of ocular discomfort, itching, or photophobia ,Minimal to mild MGD clinical signs Scattered lid margin features

Meibum quality -Mildly altered secretions: grade 4–8

Expressibility: 1

None to limited ocular surface staining:(Oxford grade 0–3)

Stage 3- Moderate lid margin features: plugging, vascularity

Meibum quality -Moderately altered secretions: grade 8 to 13 indicated

Meibum Expressibility: 2

Mild to moderate conjunctival and peripheral corneal staining, often inferior: Oxford grade 4–10

Stage 4 -Marked symptoms of ocular discomfort, itching or photophobia with definite limitation of activities, Severe MGD clinical signs- lid margin features: dropout, displacement

Meibum quality- Severely altered secretions: grade 13

Meibum Expressibility: 3

Increased conjunctival and corneal staining, including central staining: Oxford grade (11–15)

STATISTICAL ANALYSIS

Microsoft Excel and the statistical program R 4.2.0 were used to analyze the data. Frequencies and percentages were used to represent categorical variables. Constant variables are expressed in the form of Mean ± SD / Median (Min, Max). To investigate the relationship between categorical variables, the Chi-Square test was employed. The QQ plot and the Shapiro-Wilk test are used to determine whether a variable is normal.

The means and distributions of the variables were compared between the groups using the Two sample t test/Mann Whitney U test. The correlation between the variables was examined using Pearson's correlation test and Spearman's correlation test. A P-value of less than or equal to 0.05 denotes statistical significance

RESULTS

Present study included total of 140 participants fulfilling inclusion criteria and separated into two group based on history of diabetes mellitus. Group DM – with history of diabetes mellitus and group NDM – non-diabetic healthy participants.

Table 1: Comparison of mean age of patients between the groups

	Diabetes mellitus		Non-Diabetes Mellitus		p-value
	Mean	SD	Mean	SD	
AGE	57.5	10.1	57.1	12.6	0.819

The mean age of participants between the group was comparable with no significant difference.

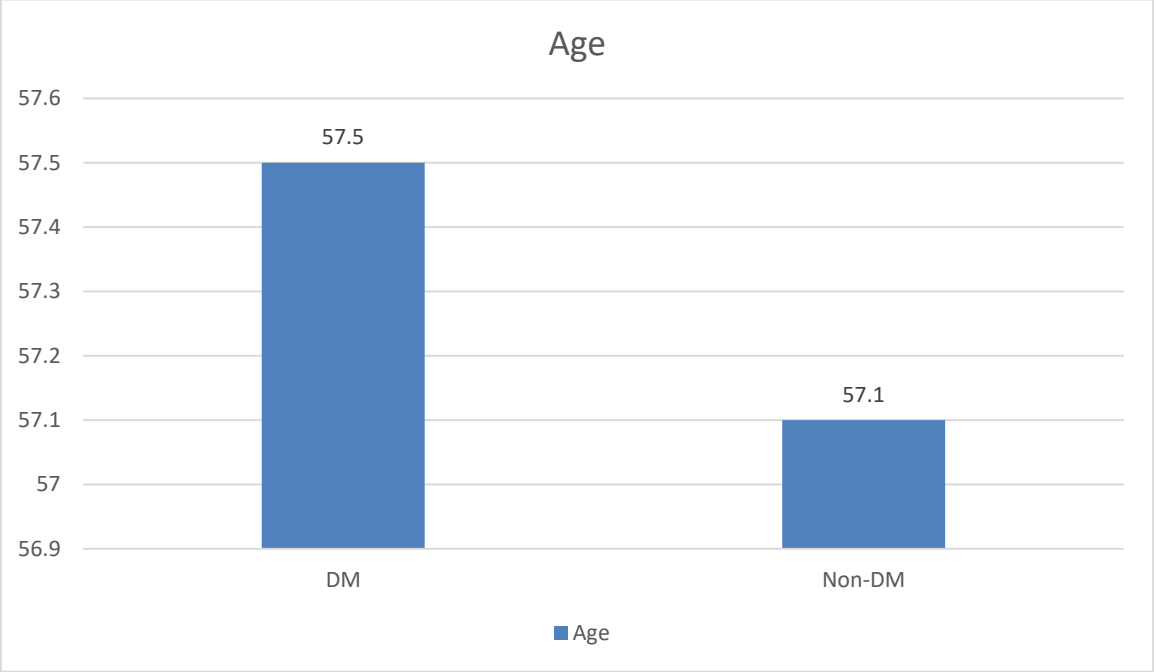


Figure 11: Comparison of mean age of patients between the groups

Table 2: Comparison of gender distribution between the groups

		Diabetes mellitus		Non-Diabetes Mellitus		Chi-square (p-value)
		Count	N %	Count	N %	
Gender	Female	38	54.3%	29	41.4%	4.2 (0.12)
	Male	32	45.7%	41	58.6%	

Among the gender distribution, there is no significant difference in male and female distribution between the group. However there is marginal male preponderance.

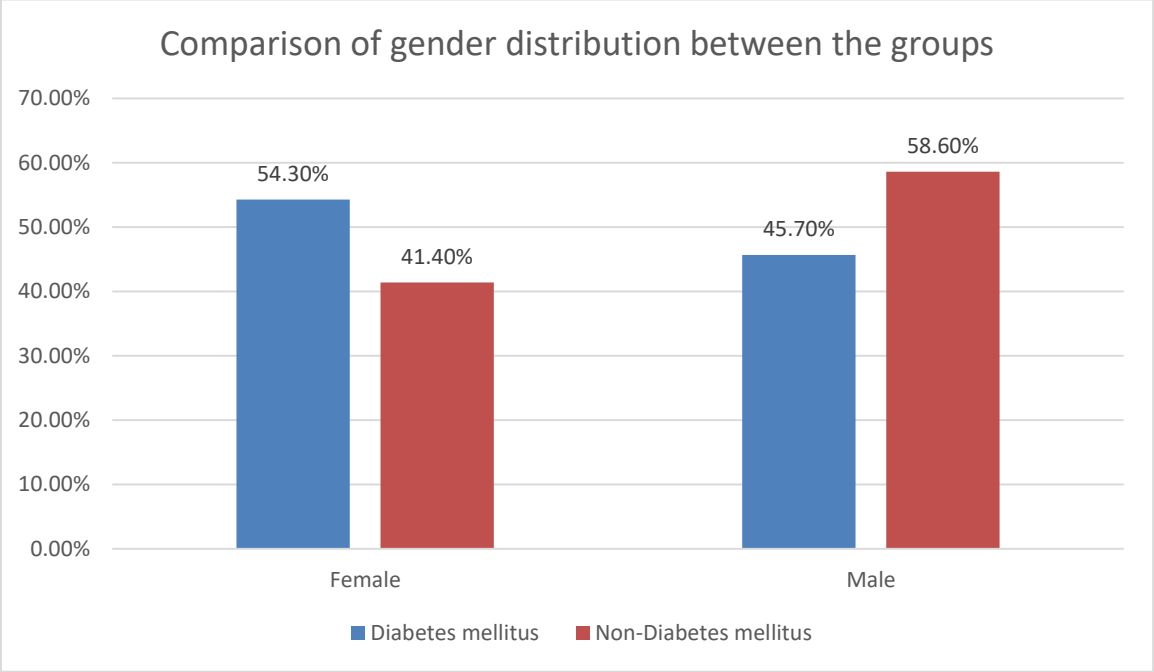


Figure 12: Comparison of gender distribution between the groups

Table 3: Comparison of the occupation of patients between the groups

		Diabetes mellitus		Non-Diabetes Mellitus		Chi-square (p-value)
		Count	N %	Count	N %	
Occupation	Unemployed	2	2.9%	6	8.6%	29.23 (0.02)*
	Analyst	0	0.0%	1	1.4%	
	Bank employee	1	1.4%	0	0.0%	
	Banker	1	1.4%	1	1.4%	

	Businessman	0	0.0%	1	1.4%	
	Driver	2	2.9%	0	0.0%	
	Employee	18	25.7%	25	35.7%	
	Farmer	1	1.4%	7	10.0%	
	Housewife	20	28.6%	18	25.7%	
	Librarian	0	0.0%	1	1.4%	
	Maid	1	1.4%	0	0.0%	
	Retired	13	18.6%	5	7.1%	
	Shopkeeper	1	1.4%	1	1.4%	
	Tailor	2	2.9%	1	1.4%	
	Teacher	8	11.4%	2	2.9%	
	Watchmaker	0	0.0%	1	1.4%	

By occupation, participants in both the groups were comparable with no significant difference noted.

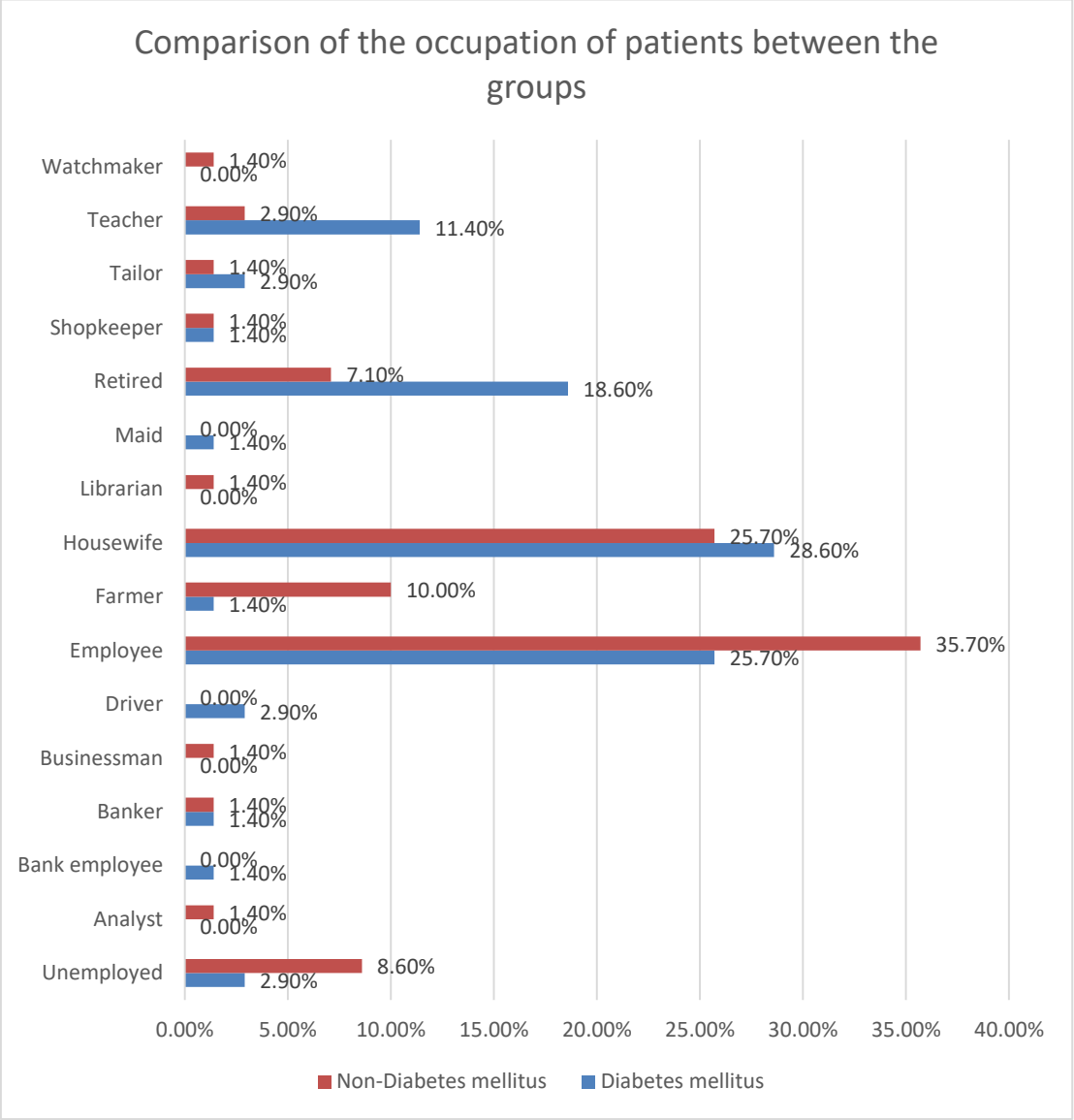


Figure 13: Comparison of the occupation of patients between the groups

Table 4: Comparison of symptoms of eye between the groups

	Diabetes mellitus		Non-Diabetes Mellitus		Chi-square (p-value)
	Count	N %	Count	N %	

Blurring of vision	No	22	31.4%	36	51.4%	5.7 (0.01)*
	Yes	48	68.6%	34	48.6%	
Sensitivity to light	No	49	70.0%	57	81.4%	2.48 (0.115)
	Yes	21	30.0%	13	18.6%	
Grittiness	No	45	64.3%	53	75.7%	2.177(0.140)
	Yes	25	35.7%	17	24.3%	
Pain	No	40	57.1%	62	88.6%	17.48 (0.01)*
	Yes	30	42.9%	8	11.4%	

There is significant higher incidence of blurring of vision in diabetic patients (68.6%) compared to non diabetic (48.6%).($p<0.05$) also there is significant higher incidence of pain among diabetic patients (42.9%)compared to non-diabetics (11.4%).($p<0.05$) there is no significant difference in the sensitivity to light and grittiness between the groups, however the incidence of both were higher among diabetic patients compared to non-diabetic individuals.

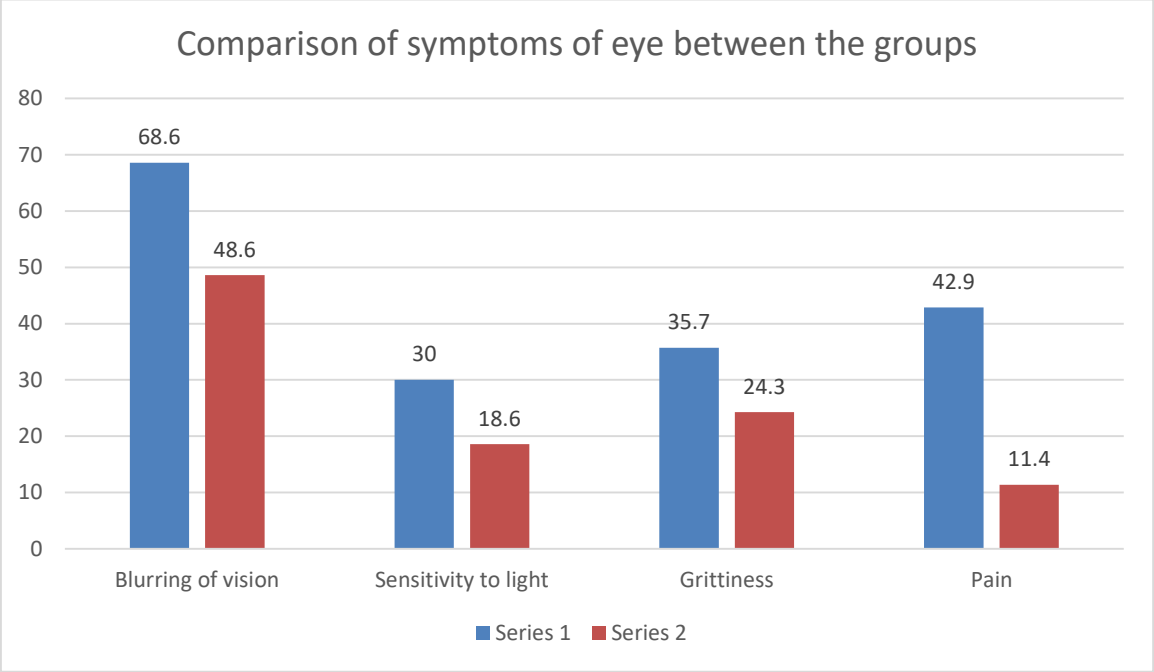


Figure 14: Comparison of symptoms of eye between the groups

Table 5: Comparison of best corrected visual acuity between the groups

		Diabetes mellitus		Non-Diabetes Mellitus		Chi-square (p-value)
		Count	N %	Count	N %	
BCVA OD	6\6	1	1.4%	8	11.4%	29.03 (0.016)*
	6\9	4	5.7%	12	17.1%	
	6\12	10	14.3%	13	18.6%	

	6\18	9	12.9%	13	18.6%	
	6\24	8	11.4%	3	4.3%	
	6\36	7	10.0%	3	4.3%	
	6\60	14	20.0%	3	4.3%	
	CF 0.5M	1	1.4%	0	0.0%	
	CF 0.5MT	1	1.4%	1	1.4%	
	CF 1M	4	5.7%	3	4.3%	
	CF 1MT	1	1.4%	2	2.9%	
	CF 2M	3	4.3%	1	1.4%	
	CF 3M	6	8.6%	3	4.3%	
	CF 3MT	0	0.0%	3	4.3%	
	CF1MT	1	1.4%	1	1.4%	
	CFCF	0	0.0%	1	1.4%	
BCVA_OS	6\6	0	0.0%	8	11.4%	32.02 (0.01)*
	6\9	10	14.3%	15	21.4%	
	6\12	7	10.0%	12	17.1%	

	6\18	7	10.0%	9	12.9%	
	6\24	7	10.0%	4	5.7%	
	6\36	13	18.6%	3	4.3%	
	6\60	11	15.7%	4	5.7%	
	CF 1.5 MT	0	0.0%	3	4.3%	
	CF 1M	2	2.9%	0	0.0%	
	CF 1MT	1	1.4%	1	1.4%	
	CF 2M	5	7.1%	4	5.7%	
	CF 2MT	1	1.4%	1	1.4%	
	CF 3M	6	8.6%	2	2.9%	
	CF 3MT	0	0.0%	3	4.3%	

There is significant difference in best corrected visual acuity between the group, with poor visual acuity among the patients with diabetes mellitus compared to the participants in non-diabetic group in both eyes.($p<0.05$)

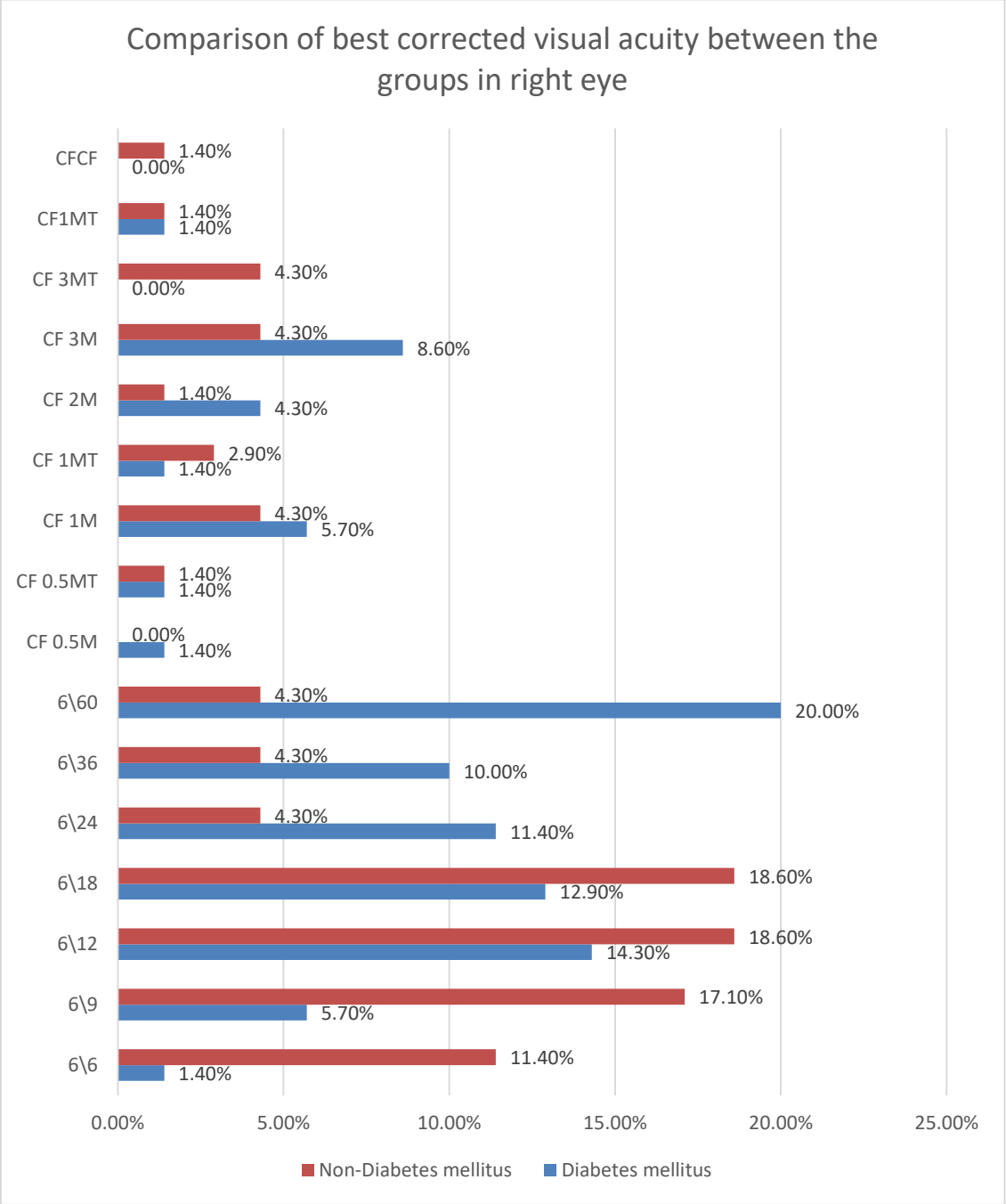


Figure 15: Comparison of best corrected visual acuity between the groups in right eye

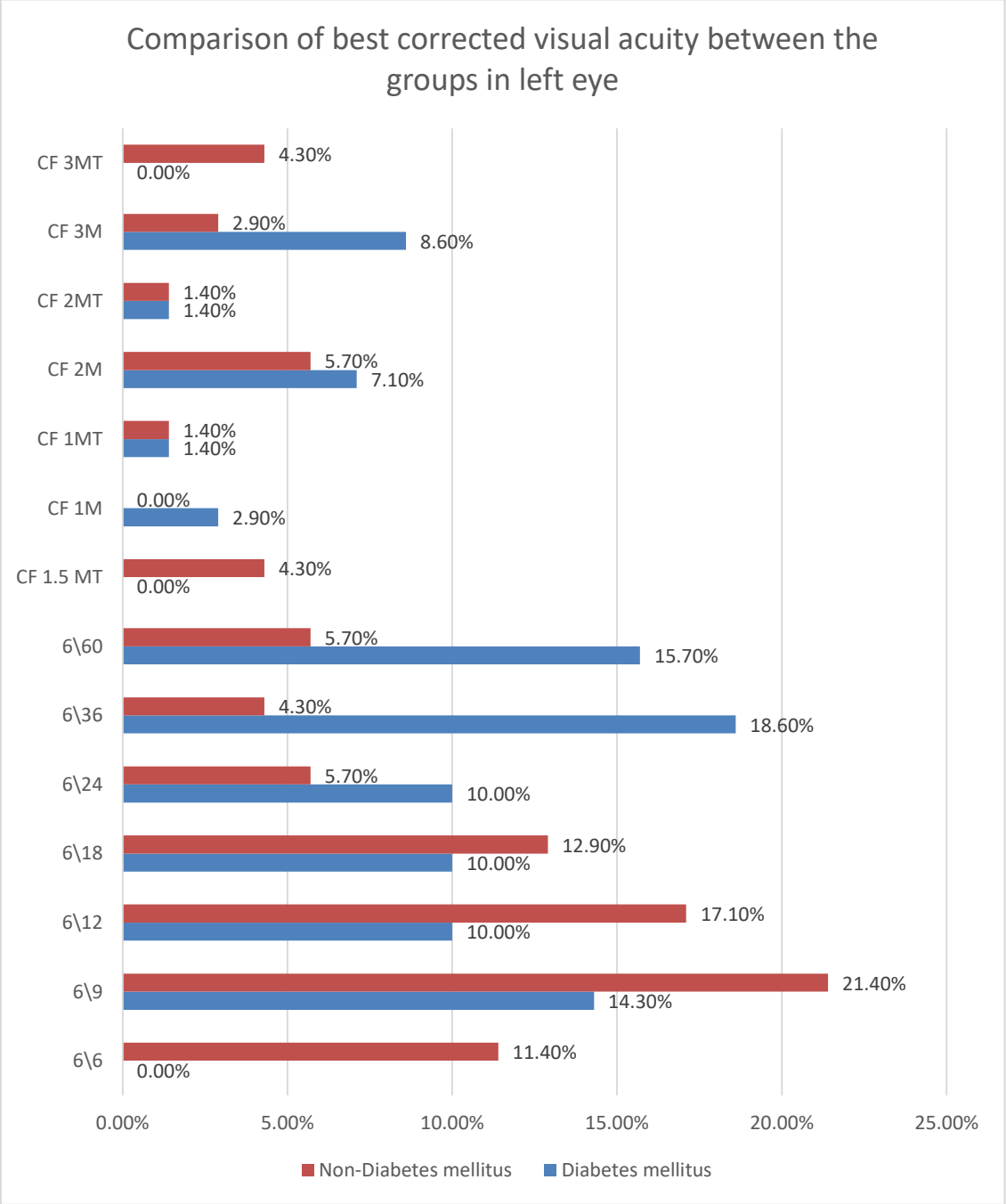


Figure 16: Comparison of best corrected visual acuity between the groups in left eye

Table 6: Comparison of the anterior segment findings between the groups

	Diabetes	Non-Diabetes	Chi-

		mellitus		Mellitus		square
		Count	N %	Count	N %	(p-value)
Anterior segment OD	Clear	0	0.0%	2	2.9%	29.16 (0.3)
	Grade 1 NS	13	18.6%	13	18.6%	
	Grade 1 NS + CC	0	0.0%	1	1.4%	
	Grade 1 NS + PSC	0	0.0%	2	2.9%	
	Grade 2 NS	12	17.1%	10	14.3%	
	Grade 2 NS + CC	3	4.3%	0	0.0%	
	Grade 2 NS + PSC	6	8.6%	3	4.3%	
	Grade 3 NS	6	8.6%	8	11.4%	
	Grade 3 NS + PSC	2	2.9%	2	2.9%	
	Grade 4 NS	2	2.9%	2	2.9%	

	LID MARGINS INFLAMED	1	1.4%	2	2.9%	
	Mature Cataract	0	0.0%	1	1.4%	
	MG cyst	0	0.0%	1	1.4%	
	Mild PSC	6	8.6%	7	10.0%	
	Normal	1	1.4%	9	12.9%	
	Pouting of MG orifice	0	0.0%	2	2.9%	
	PSC	12	17.1%	5	7.1%	
	Pseudophakia	6	8.6%	0	0.0%	
Anteriorsegment_OS	Clear	0	0.0%	2	2.9%	26.94 (0.137)
	Grade 1 NS	0	0.0%	1	1.4%	
	Grade 1 NS	8	11.4%	9	12.9%	
	Grade 1 NS + CC	0	0.0%	1	1.4%	

	Grade 1 NS + CC	3	4.3%	1	1.4%	
	Grade 2 NS	12	17.1%	8	11.4%	
	Grade 2 NS + CC	1	1.4%	0	0.0%	
	Grade 2 NS + PSC	6	8.6%	3	4.3%	
	Grade 3 NS	6	8.6%	6	8.6%	
	Grade 3 NS + PSC	4	5.7%	5	7.1%	
	Grade 4 NS + PSC	0	0.0%	2	2.9%	
	Lid Margins Inflamed	1	1.4%	2	2.9%	
	MG cyst	0	0.0%	1	1.4%	
	Mild CC	1	1.4%	0	0.0%	
	Mild PSC	8	11.4%	9	12.9%	
	Normal	3	4.3%	9	12.9%	

	Pouting of mg orifice	0	0.0%	2	2.9%	
	PSC	13	18.6%	6	8.6%	
	PSC+CC	0	0.0%	1	1.4%	
	Pseudophakia	4	5.7%	2	2.9%	

On assessment of the anterior segment of both the eye, there is no significant difference noted between the groups.

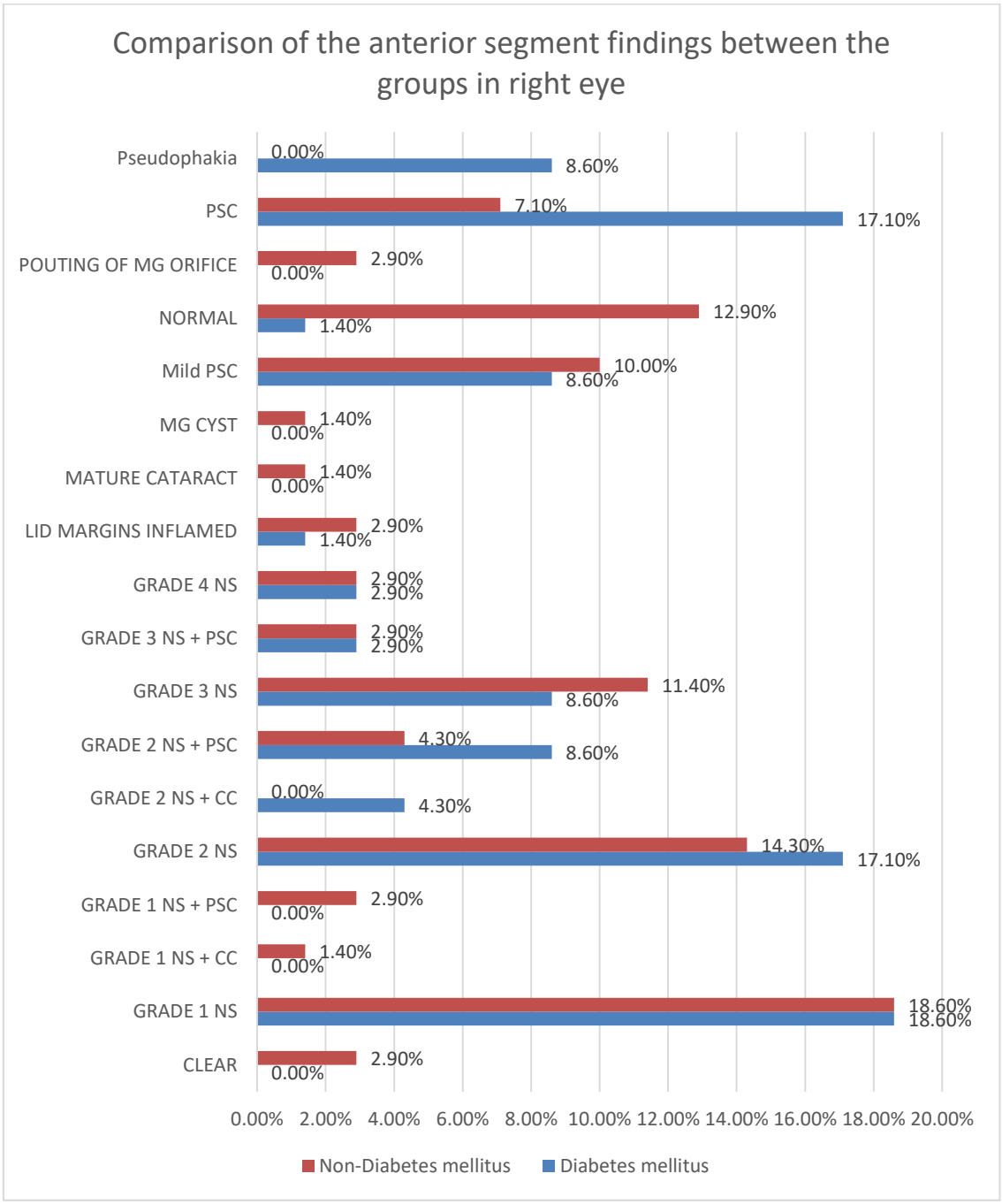


Figure 17: Comparison of the anterior segment findings between the groups in right eye

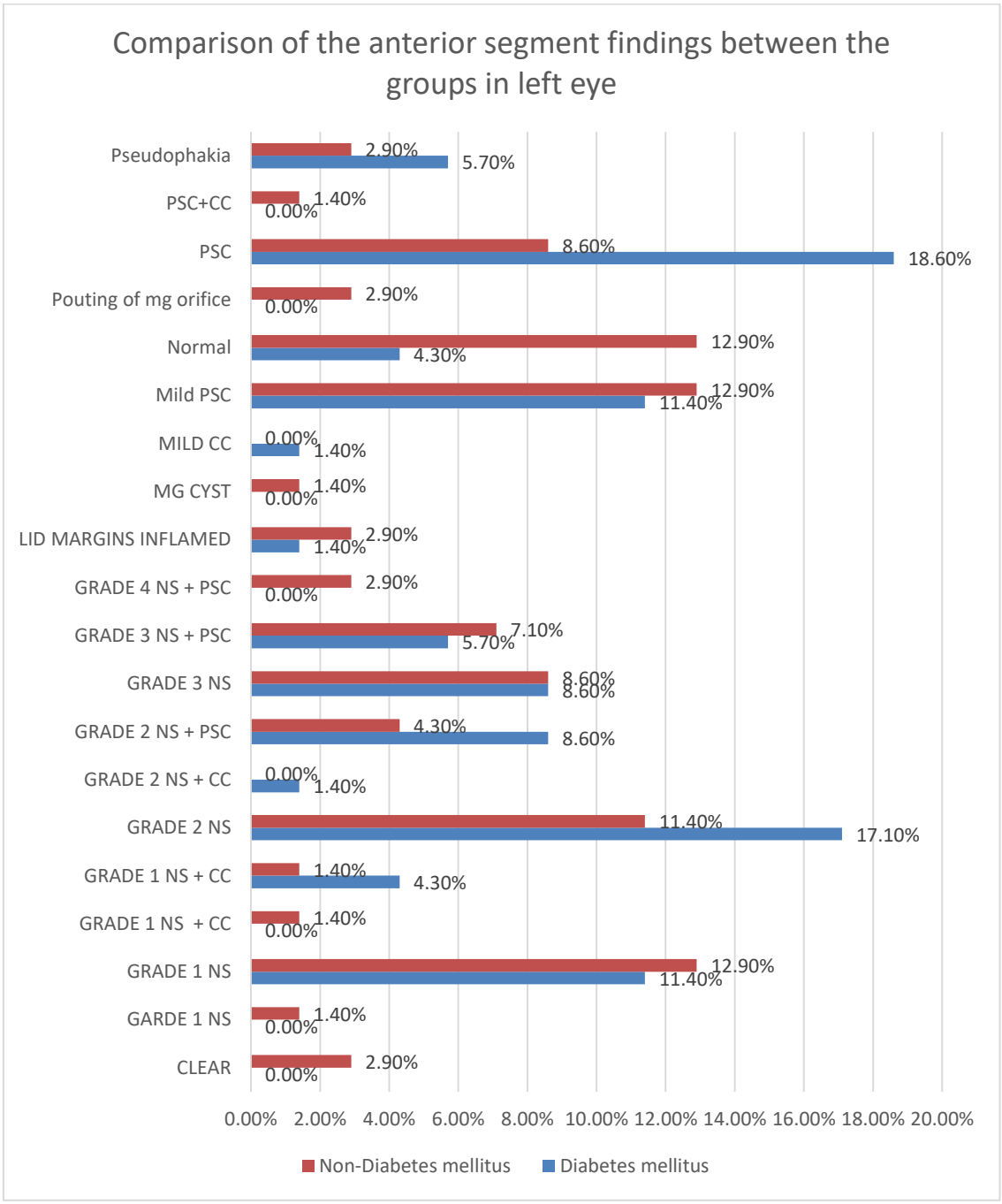


Figure 18: Comparison of the anterior segment findings between the groups in left eye

Table 7: Comparison of the mean OSDI score between the groups

	Diabetes mellitus		Non-Diabetes Mellitus		p-value
	Mean	SD	Mean	SD	
OSDI	14.7	10.2	8.4	10.5	0.01*

On comparison of the mean score of OSDI, there is significant higher mean score among the diabetic patients compared to non-diabetic individuals. ($p<0.05$)

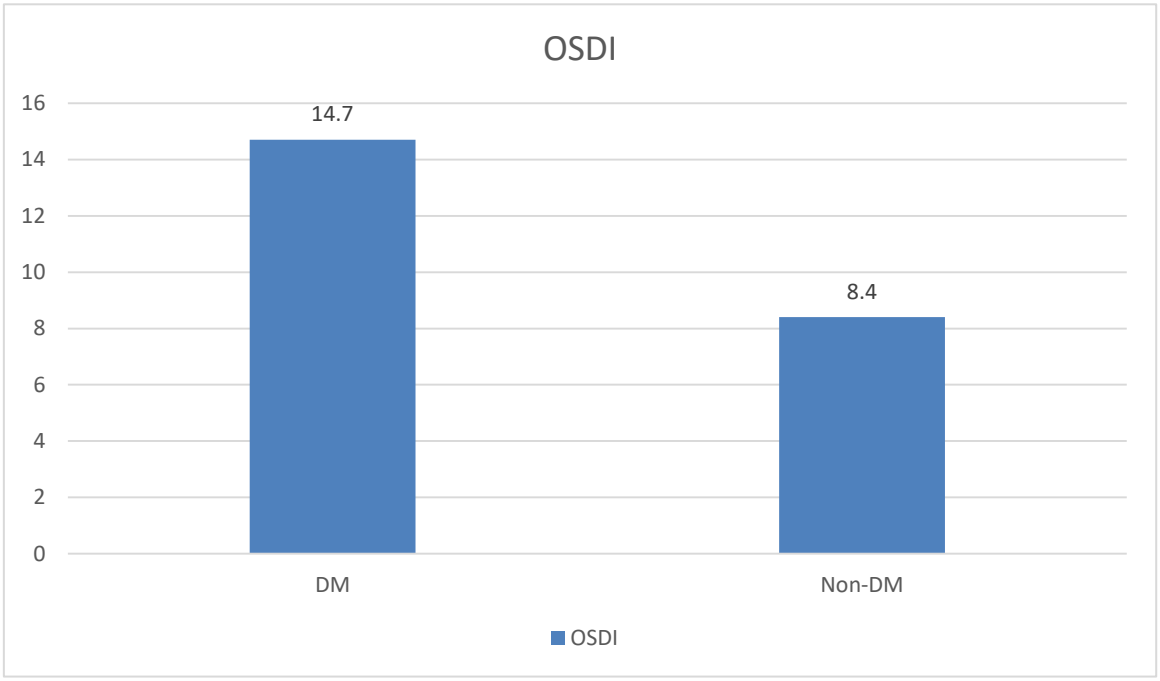


Figure 19: Comparison of the mean OSDI score between the groups

Table 8: Comparison of the Schirmer's test result between the groups

	Diabetes mellitus		Non-Diabetes Mellitus		p-value
	Mean	SD	Mean	SD	
Schirmer’s Test OD	10.6	4.8	18.0	6.5	0.01*
Schirmer’s Test OS	11.0	5.1	18.8	7.4	0.01*

On assessment of schirmer’s test there is significant lower mean level among diabetic patients compared to the non-diabetic individuals.

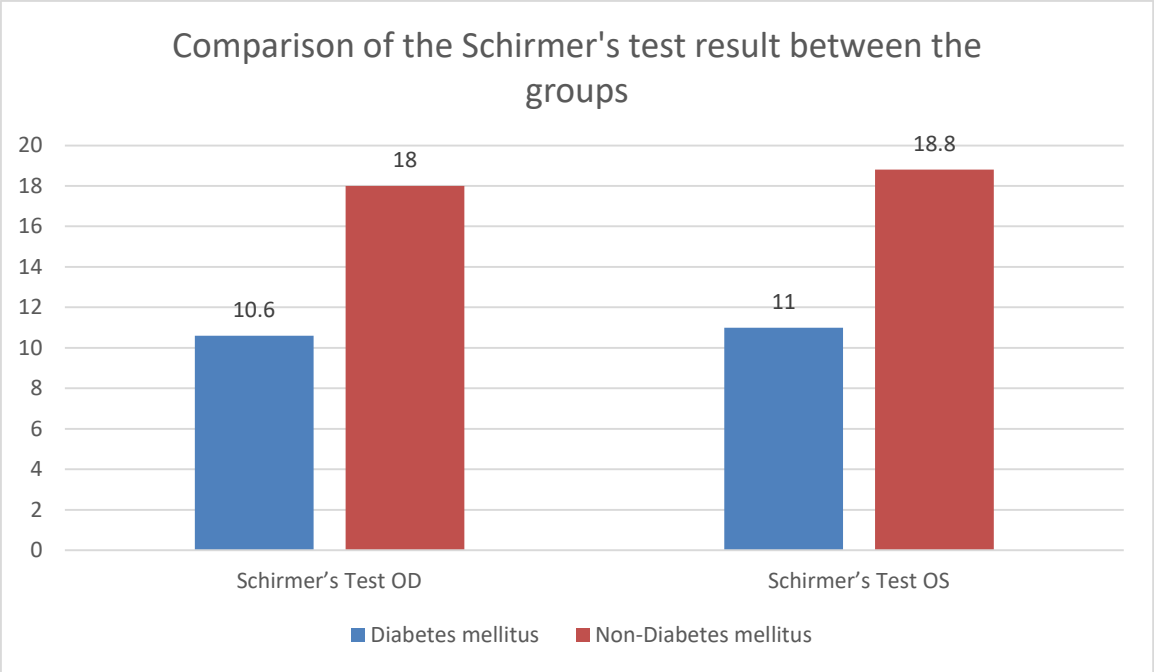


Figure 20: Comparison of the Schirmer's test result between the groups

Table 9: Comparison mean level of TBUT between the groups

	Diabetes mellitus		Non-Diabetes Mellitus		p-value
	Mean	SD	Mean	SD	
TBUT OD	10.0	4.1	9.5	2.7	0.39
TBUT OS	10.1	4.2	9.0	1.7	0.34

On assessment of TBUT score, there is no significant difference in the mean level between the groups.

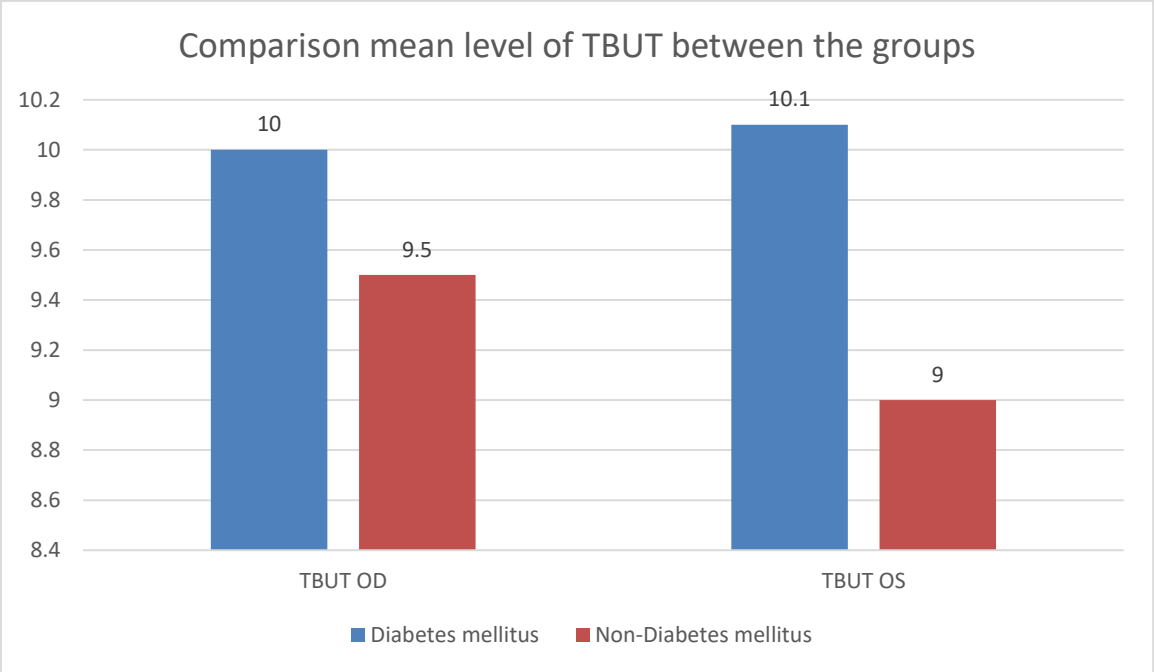


Figure 21: Comparison mean level of TBUT between the groups

Table 10: Comparison of the blink interval between the groups.

	Diabetes mellitus		Non-Diabetes Mellitus		p-value
	Mean	SD	Mean	SD	
Blink Interval OD	8.6	1.7	9.1	2.7	0.56
Blink Interval OS	8.9	2.8	9.1	2.7	0.669

There is no significant difference in the mean blink interval among the patients between the groups.

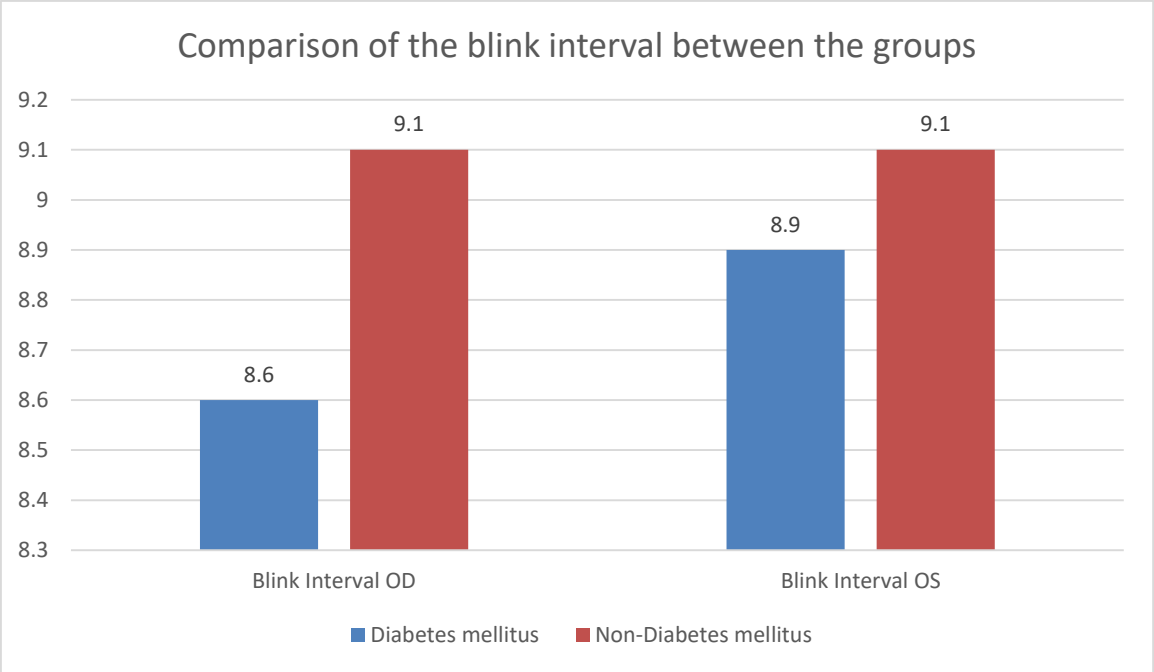


Figure 22: Comparison of the blink interval between the groups

Table 11: Comparison of the oxford staining score between the groups

	Diabetes mellitus		Non-Diabetes Mellitus		p-value
	Mean	SD	Mean	SD	
Oxford staining score OD	2.9	3.6	3.4	3.2	0.554
Oxford staining score OS	3.1	3.5	3.5	3.3	0.570

There is no significant difference in the Oxford staining score between the groups, however the mean level of staining score was lower in diabetic patients compared to non-diabetic individuals.($p>0.05$)

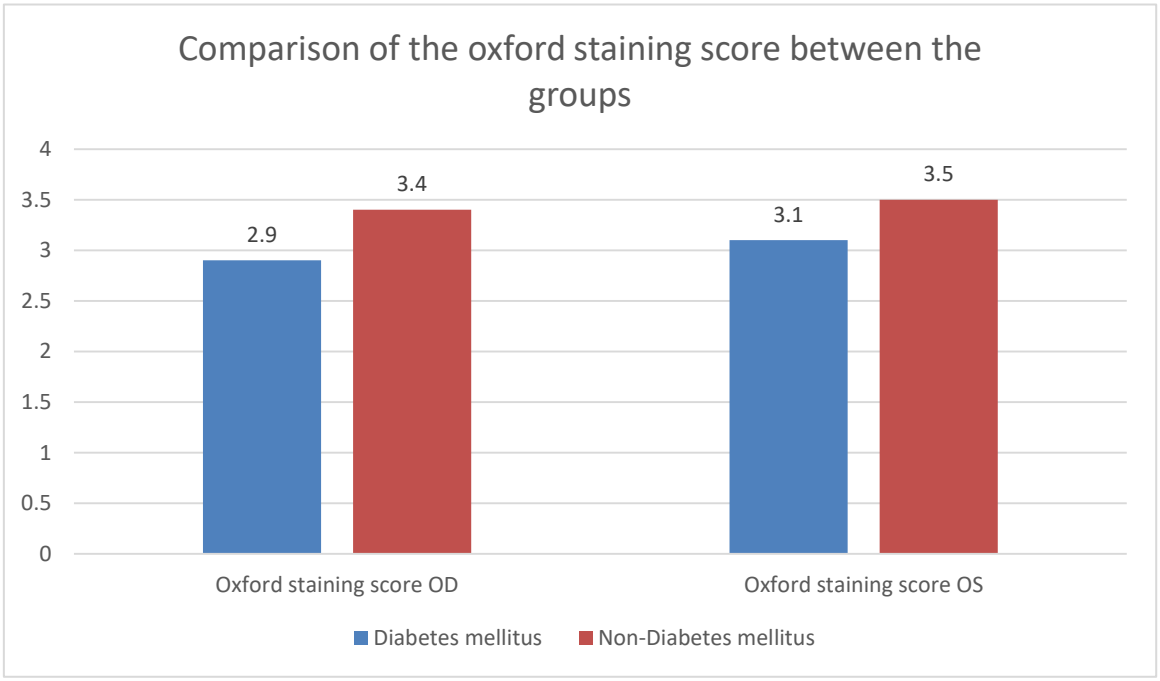


Figure 23: Comparison of the oxford staining score between the groups

Table 12: Comparison of the Meibum expressibility scale between the groups

		Diabetes mellitus		Non-Diabetes Mellitus		Chi-square (p-value)
		Count	N %	Count	N %	
Meibum Expressibility Scale OD	.0	53	75.7%	55	78.6%	1.069 (0.58)
	1.0	16	22.9%	15	21.4%	
	2.0	1	1.4%	0	0.0%	
Meibum Expressibility Scale OS	.0	53	75.7%	56	80.0%	1.21 (0.544)
	1.0	16	22.9%	14	20.0%	
	2.0	1	1.4%	0	0.0%	

In study, there is no significant difference in meibum expressibility scale score between the group in both eye.

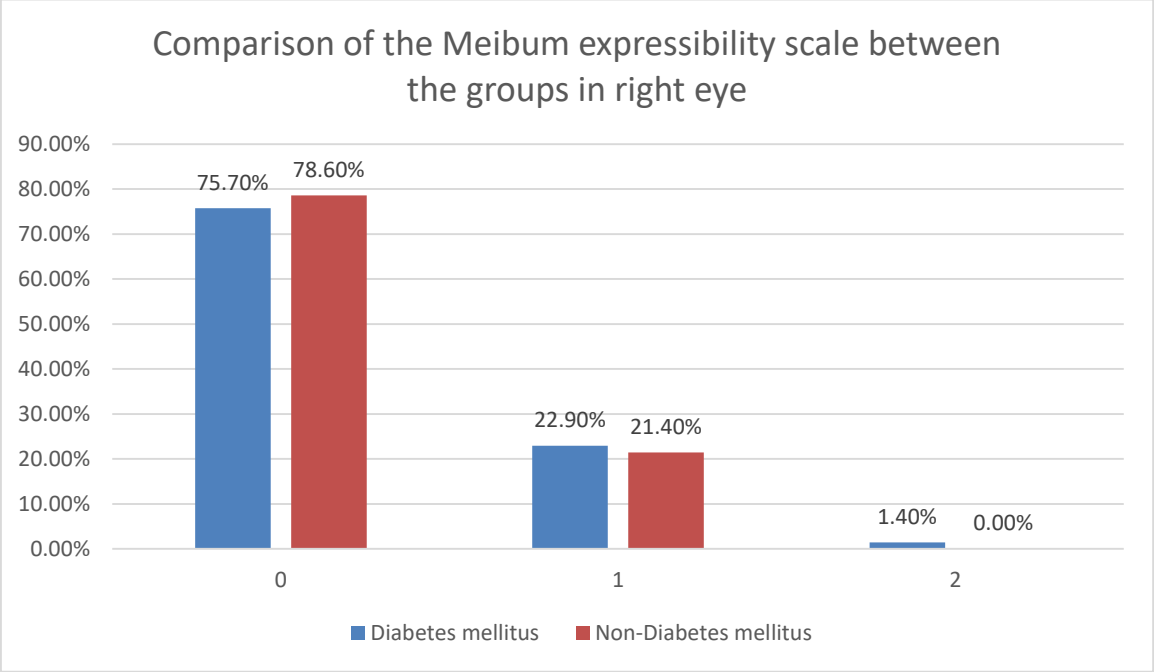


Figure 24: Comparison of the Meibum expressibility scale between the groups in right eye

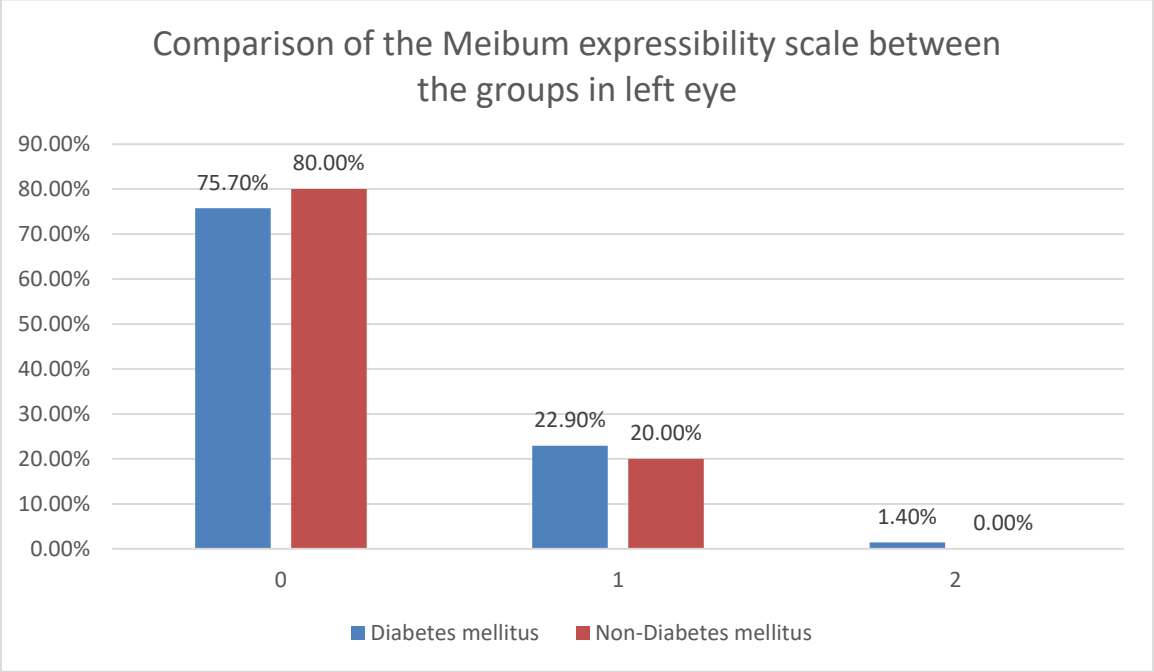


Figure 25: Comparison of the Meibum expressibility scale between the groups in left eye

Table 13: Comparison of the meibum quality score between the groups

	Diabetes mellitus		Non-Diabetes Mellitus		p-value
	Mean	SD	Mean	SD	
Meibum Quality Score OD	2.5	3.7	2.5	4.2	0.966
Meibum Quality Score OS	2.5	3.7	2.5	4.2	0.992

There is no significant difference in meibum quality score between the groups.

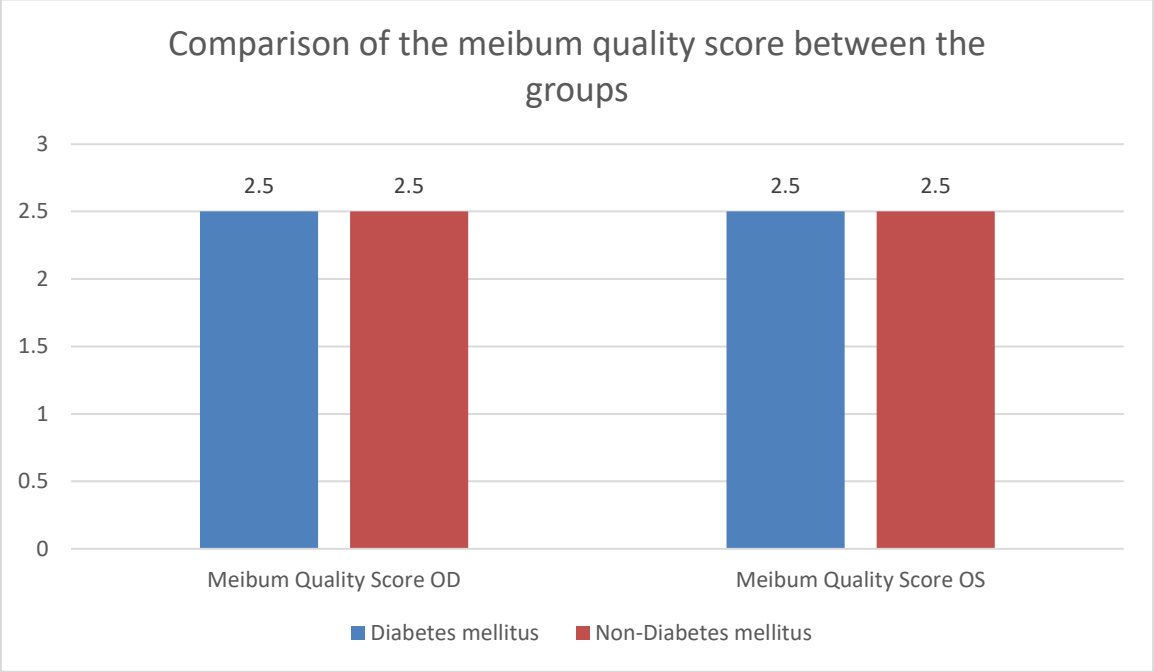


Figure 26: Comparison of the meibum quality score between the groups

Table 14: Comparison of the dry eye severity between the groups

		Diabetes mellitus		Non-Diabetes Mellitus		Chi-square (p-value)
		Count	N %	Count	N %	
Dry Eye Severity OD	Nil	33	47.1%	39	55.7%	5.38 (0.01*)
	Mild	11	15.7%	17	24.3%	
	Moderate	24	34.3%	13	18.6%	
	Severe	2	2.9%	1	1.4%	

Dry Eye Severity OS	Nil	33	47.1%	39	55.7%	5.38 (0.01)*
	Mild	11	15.7%	17	24.3%	
	Moderate	24	34.3%	13	18.6%	
	Severe	2	2.9%	1	1.4%	

There is significant higher incidence of the dry eye severity grade of moderate and severe among the patients with diabetes mellitus compared to non-diabetic individuals. ($p<0.05$)

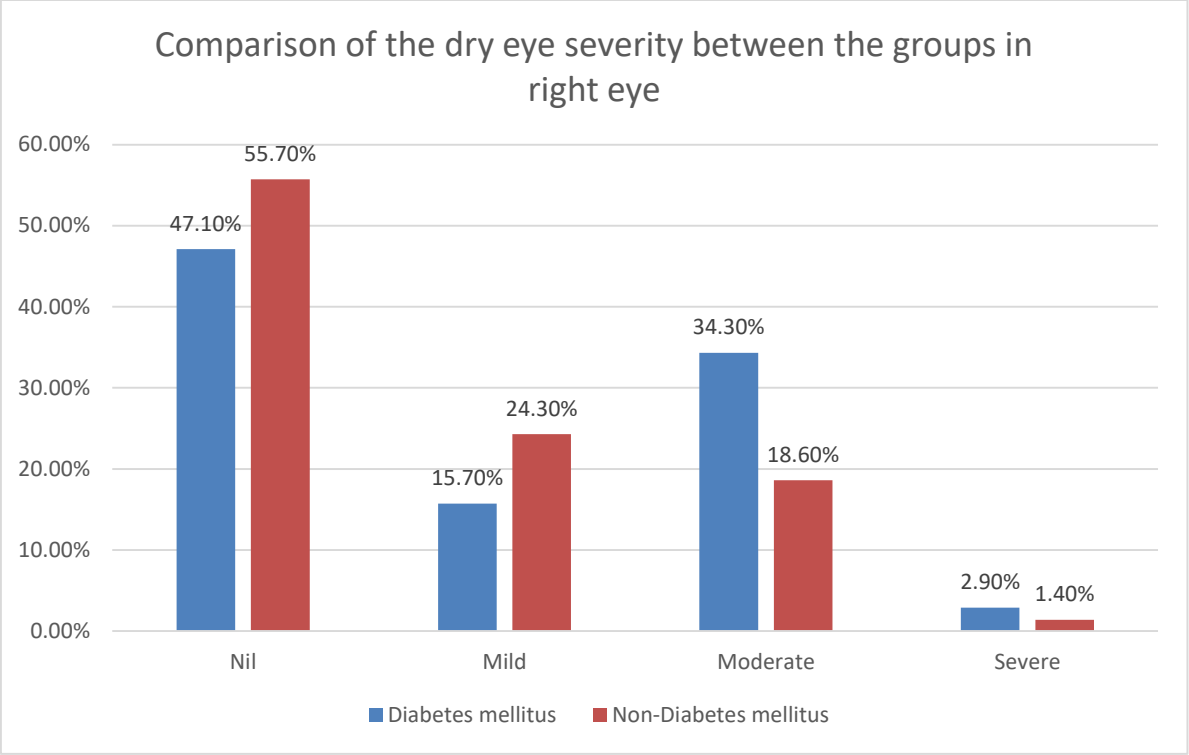


Figure 27: Comparison of the dry eye severity between the groups in right eye

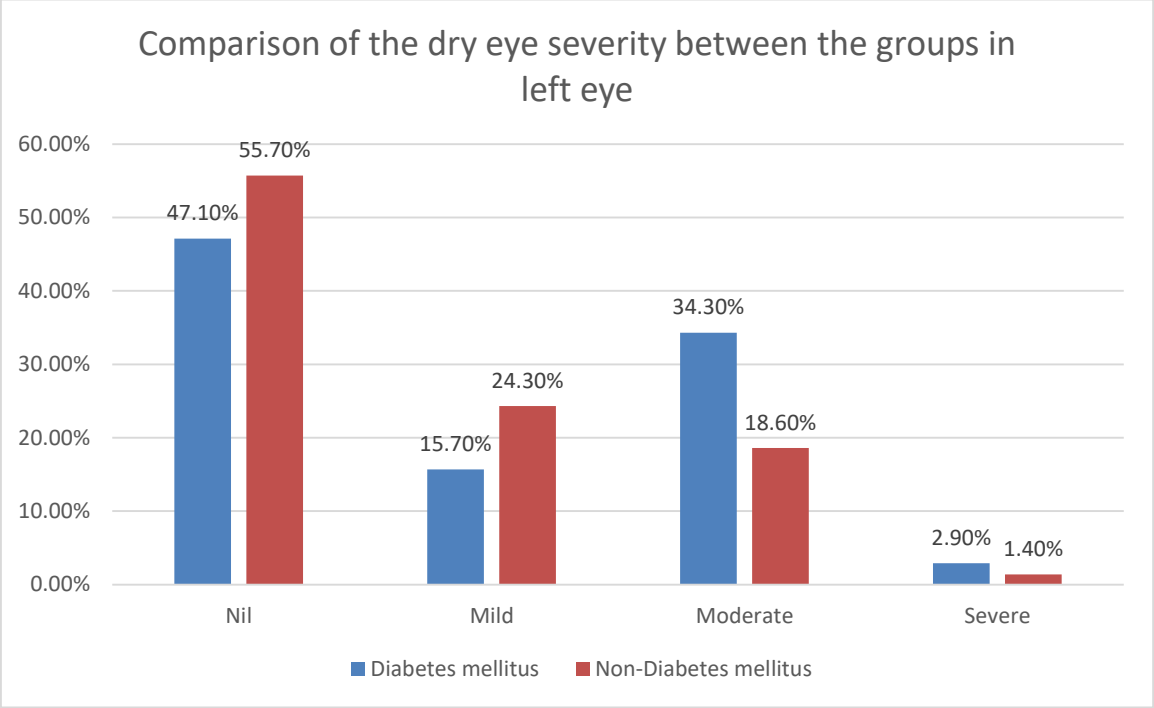


Figure 28: Comparison of the dry eye severity between the groups in left eye

Table 15: Comparison of the Meibomian gland dysfunction stage between the groups

	Diabetes mellitus		Non-Diabetes Mellitus		p-value
	Mean	SD	Mean	SD	
Meibomian Gland Dysfunction Stage OD	2.2	1.0	1.8	1.1	0.082
Meibomian Gland Dysfunction Stage OS	2.2	1.0	1.6	1.2	0.064

There is higher mean stage of the meibomian gland dysfunction in patients with diabetes mellitus compared to the patients with non-diabetics.

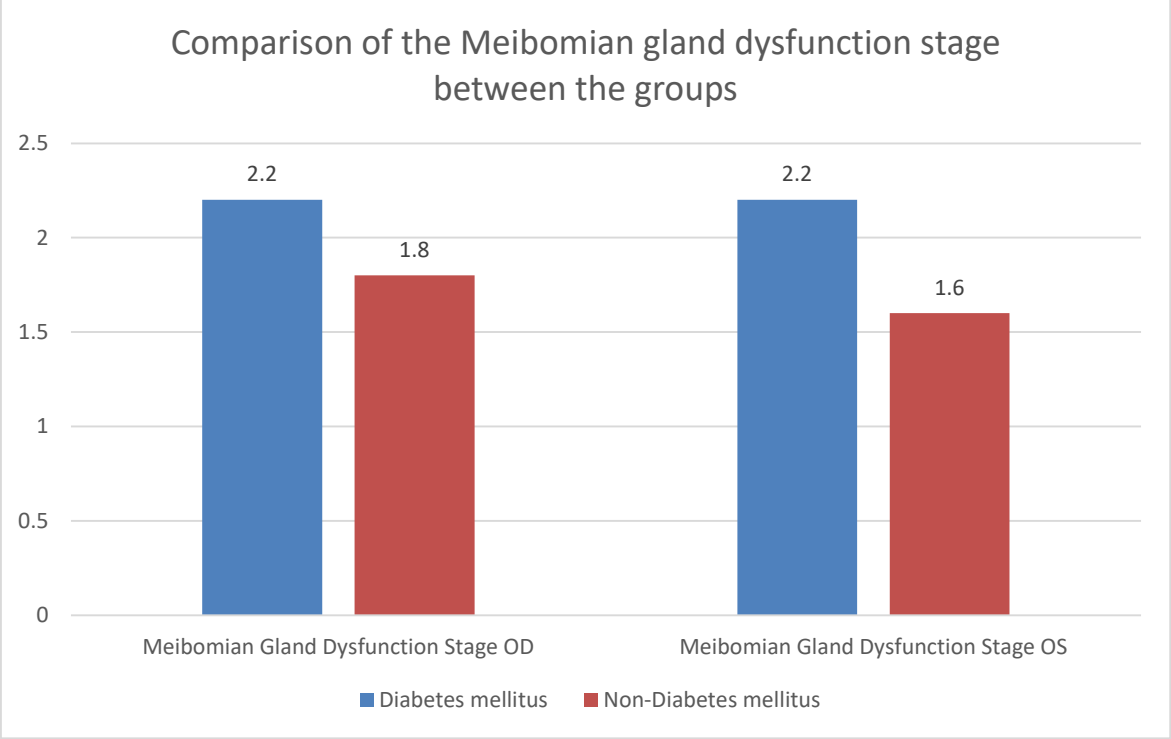


Figure 29: Comparison of the Meibomian gland dysfunction stage between the groups

DISCUSSION

“Dry eye disease (DED) and meibomian gland dysfunction (MGD) are prevalent and often debilitating conditions affecting the ocular surface and tear film stability, characterized by symptoms such as discomfort, visual disturbance, and tear film instability, DED can significantly impair quality of life. MGD, a leading cause of evaporative dry eye, involves the dysfunction of the meibomian glands, which are responsible for secreting lipids that prevent tear evaporation. Understanding the factors that exacerbate these conditions is crucial for developing effective treatment strategies.”

“Diabetes mellitus (DM) is a chronic metabolic disorder that affects millions worldwide and is associated with various ocular complications, including diabetic retinopathy and cataracts. Emerging evidence suggests that DM may also be a significant risk factor for DED and MGD. The metabolic and inflammatory changes associated with diabetes can potentially disrupt the homeostasis of the ocular surface and meibomian gland function, leading to increased severity of these conditions. However, the precise relationship between DM and the severity of DED and MGD remains inadequately explored.”

“Several studies have highlighted the potential impact of diabetes on the ocular surface. Hyperglycemia can lead to microvascular damage and neuropathy, affecting the lacrimal gland's function and reducing tear production. Additionally, diabetes-induced oxidative stress and inflammation can further exacerbate ocular surface damage and meibomian gland dysfunction. Despite these insights, there is a need for more comprehensive research to compare the severity of DED and MGD between diabetic and non-diabetic populations systematically.”

The present study compared the severity of dry eye and meibomian gland dysfunction (MGD) between diabetic (DM) and non-diabetic (NDM) participants, encompassing a total of 140 individuals. The mean age and gender distribution between the groups were comparable, with a slight male predominance observed. Occupational backgrounds also showed no significant differences.

In study by Johanna S et al., the mean age of the patients was 59.8yrs. [68] In study by Manjula et al., majority of patients were in age group of 50-60yrs with male preponderance in their study. [69] In line another study by Shamsheer et al., found the mean age of patients was 52.6yrs with comparable mean age difference between the groups and also the male preponderance was seen in overall study participants.[76] In study by Aljarousha M et al., documented mean age of 52yrs with comparable between the group. also the male preponderance in the study with similar distribution between the groups.[77]

Present study findings indicate that diabetic patients exhibit a significantly higher incidence of blurred vision (68.6%) and ocular pain (42.9%) compared to non-diabetic participants (48.6% and 11.4%, respectively), with both symptoms demonstrating statistical significance ($p<0.05$). Although the sensitivity to light and grittiness were more common among diabetics, these differences were not statistically significant. Notably, diabetics showed poorer best corrected visual acuity in both eyes ($p<0.05$).

In concordance study by Aljarousha M et al., documented higher prevalence of the more than one dry eye symptoms among the diabetes mellitus participants compared to the non-diabetic participants.[77]

There is significant difference in best corrected visual acuity between the group, with poor visual acuity among the patients with diabetes mellitus compared to the participants in non-diabetic group in both eyes.($p<0.05$) Evaluations of the anterior segment of the eye revealed no significant differences between the groups. However, the mean Ocular Surface Disease Index (OSDI) score was significantly higher in diabetics ($p<0.05$), indicating more severe dry eye symptoms.

In line to present study findings, study by Jurangal A et al., documented the poor visual acuity among the patients with diabetes mellitus compared to the non-diabetic individual and the findings were statistically significant. [78] Another study by Sood R et al., documented that the maximum number of diabetic patients had best corrected visual acuity of 6/12 and in non-diabetic group it was 6/9, and these findings were statistically significant. [79]

In concordance to present study Johanna S et al., documented significant higher mean level of OSDI score among diabetic patients compared to controls. [68] Another study by Wu H et al., documented that HbA1c levels were linked with OSDI, BUT, LLT, FL, and MGD characteristics. Asymptomatic MGD may be an early indicator of T2D dry eye and ocular pain. MGD characteristics were linked to HbA1c levels and diabetes duration. [73]

In present study, Schirmer's test results were also significantly lower among diabetics, suggesting reduced tear production ($p<0.05$). Conversely, the Tear Break-Up Time (TBUT) score and blink interval did not differ significantly between groups. Oxford staining scores, although not significantly different, were lower in diabetics. Meibum expressibility and quality scores were also comparable between the groups. Nevertheless, diabetic patients

exhibited a higher incidence of moderate to severe dry eye severity grades and a greater mean stage of meibomian gland dysfunction compared to non-diabetics ($p<0.05$).

In study by Aljarousha M et al., documented significant lower mean TBUT score and TMH score among the diabetic patients compared to non-diabetic individuals. [77] In study by Mangoli M et al., documented Mean value of Schirmer's II test was 11.61 ± 5.69 mm in diabetic patients and 17.89 ± 7.07 mm in non-diabetic patients. Based on TBUT measurements, 8.5% of diabetics and 3% of non-diabetics exhibited low tear film stability. Marginal tear film stability was observed in 42% of diabetics and 10.5% of non-diabetics. In contrast, 49.5% of diabetics and 86.25% of non-diabetics showed normal tear film stability. The mean TBUT values were 12.43 ± 5.32 seconds for diabetic patients and 16.46 ± 4.55 seconds for non-diabetic patients. [27]

In study by Johanna S et al., documented with 71% of the patients presented with meibomian gland dysfunction, which was 76% among diabetic patients and 67% in controls. The control group had lower NIBUT compared to the diabetic patients. Also found significant lower mean level of the Lissamjne staining and Fluorescein staining among controls compared to the patients with diabetes mellitus.[68] In their study, Shamsheer et al., found that the diabetic group, consisting of 58 eyes, had a significantly higher number of eyes with Grade I–IV lissamine green and fluorescein staining compared to the control group, which included 14 eyes. This difference was statistically significant.[76]

In concordance to present study Tao V et al., documented the T2DM patients with more unstable tear film, severe symptoms of dry eye and significant morphological and cytological changes. Also there is higher incidence of the dysfunction in meibomian gland in diabetic patients when compared to the non-diabetic individuals. [65] In another study by

Rathnakumar K et al., documented the significant relation of the dry eye with the dyslipidemia among the patients with diabetes mellitus. [66] Meibomian gland dysfunction is the most common and significant cause for dry eye disease. [67]

MGD is more severe in type 2 diabetes people than in nondiabetic ones. Diabetes over a longer period of time is connected with more severe symptoms and alterations in MG. The diabetic group demonstrated significant alterations in lid and tear function, accounting for evaporative dry eye and demonstrating a strong association with MG inflammation. [68]

Of the 100 diabetics, 56 (56%) had dry eye disease; 24 of them also had MGD. with 56 cases with dry eyes, or 42% of all cases, MGD is the cause in study by Manjula TR et al. also, Six of the 100 non-diabetics with dry eye disease also had MGD, making up 15% of the group. Diabetes can change both the qualitative and quantitative characteristics of the ocular surface. Diabetic people are more likely to have dry eye problems than the general population. Compared to the non-diabetic population, the prevalence of MGD among diabetics is significantly greater. The frequency and intensity of MGD increase with the duration of DM. [69]

In study by Mussi N et al., the patients with dry eye group, MGD was not linked with BMI, smoking, type 2 diabetes, hypertension, or hyperlipidemia. MGD was linked to male sex and getting older. [71]

Another study by Shamsheer et al., found significant higher grade of MGD among diabetic patients compared to non-diabetic patients.[76]

The study included 140 participants divided into two groups based on diabetes mellitus history: Group DM (diabetic) and Group NDM (non-diabetic). The mean age and gender distribution were comparable between the groups, with a slight male predominance. Occupational backgrounds were similar as well. Diabetic patients showed a significantly higher incidence of blurred vision (68.6% vs. 48.6%) and ocular pain (42.9% vs. 11.4%) compared to non-diabetics ($p<0.05$). Although sensitivity to light and grittiness were more common in diabetics, the differences were not significant. Diabetics had poorer best corrected visual acuity in both eyes ($p<0.05$). The Ocular Surface Disease Index (OSDI) scores were significantly higher in diabetics ($p<0.05$), and Schirmer's test results indicated lower tear production in diabetics. Tear Break-Up Time (TBUT) and blink intervals showed no significant differences. Oxford staining scores were lower in diabetics, but the difference was not significant. Meibum expressibility and quality scores were also similar. However, diabetics exhibited a significantly higher incidence of moderate to severe dry eye ($p<0.05$) and a more advanced stage of meibomian gland dysfunction compared to non-diabetics. Meibomian gland dysfunction (MGD) is a major contributor to dry eye disease, and its more severe forms are significantly more common in diabetics. This heightened severity of MGD may be a key factor in the increased prevalence of dry eye observed in diabetic patients.

SUMMARY

- Present study included total of 140 participants fulfilling inclusion criteria and separated into two group based on history of diabetes mellitus. Group DM – with history of diabetes mellitus and group NDM – non-diabetic healthy participants.
- The mean age of participants between the group was comparable with no significant difference.
- Among the gender distribution, there is no significant difference in male and female distribution between the group. However there is marginal male preponderance.
- By occupation, participants in both the groups were comparable with no significant difference noted.
- There is significant higher incidence of blurring of vision in diabetic patients (68.6%) compared to non diabetic (48.6%).($p<0.05$) also there is significant higher incidence of pain among diabetic patients (42.9%)compared to non-diabetics (11.4%).($p<0.05$) there is no significant difference in the sensitivity to light and grittiness between the groups, however the incidence of both were higher among diabetic patients compared to non-diabetic individuals.
- There is significant difference in best corrected visual acuity between the group, with poor visual acuity among the patients with diabetes mellitus compared to the participants in non-diabetic group in both eyes.($p<0.05$)
- On assessment of the anterior segment of both the eye, there is no significant difference noted between the groups.
- On comparison of the mean score of OSDI, there is significant higher mean score among the diabetic patients compared to non-diabetic individuals. ($p<0.05$)

- On assessment of schirmer's test there is significant lower mean level among diabetic patients compared to the non-diabetic individuals.
- On assessment of TBUT score, there is no significant difference in the mean level between the groups.
- There is no significant difference in the mean blink interval among the patients between the groups.
- There is no significant difference in the Oxford staining score between the groups, however the mean level of staining score was lower in diabetic patients compared to non-diabetic individuals.($p>0.05$)
- In this study, there is no significant difference in meibum expressibility scale score between the group in both eye.
- There is no significant difference in meibum quality score between the groups.
- There is significant higher incidence of the dry eye severity grade of moderate and severe among the patients with diabetes mellitus compared to non-diabetic individuals. ($p<0.05$)
- There is higher mean stage of the meibomian gland dysfunction in patients with diabetes mellitus compared to the patients with non-diabetics.

CONCLUSION

In conclusion, the study demonstrates that diabetic individuals suffer from more severe dry eye and meibomian gland dysfunction than non-diabetic individuals. The increased severity of symptoms and functional impairments in the diabetic group underscores the importance of diligent ocular surface assessment and targeted management strategies in diabetic patients to alleviate discomfort and prevent further visual deterioration.

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ANNEXURE

Title of Research study

"COMPARISON OF SEVERITY OF DRY EYE AND MEIBOMIAN GLAND DYSFUNCTION IN DIABETICS AND NON- DIABETICS – ONE YEAR CROSS SECTIONAL STUDY IN A TERTIARY CARE CENTER''

Name of Student/Principal Investigator:

Name of Guide/Co Investigators:

Objective: To compare the severity of dry eye and meibomian gland dysfunction in diabetics and non- diabetics

Introduction: Various systemic and environmental causes has been suggested as the etiology for dry eyes, diabetes being one of the significant causes hence it is important to understand the relationship between diabetes mellitus, meibomian gland dysfunction and dry eyes. This study aims at correlating the severity of dry eye and meibomian gland dysfunction in diabetics and non-diabetics

Explanation of procedure: If, you agree to be part of the research study, you will be asked the relevant history and will be subjected to relevant clinical examination and investigations.

Withdrawal from participation in the study: Participation in this study is voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the principal investigator.

Possible benefits from participating in the study: You will/will not have nor get any benefits by participating in this study. The data gathered will help the population at large.

Possible risks from participating in the study: There are no risks involved in participating in this study.

Privacy and confidentiality: The information collected from you will be coded, to prevent any person from identifying you. Your identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

Financial incentives: You will not receive any payment for participating in this study.

Authorization for publication of aggregated data: Results obtained after processing of the aggregated data will be published for scientific purposes and or presented to scientific groups. However, your identity will never be revealed.

Questions:

If you have any question or complaints with regard to your right as study participant you may contact Dr Harsha Hegde, Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052.

Legal rights: By signing this consent form, we are not waving any of your legal rights.

CONSENT STATEMENT

I am making a voluntary decision to participate in the study comparison of severity of dry eye and meibomian gland dysfunction in diabetics and non- diabetics – One year cross sectional study in a tertiary care centre

My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name of the participant:

Signature or left thumb impression of the participant:

Name of the witness:

Signature or left thumb impression of the witness:

Name of the investigator:

Signature of the investigator:

PROFORMA

Hospital ID: Study ID:

NAME: _____

AGE:_____Years

GENDER: MALE ☐ FEMALE ☐

ADDRESS: _____

_____

OCCUPATION: _____

CONTACT NUMBER: ☐☐☐☐☐☐☐☐☐☐

DATE OF EXAMINATION: / /

IS THE PATIENT ELIGIBLE FOR STUDY? YES ☐ NO ☐

HAS INFORMED CONSENT BEEN GIVEN? YES ☐ NO ☐

CHIEF COMPLAINTS:

1. DIMINUTION OF VISION: YES ☐ NO ☐
   RE: DURATION _____ Days/Months/Years
   LE: DURATION _____ Days/Months/Years

   GRADUAL ☐ PROGRESSIVE ☐ SUDDEN ☐ NON-PROGRESSIVE ☐

2. OSDI QUESTIONNAIRE:
   HAVE YOU EXPERIENCED ANY OF THE FOLLOWING DURING THE LAST WEEK

	ALL OF THE TIME	MOST OF THE TIME	HALF OF THE TIME	SOME OF THE TIME	NONE OF THE TIME	N/A
1.Eyes that are sensitive to light						
2.Eyes that feel gritty						
3.Painful or sore eyes						
4.Blurred vision						
5.Poor vision						

Subtotal score for answers 1-5 ( )

Have problems with your eyes limited you in performing any of the following in last week

	ALL OF THE TIME	MOST OF THE TIME	HALF OF THE TIME	SOME OF THE TIME	NONE OF THE TIME	N/A
6.Reading						
7.Driving at night						
8.Working with computer or bank machine						
9.Watching TV						

Subtotal score for answers 6-9 ( )

Have your eyes felt uncomfortable in any of the situations during the last week

	ALL OF THE TIME	MOST OF THE TIME	HALF OF THE TIME	SOME OF THE TIME	NONE OF THE TIME	N/A
10.windy conditions						
11. places or areas with low humidity						
12. areas that are air conditioned						

Subtotal score for answers 10-12 ( )

OSDI = Sum of all questions answered/ total number of questions answered x 100/25

=

MEDICAL HISTORY:

1. DIABETES: PRESENT ☐ ABSENT ☐

   DURATION OF DIABETES: _____ Months/Years

   ANY MEDICATION: YES ☐ NO ☐ IF YES, DRUGS TAKEN

   _____

2. HYPERTENSION: PRESENT ☐ ABSENT ☐
   ANY MEDICATION :
   _____

3. OCULAR TRAUMA: PRESENT ☐ ABSENT ☐

4. SPECTACLE USE: YES ☐ NO ☐
   IF YES, DURATION:_____

5. H/O CONTACT LENS USE: YES ☐ NO ☐
   IF YES, DURATION: _____

6. H/O JOINT PAIN: YES ☐ NO ☐ IF YES, DURATION: _____

7. ANY TOPICAL /SYSTEMIC MEDICATION/OCP'S/STEROIDS
   _____

8. RECENT OCCULAR SURGERY YES ☐ NO ☐
9. HISTORY OF SMOKING YES ☐ NO ☐
10. ANY RECENT OCULAR INFECTION/ DISEASE YES ☐ NO ☐

OCULAR EXAMINATION:

ANTERIOR SEGMENT:	RIGHT EYE	LEFT EYE
VISUAL ACUITY		
PINHOLE		
WITH GLASSES		
EXTRA OCULAR MOVEMENTS		
EYELIDS		
EYELASHES		
CONJUNCTIVA		
SCLERA		
PRECORNEAL TEAR FILM		

CORNEA

ANTERIOR CHAMBER

IRIS

PUPIL

LENS

POSTERIOR SEGMENT:

GLOW

MEDIA

DISC

C:D

B/V

B/G

MACULA

a. **SCHIRMER'S I TEST : RE ---------- LE----------**

b. **TBUT (sec) : RE ---------- LE----------**

c. **NASOLACRIMAL DUCT PATENCY: RE ---------- LE----------**

d. **Blink interval : RE ---------- LE----------**

e. **Ocular surface staining (oxford staining score) RE---------- LE----------**

f. **Meibum expressibility RE LE**

All glands Expressible		
3–4 glands expressible		
1–2 glands expressible		
no glands expressible		
GRADE		

scale 0 (normal)= all glands expressible; 1 = 3–4 glands expressible;
2 = 1–2 glands expressible; 3= no glands expressible
(scale of 0-3 in five glands in lower or upper lid)

g. Meibum quality **RE** **LE**

Clear fluid		
Cloudy fluid		
Cloudy and particulate fluid		
Opaque tooth paste like		
Total score		

0(normal)=clear fluid; 1= cloudy fluid; 2= cloudy and particulate fluid;

3= opaque, toothpaste-like meibum.

Total score-(assessed in each of the eight glands of central third of lower lid of a scale of 0-3 for each gland ,total score range 0-24)

IMPRESSION:

DIABETIC / NON-DIABETIC :

If diabetic – duration of diabetics-

	RIGHT EYE	**LEFT EYE**
DRY EYE SEVERITY		
MEBOMIAN GLAND DYSFUNCTION		

NAME OF THE INVESTIGATOR : **DR. ASHLY BIJU**

SIGNATURE : _____

NAME OF THE GUIDE : **DR. ARVIND L TENAGI**

SIGNATURE : _____

MASTERCHART

STUDY ID	Group	AGE	GENDER	OCCUPATION	BLURRING OF VISION	SENSITIVITY TO LIGHT	GRITTINESS	PAIN	H/O DM	DURATION	TREATMENT	BCVA_OD	BCVA_OS	Anterior segment_OD	Anterior segment_OS
1	NDM	74	M	FARMER	Y	N	N	N	NO			6 \36	6\6	NORMAL	NORMAL
2	NDM	42	F	HOMEMAKER	Y	N	N	N	NO			6\24	6\6	NS 1	NORMAL
3	NDM	75	M	FARMER	Y	N	N	N	NO			6\18	6\60	NS 1	NS2
4	NDM	70	M	-	Y	N	N	N	NO			6\18	CF2MT	NS1	NS3 + PSC
5	NDM	52	M	ANALYST	Y	N	N	N	NO			6\6	CF1.5 MT	NORMAL	NS4 + PSC
6	NDM	52	F	HOMEMAKER	N	Y	Y	Y	NO			6\18	6\18	NORMAL	NORMAL
7	NDM	70	F	HOMEMAKER	Y	N	Y	N	NO			CF1MT	6\9	NS 4	NORMAL
8	NDM	70	M	FARMER	Y	Y	Y	Y	NO			CF 3MT	6\36	NS3	NS1
9	NDM	66	F	HOMEMAKER	Y	N	N	N	NO			6\24	6\6	NS 1	NORMAL
10	NDM	74	F	HOMEMAKER	Y	Y	Y	Y	NO			CF 0.5MT		NS4	NS2
11	ND	51	M	BANKER	N	Y	Y	N	N			6\9	6\9	LID MARGINS	LID MARGINS

	M								O					INFLAMED	INFLAMED
12	ND M	48	M	BUSINESSMA N	Y	Y	Y	N	N O			6\9	6\36	NORMAL	PSC
13	ND M	48	F	HOMEMAKER	Y	Y	Y	N	N O			CFCF	6\18	MATURE CATARACT	PSC+CC
14	ND M	48	F	FARMER	N	Y	Y	N	N O			6\6	6\6	MG CYST	MG CYST
15	ND M	73	F	HOMEMAKER	Y	Y	Y	N	N O			CF 1MT	6\12	NS2 + PSC + CC	NS2
16	ND M	60	F	HOMEMAKER	Y	Y	Y	N	N O			CF 3MT	CF 1.5 MT	NS3	NS4 + PSC
17	ND M	55	M	SHOPKEEPER	Y	Y	Y	N	N O			6\6	CF 1MT	NS 1	NS3 +PSC
18	ND M	57	M	HOMEMAKER	Y	N	N	N	N O			6\60	6\18	NS3	NS2
19	ND M	44	M	LIBRARIAN	N	Y	Y	Y	N O			6\6	6\6	NS1	NS1
20	ND M	75	M	FARMER	Y	n	n	n	N O			6\18	CF 3MT	NS 2	NS3 +PSC
21	ND M	70	M	-	Y	N	N	Y	N O			CF 3MT	6\ 36	LID MARGINS INFLAMED	LID MARGINS INFLAMED
22	ND M	70	F	HOMEMAKER	Y	N	Y	N	N O			CF 1MT	6\ 9	NS2 + PSC	NORMAL
23	ND M	52	F	HOMEMAKER	N	Y	Y	Y	N O			6\ 18	6\ 18	POUTING OF MG ORIFICE	POUTING OF MG ORIFICE
24	ND M	70	M	-	Y	N	N	N	N O			6\ 18	CF 2M	NORMAL	NORMAL
25	ND M	52	M	ENGINEER	Y	N	N	N	N O			6\ 6	CF1.5 MT	NORMAL	NS3 +PSC
26	ND	42	F	TEACHER	Y	N	N	N	N			6\ 24	6\ 6	NORMAL	NORMAL

	M								O						
27	ND M	75	M	-	Y	N	N	N	N O			6\18	CF 3MT	NORMAL	NS3
28	ND M	75	M	FARMER	Y	n	n	n	N O			6\18	CF 3MT	NS 2	NS3 +PSC
29	ND M	59	M	-	N	Y	Y	N	N O			6\6	6 \6	POUTING OF MG ORIFICE	POUTING OF MG ORIFICE
30	ND M	46	M	-	N	N	N	N	N O			6\6	6\9	NORMAL	NORMAL
31	ND M	68	M	Farmer	Y	N	N	N	N O			CF 1M	CF 2M	GRADE 3 NS + PSC	GRADE 2 NS + PSC
32	ND M	54	M	Employee	N	N	N	N	N O			6\9	6\12	GRADE 2 NS	GRADE 2 NS + PSC
33	ND M	40	M	Employee	N	N	N	N	N O			6\9	6\6	Mild PSC	Mild PSC
34	ND M	36	M	Employee	N	N	N	N	N O			6\6	6\12	Mild PSC	PSC
35	ND M	45	M	Employee	N	N	N	N	N O			6\12	6\12	PSC	PSC
36	ND M	35	M	Employee	N	N	N	N	N O			6\9	6\9	CLEAR	CLEAR
37	ND M	50	F	Tailor	N	N	N	N	N O			6\18	6\24	GRADE 1 NS	GRADE 1 NS
38	ND M	47	M	Watchmaker	N	N	N	N	N O			6\12	6\9	PSC	Mild PSC
39	ND M	53	M	Employee	N	N	N	Y	N O			6\9	6\9	Mild PSC	Mild PSC
40	ND M	54	M	Employee	Y	N	N	N	N O			6\36	6\24	Mild PSC	Mild PSC
41	ND	78	M	Retired	Y	N	N	N	N			CF 3M	6\24	GRADE 3 NS	PSEUDOPHAK\A

	M								O					
42	ND M	80	M	Retired	Y	N	N	N	N O			CF 1M	CF 2M	GRADE 2 NS	GRADE 3 NS
43	ND M	56	F	Teacher	N	N	N	N	N O			6\12	6\18	GRADE 1 NS + PSC	GRADE 2 NS
44	ND M	39	F	Employee	N	N	N	N	N O			6\9	6\9	GRADE 1 NS	GRADE 1 NS
45	ND M	44	M	Employee	N	N	N	N	N O			6\12	6\18	GRADE 2 NS	GRADE 2 NS
46	ND M	76	F	Retired	Y	N	N	N	N O			6\60	6\24	GRADE 3 NS	PSEUDOPHAK\A
47	ND M	66	F	Housewife	Y	N	N	N	N O			CF 2M	CF 2M	GRADE 3 NS + PSC	GRADE 3 NS
48	ND M	55	F	Housewife	N	N	N	N	N O			6\9	6\12	GRADE 1 NS	GRADE 1 NS
49	ND M	56	M	Employee	N	N	N	N	N O			6\12	6\12	GRADE 2 NS	GRADE 2 NS
50	ND M	67	M	Retired	Y	N	N	N	N O			6\36	6\60	GRADE 2 NS + PSC	GRADE 3 NS
51	ND M	80	F	Housewife	Y	N	Y	N	N O			CF 3M	CF 3M	GRADE 3 NS	GRADE 3 NS
52	ND M	35	F	Employee	N	N	N	N	N O			6\9	6\9	CLEAR	CLEAR
53	ND M	43	F	Employee	N	N	N	N	N O			6\12	6\18	Mild PSC	Mild PSC
54	ND M	44	M	Employee	N	N	N	N	N O			6\12	6\9	Mild PSC	Mild PSC
55	ND M	56	F	Housewife	N	N	N	Y	N O			6\18	6\18	GRADE 2 NS	GRADE 1 NS + CC
56	ND	56	M	Employee	N	N	N	N	N			6\12	6\12	GARDE 1 NS + PSC	Mild PSC

	M								O						
57	ND M	77	F	Housewife	Y	N	N	N	N O			CF 3M	CF 3M	GRADE 3 NS	GRADE 3 NS
58	ND M	45	F	Employee	N	N	N	N	N O			6\18	6\12	GRADE 1 NS	GRADE 1 NS
59	ND M	55	F	Employee	N	N	N	N	N O			6\9	6\9	GRADE 1 NS	GRADE 1 NS + CC
60	ND M	56	F	Employee	N	N	Y	N	N O			6\18	6\12	GRADE 1 NS + CC	GARDE 1 NS
61	ND M	39	M	Employee	N	N	N	N	N O			6\12	6\9	GRADE 1 NS	Mild PSC
62	ND M	56	F	Housewife	N	N	N	N	N O			6\12	6\12	PSC	PSC
63	ND M	48	M	Employee	N	N	N	N	N O			6\12	6\18	PSC	PSC
64	ND M	56	F	Employee	N	N	N	N	N O			6\9	6\9	Mild PSC	Mild PSC
65	ND M	67	M	Housewife	Y	N	N	N	N O			6\60	6\60	GRADE 2 NS	GRADE 2 NS
66	ND M	55	M	Employee	N	N	N	N	N O			6\12	6\9	GRADE 2 NS	GRADE 1 NS
67	ND M	57	F	Employee	N	N	N	N	N O			6\9	6\9	PSC	PSC
68	ND M	44	M	Employee	N	N	N	N	N O			6\18	6\12	GRADE 2 NS	GRADE 1 NS
69	ND M	67	M	Retired	Y	N	N	N	N O			CF 1 M	6\60	GRADE 3 NS	GRADE 2 NS + PSC
70	ND M	44	M	Employee	N	N	N	N	N O			6\12	6\12	GRADE 1 NS	GRADE 1 NS
71	DM	56	F	HOUSEWIFE	Y	Y	N	Y	Y	7	Y	6\18	6\12	GRADE 2 NS	GRADE 1 NS

72	DM	55	M	EMPLOYEE	Y	Y	Y	Y	Y	0.1	Y	6\12	6\9	MILD PSC	MILD PSC
73	DM	67	M	RETIRED	Y	Y	Y	Y	Y	13	Y	6\9	6\9	PSEUDOPHAKIA	PSEUDOPHAKIA
74	DM	36	M	TEACHER	y	N	N	Y	Y	6	Y	6\24	6\24	PSC	PSC
75	DM	58	F	RETIRED	y	N	Y	Y	Y	12	Y	6\60	6\60	GRADE 2 NS + PSC	GRADE 2 NS + PSC
76	DM	45	M	RETIRED	y	N	Y	Y	Y	7	Y	6\60	6\36	GRADE 2 NS + PSC	GRADE 2 NS
77	DM	48	M	EMPLOYEE	y	N	N	N	Y	0.5	Y	6\24	6\18	PSC	PSC
78	DM	75	F	EMPLOYEE	N	N	N	N	Y	0	Y	6\12	6\12	MILD PSC	MILD PSC
79	DM	56	F	EMPLOYEE	y	N	Y	Y	Y	2	Y	6\36	6\36	PSC	PSC
80	DM	55	M	EMPLOYEE	n	N	N	Y	Y	0	Y	6\12	6\9	MILD PSC	MILD CC
81	DM	67	F	EMPLOYEE	N	N	N	Y	Y	0	Y	6\9	6\9	MILD PSC	MILD PSC
82	DM	59	F	RETIRED	y	Y	Y	N	Y	14	Y	6\60	CF 2M	PSEUDOPHAKIA	GRADE 3 NS
83	DM	44	F	EMPLOYEE	N	N	N	Y	Y	0.5	Y	6\12	6\12	GRADE 1 NS	GRADE 1 NS
84	DM	65	M	TEACHER	N	N	N	N	Y	1	Y	6\18	6\12	GRADE 1 NS	GRADE 1 NS
85	DM	56	F	HOUSEWIFE	N	N	Y	Y	Y	4	Y	6\36	6\36	PSC	PSC
86	DM	65	F	HOUSEWIFE	y	N	N	N	Y	0.3	Y	6\60	6\24	GRADE 2 NS + PSC	GRADE 1 NS
87	DM	66	M	DRIVER	N	Y	N	N	Y	1	Y	6\24	6\24	GRADE 1 NS	GRADE 1 NS
88	DM	48	M	EMPLOYEE	N	Y	N	Y	Y	0.4	Y	6\18	6\12	PSC	MILD PSC
89	DM	43	M	TECHNICIAN	N	Y	Y	Y	Y	0	N	6\12	6\12	MILD PSC	MILD PSC
90	DM	54	F	EMPLOYEE	N	N	N	N	Y	0	N	6\9	6\9	GRADE 1 NS	MILD PSC
91	DM	50	F	HOUSEWIFE	y	N	Y	Y	Y	3	N	6\36	6\60	PSC	PSC
92	DM	44	M	RETIRED	y	N	N	Y	Y	7	Y	6\60	6\60	GRADE 2 NS	GRADE 2 NS
93	DM	67	F	HOUSEWIFE	y	N	N	Y	Y	0.5	Y	CF 2M	6\60	GRADE 3 NS + PSC	GRADE 2 NS
94	DM	45	F	HOUSEWIFE	y	N	N	N	Y	0	Y	CF 1M	6\9	GRADE 3 NS	PSEUDOPHAKIA

95	DM	46	M	DRIVER	y	N	Y	Y	Y	0	N	CF 3M	CF 3M	GRADE 3 NS	GRADE 3 NS
96	DM	56	M	FARMER	y	Y	N	Y	Y	10	Y	CF 3M	6\60	GRADE 2 NS	GRADE 2 NS
97	DM	46	F	HOUSEWIFE	y	Y	N	Y	Y	0	N	6\60	6\18	PSC	PSC
98	DM	55	F	HOUSEWIFE	y	N	Y	Y	Y	5	Y	6\60	6\36	PSC	PSC
99	DM	46	F	RETIRED	y	Y	Y	N	Y	0	N	CF 0.5M	CF 3M	GRADE 2 NS	GRADE 2 NS
100	DM	39	M	EMPLOYEE	y	N	N	Y	Y	0.5	Y	6\60	6\24	GRADE 2 NS	GRADE 1 NS + CC
101	DM	43	M	EMPLOYEE	Y	Y	Y	Y	Y	0	Y	6\36	6\24	GRADE 1 NS	PSC
102	DM	55	M	TEACHER	N	Y	N	N	Y	2	Y	6\12	6\36	PSC	PSC
103	DM	65	F	HOUSEWIFE	Y	Y	N	N	Y	12	Y	6\60	CF 3M	GRADE 2 NS	GRADE 3 NS
104	DM	60	F	HOUSEWIFE	Y	Y	N	Y	Y	5	Y	CF 2M	CF 2M	GRADE 2 NS + CC	GRADE 2 NS
105	DM	68	F	RETIRED	y	N	N	N	Y	15	Y	6\18	CF 1M	PSEUDOPHAKIA	GRADE 2 NS + PSC
106	DM	52	F	EMPLOYEE	y	N	N	N	Y	10	Y	6\12	6\18	PSC	PSC
107	DM	60	M	EMPLOYEE	n	N	N	Y	Y	0	N	CF 3M	6\36	GRADE 3 NS	GRADE 2 NS + PSC
108	DM	50	F	EMPLOYEE	N	N	N	N	Y	0	N	6\18	6\12	PSC	PSC
109	DM	50	F	HOUSEWIFE	y	Y	N	N	Y	8	Y	CF 3M	6\24	GRADE 3 NS	PSC
110	DM	80	M	TEACHER	N	N	N	N	Y	5	Y	6\24	6\36	PSC	PSC
111	DM	52	M	RETIRED	y	N	N	N	Y	15	Y	CF 2M	CF 3M	GRADE 3 NS	GRADE 2 NS + PSC

112	DM	44	F	TEACHER	y	N	N	N	Y	0.9	Y	6\60	6\36	GRADE 2 NS + CC	GRADE 2 NS
113	DM	54	F	EMPLOYEE	y	N	N	N	Y	2	Y	6\36	6\36	GRADE 2 NS	GRADE 2 NS
114	DM	65	F	HOUSEWIFE	y	Y	N	N	Y	4	Y	CF 1M	CF 3M	GRADE 3 NS	GRADE 2 NS + PSC
115	DM	66	M	RETIRED	Y	N	Y	N	Y	12	Y	6\60	6\60	PSEUDOPHAKIA	PSEUDOPHAKIA
116	DM	76	M	TAILOR	y	N	N	Y	Y	5	Y	6\36	6\36	GRADE 2 NS	GRADE 2 NS
117	DM	54	M	TEACHER	y	N	N	N	Y	2	Y	6\60	6\60	GRADE 2 NS + CC	GRADE 2 NS
118	DM	57	M	HOUSEWIFE	y	N	N	Y	Y	5	Y	CF 3M	CF 2M	GRADE 2 NS + PSC	GRADE 3 NS
119	DM	43	F	EMPLOYEE	N	N	N	N	Y	0	Y	6\24	6\18	GRADE 1 NS	GRADE 1 NS + CC
120	DM	52	M	BANK EMPLOYEE	N	N	Y	N	Y	18	Y	6\24	6\36	GRADE 2 NS	MILD PSC
121	DM	55	F	RETIRED	N	N	N	N	Y	0	N	6\12	CF 3M	PSEUDOPHAKIA	GRADE 3 NS
122	DM	67	F	MAID	y	N	Y	N	Y	0.5	Y	CF 1M	CF 1M	GRADE 2 NS	GRADE 3 NS + PSC
123	DM	58	F	HOUSEWIFE	y	N	Y	Y	Y	0	Y	6\24	6\24	GRADE 1 NS	GRADE 2 NS
124	DM	56	M	EMPLOYEE	N	N	N	N	Y	0.2	Y	6\12	6\9	MILD PSC	MILD PSC
125	DM	67	F	RETIRED	Y	Y	Y	N	Y	12	Y	CF 1 M	6\60	PSEUDOPHAKIA	PSEUDOPHAKIA
126	DM	77	F	TEACHER	Y	N	Y	N	Y	5	Y	6\60	6\36	GRADE 2 NS	GRADE 2 NS + CC

127	DM	56	M	TAILOR	N	N	N	N	Y	2	Y	6\12	6\18	GRADE 1 NS	GRADE 1 NS + CC
128	DM	60	F	HOUSEWIFE	y	N	N	N	Y	10	Y	CF 3M	CF 2M	GRADE 3 NS + PSC	GRADE 3 NS + PSC
129	DM	66	M	RETIRED	N	N	N	N	Y	6	Y	6\24	6\36	GRADE 2 NS + PSC	GRADE 3 NS
130	DM	52	M	EMPLOYEE	Y	Y	Y	Y	Y	0	N	6\36	6\60	GRADE 1 NS	GRADE 1 NS
131	DM	66	F	RETIRED	y	N	N	N	Y	1	Y	6\60	6\60	GRADE 2 NS	GRADE 2 NS + PSC
132	DM	72	F	HOUSEWIFE	N	N	N	Y	Y	0	N	6\18	6\18	GRADE 1 NS	GRADE 1 NS
133	DM	55	M	HOUSEWIFE	Y	N	N	N	Y	0	N	6\18	6\18	GRADE 1 NS	GRADE 1 NS
134	DM	70	M	UNEMPLOYED	Y	N	N	N	YES	4	YES	6\18	CF2MT	NS1	NS3 +PSC
135	DM	70	M	HOMEMAKER	Y	N	Y	N	YES	6	YES	CF1MT	6\9	NS 4	NORMAL
136	DM	74	F	HOMEMAKER	y	Y	Y	Y	YES	1	YES	CF 0.5MT	6\60	NS4	NS2
137	DM	51	F	BANKER	n	Y	Y	N	YES	2	YES	6\9	6\9	LID MARGINS INFLAMED	LID MARGINS INFLAMED
138	DM	55	M	SHOPKEEPER	Y	Y	Y	N	YES	6	YES	6\6	CF 1MT	NS 1	NS3 +PSC
139	DM	70	F	HOMEMAKER	Y	N	Y	N	YES	6	NO	CF 1MT	6\ 9	NS2 + PSC	NORMAL
140	DM	70	F	UNEMPLOYED	Y	N	N	N	YES	4	YES	6\ 18	CF 2M	NORMAL	NORMAL

STUDY ID	Group	OSDI	SCHIRMERS I TEST_OD	SCHIRMERS I TEST_OS	TBUT_OD	TBUT_OS	BlinkInterval_OD	BlinkInterval_OS	OXFORD STAINING SCORE_OD	OXFORD STAINING SCORE_OS	MEIBUM EXPRESSIBILITY SCALE_OD	MEIBUM EXPRESSIBILITY SCALE_OS	MEIBUM QUALITY SCORE_OD	MEIBUM QUALITY SCORE_OS	DRY EYE SEVERITY_OD	DRY EYE SEVERITY_OS	GLAND DYSFUNCTION	GLAND DYSFUNCTION
1	NDM	5.5	10	10	8	8	7	7	6	6	0	0	2	2	Moderate	Moderate	1	1
2	NDM	8.3	25	25	12	5	12	12	-	-	0	0	3	3	-	-	1	1
3	NDM	4	25	25	12	5	10	10	-	-	0	0	2	2	-	-	1	1
4	NDM	4	15	15	6	5	10	10	-	-	0	0	2	2	-	-	1	1
5	NDM	8.3	20	25	11	5	10	10	-	-	0	0	3	3	-	-	1	1
6	NDM	25	8	8	8	8	8	8	7	7	0	0	2	2	Moderate	Moderate	1	1
7	NDM	13.8	14	13	11	11	4	11	0	0	0	0	0	0	Mild	Mild	0	0
8	NDM	27.7	13	13	11	11	6	6	0	0	0	0	3	3	Mild	Mild	1	1
9	NDM	5.5	25	25	12	5	12	12	-	-	0	0	0	0	-	-	-	-
10	NDM	60	20	25	11	5	10	10	-	-	0	0	0	-	-	-	-	-
11	NDM	13.8	24	25	14	5	10	10	-	-	1	1	2	2	-	-	1	1
12	NDM	22.2	8	8	10	10	12	12	6	6	0	0	0	0	moderate	moderate	0	0
13	NDM	28.1	24	22	12	5	12	12	-	-	0	0	0	0	-	-	-	-
14	NDM	16.6	30	35	12	5	10	10	-	-	0	0	0	0	-	-	0	0
15	NDM	25	20	19	14	5	18	18	2	2	1	1	2	2	-	-	1	1
16	NDM	16.6	8	8	7	7	5	5	6	7	0	0	0	0	Moderate	Moderate	-	0
17	NDM	28.1	25	20	11	5	10	10	8	8	0	0	2	2	-	-	1	1
18	NDM	5.5	14	12	9	7	10	10	0	0	0	0	0	0	Mild	Mild	-	0
19	NDM	22.5	25	28	7	6	5	5	0	0	0	0	8	8	Mild	Mild	2	2
20	NDM	8.3	25	30	12	5	9	9	-	-	0	0	0	0	-	-		
21	NDM	16.6	12	13	6	5	6	6	2	2	0	0	8	8	Mild	Mild	2	2

22	NDM	13.8	15	15	8	5	4	4	0	0	0	0	0	0	Mild	Mild		
23	NDM	28.1	9	9	8	9	8	8	7	7	1	1	8	8	MODERATE	Moderate	2	2
24	NDM	8.3	15	15	6	5	10	10	-	-	0	0	0	0	-	-	-	-
25	NDM	8.3	20	25	12	5	10	10	-	-	0	0	0	0	-	-	-	-
26	NDM	5.5	25	25	12	5	12	12	-		0	0	0	0	-	-	-	-
27	NDM	5.5	25	25	12	5	10	10	-	-	0	0	0	0	-	-	-	-
28	NDM	8.3	25	30	12	5	9	9	-	-	0	0	0	0	-	-	-	-
29	NDM	16.6	5	7	3	3	5	5	10	10	1	1	13	13	Severe	Severe	3	3
30	NDM	0	15	15	6	7	4	4	2	0	1	0	8	8	Mild	Mild	3	3
31	NDM	5.5	13	13	8	8	5	5	6	7	1	1	11	12	Moderate	Moderate	3	3
32	NDM	0	10	9	7	7	9	8	6	7	1	1	13	12	Moderate	Moderate	3	3
33	NDM	0	9	9	7	8	10	10	5	6	1	1	11	11	Moderate	Moderate	3	3
34	NDM	0	8	9	9	9	8	8	4	4	0	0	0	0	Moderate	Moderate	-	-
35	NDM	0	10	9	7	8	10	10	5	6	0	0	0	0	Moderate	Moderate	-	-
36	NDM	0	8	8	10	10	12	12	6	6	1	1	4	4	moderate	moderate	1	1
37	NDM	0	8	8	8	9	8	8	7	7	0	0	16	16	MODERATE	Moderate	-	-
38	NDM	0	8	8	9	9	8	8	4	4	1	1	4	4	Moderate	Moderate	2	2
39	NDM	5.5	14	12	9	7	10	10	0	0	0	0	0	0	Mild	Mild	-	-
40	NDM	5.5	25	28	4	5	5	5	0	0	1	1	8	8	Mild	Mild	3	3
41	NDM	8.3	14	14	8	8	9	9	-	-	0	0	0	0	Mild	Mild	-	-
42	NDM	5.5	12	13	6	5	6	6	2	2	1	1	8	8	Mild	Mild	3	3
43	NDM	0	15	15	8	5	4	4	0	0	0	0	0	0	Mild	Mild		
44	NDM	0	25	20	11	5	10	10	8	8	0	0	0	0	-	-	-	-
45	NDM	0	14	12	9	7	10	10	0	0	0	0	0	0	Mild	Mild	-	-
46	NDM	5.5	25	28	4	5	5	5	0	0	1	1	8	8	Mild	Mild	3	3
47	NDM	5.5	25	30	12	5	9	9	-	-	0	0	0	0	-	-	-	-
48	NDM	0	12	13	6	5	6	6	2	2	1	1	16	16	Mild	Mild	4	4

49	NDM	0	15	15	8	5	4	4	0	2	1	1	5	5	Mild	Mild	2	2
50	NDM	8.3	25	25	12	5	12	12	-	-	0	0	0	0	-	-	-	-
51	NDM	25	25	25	12	5	10	10	-	-	0	0	0	0	-	-	-	-
52	NDM	0	15	15	6	5	10	10	-	-	0	0	0	0	-	-	-	-
53	NDM	0	20	25	11	5	10	10	-	-	0	0	0	0	-	-	-	-
54	NDM	0	20	25	12	5	10	10	-	-	0	0	0	0	-	-	-	-
55	NDM	5.5	25	25	12	5	12	12	-		0	0	0	0	-	-	-	-
56	NDM	0	20	25	12	5	10	10	-	-	0	0	0	0	-	-	-	-
57	NDM	8.3	25	25	12	5	12	12	-		0	0	0	0	-	-	-	-
58	NDM	4	25	25	12	5	12	12	-	-	0	0	0	0	-	-	-	-
59	NDM	4	25	25	12	5	10	10	-	-	0	0	0	0	-	-	-	
60	NDM	4	15	15	6	5	10	10	-	-	0	0	0	0	-	-	-	-
61	NDM	0	20	25	11	5	10	10	-	-	0	0	0	0	-	-	-	-
62	NDM	0	15	15	8	5	4	4	0	0	0	0	0	0	Mild	Mild		
63	NDM	0	20	25	12	5	10	10	-	-	0	0	0	0	-	-	-	-
64	NDM	0	25	25	12	5	12	12	-		0	0	0	0	-	-	-	-
65	NDM	8.3	20	25	12	5	10	10	-	-	0	0	0	0	-	-	-	-
66	NDM	0	25	25	12	5	12	12	-		0	0	0	0	-	-	-	-
67	NDM	4	25	25	12	5	12	12	-	-	0	0	0	0	-	-	-	-
68	NDM	4	25	25	12	5	10	10	-	-	0	0	0	0	-	-	-	-
69	NDM	4	15	15	6	5	10	10	-	-	0	0	0	0	-	-	-	-
70	NDM	4	15	15	6	5	10	10	-	-	0	0	0	0	-	-	-	-
71	DM	25	11	11	11	14	7	10	2	2	0	0	0	0	MILD	MILD	-	-
72	DM	30.5	11	11	13	12	5	5	0	2	0	0	0	0	MILD	MILD	-	-
73	DM	27.7	13	12	12	12	8	9	0	2	0	0	0	0	MILD	MILD	-	-
74	DM	8.3	13	13	13	12	5	6	0	2	1	1	4	4	MILD	MILD	2	2
75	DM	16.6	11	14	12	12	5	4	1	3	1	1	4	4	MILD	MILD	2	2

76	DM	13.8	14	12	11	13	5	10	1	2	1	1	4	4	MILD	MILD	2	2
77	DM	5.5	14	14	11	10	7	10	1	2	0	0	4	4	MILD	MILD	2	2
78	DM	0	16	16	11	12	5	5	1	2	0	0	2	2	MILD	MILD	1	1
79	DM	25	12	12	12	11	5	9	1	2	1	1	2	2	MILD	MILD	1	1
80	DM	25	6	6	8	9	5	6	5	5	1	1	4	4	MODERATE	MODERATE	2	2
81	DM	25	9	10	6	6	5	4	8	8	1	1	4	4	MODERATE	MODERATE	2	2
82	DM	16.6	5	5	7	7	5	12	6	6	1	1	8	8	MODERATE	MODERATE	3	3
83	DM	28.1	9	9	5	5	5	10	6	6	1	1	4	4	MODERATE	MODERATE	2	2
84	DM	0	8	9	8	8	5	10	6	6	2	2	8	8	MODERATE	MODERATE	3	3
85	DM	16.6	9	9	5	5	5	10	6	6	0	0	0	0	MODERATE	MODERATE	-	-
86	DM	5.5	9	7	8	8	5	10	8	8	1	1	3	3	MODERATE	MODERATE	1	1
87	DM	22.2	8	9	6	6	5	12	7	7	1	1	4	4	MODERATE	MODERATE	2	2
88	DM	13.8	7	7	6	6	5	10	6	6	1	1	0	0	MODERATE	MODERATE	1	1
89	DM	22.2	8	8	6	6	5	12	8	8	1	1	4	4	MODERATE	MODERATE	2	2
90	DM	0	7	7	6	6	5	12	8	8	1	1	3	3	MODERATE	MODERATE	1	1
91	DM	25	9	8	8	8	5	10	7	7	1	1	8	8	MODERATE	MODERATE	3	3
92	DM	13.8	9	9	7	7	5	10	8	8	0	0	2	2	MODERATE	MODERATE	1	1
93	DM	13.8	6	6	6	6	5	10	8	8	0	0	0	0	MODERATE	MODERATE	-	-
94	DM	8.3	9	9	8	8	5	4	9	9	1	1	8	8	MODERATE	MODERATE	3	3
95	DM	28.1	6	6	8	8	5	10	8	8	0	0	8	8	MODERATE	MODERATE	3	3
96	DM	16.6	9	8	7	7	5	12	8	8	0	0	4	4	MODERATE	MODERATE	2	2
97	DM	28.1	4	4	8	8	5	10	9	9	0	0	14	14	MODERATE	MODERATE	4	4
98	DM	25	9	9	8	8	5	12	8	8	0	0	4	4	MODERATE	MODERATE	2	2
99	DM	28.1	6	6	9	9	5	12	6	6	0	0	8	8	MODERATE	MODERATE	3	3
100	DM	16.6	8	8	8	8	5	10	6	6	0	0	8	8	MODERATE	MODERATE	3	3
101	DM	30.5	6	6	8	8	8	7	6	6	0	0	8	8	MODERATE	MODERATE	3	3
102	DM	8.3	7	8	9	9	5	12	8	8	0	0	8	8	MODERATE	MODERATE	3	3

103	DM	16.6	3	3	6	6	5	10	7	7	0	0	0	0	MODERATE	MODERATE	-	-
104	DM	28.1	2	2	4	4	5	10	9	9	0	0	8	8	SEVERE	SEVERE	3	3
105	DM	5.5	3	4	3	3	5	10	9	9	0	0	8	8	SEVERE	SEVERE	3	3
106	DM	8.3	11	16	21	19	8	8	0	0	0	0	0	0	-	-	-	-
107	DM	5.5	9	8	8	8	6	4	0	0	0	0	0	0	-	-	-	-
108	DM	0	16	16	15	14	5	6	0	0	0	0	0	0	-	-	-	-
109	DM	16.6	9	9	10	10	5	12	0	0	0	0	0	0	-	-	-	-
110	DM	0	15	15	18	17	5	10	0	0	0	0	0	0	-	-	-	-
111	DM	8.3	10	10	14	15	5	10	0	0	0	0	0	0	-	-	-	-
112	DM	5.5	17	19	15	15	10	12	0	0	0	0	0	0	-	-	-	-
113	DM	5.5	6	6	8	8	5	12	0	0	0	0	0	0	-	-	-	-
114	DM	16.6	8	8	10	10	5	10	0	0	0	0	0	0	-	-	-	-
115	DM	13.8	6	6	5	7	5	18	0	0	0	0	0	0	-	-	-	-
116	DM	13.8	12	14	16	16	7	5	0	0	0	0	0	0	-	-	-	-
117	DM	5.5	7	8	7	7	5	10	0	0	0	0	0	0	-	-	-	-
118	DM	13.8	10	13	12	14	7	10	0	0	0	0	0	0	-	-	-	-
119	DM	0	19	21	18	18	6	5	0	0	0	0	0	0	-	-	-	-
120	DM	8.3	6	8	10	10	5	9	0	0	0	0	0	0	-	-	-	-
121	DM	0	9	9	10	10	5	6	0	0	0	0	0	0	-	-	-	-
122	DM	25	9	9	8	8	5	4	0	0	0	0	0	0	-	-	-	-
123	DM	16.6	12	15	16	16	9	8	0	0	0	0	0	0	-	-	-	-
124	DM	0	15	16	16	16	5	10	0	0	0	0	0	0	-	-	-	-
125	DM	28.1	5	5	7	6	5	10	0	0	0	0	0	0	-	-	-	-
126	DM	16.6	9	9	10	10	5	12	0	0	0	0	0	0	-	-	-	-
127	DM	0	17	18	18	20	5	10	0	0	0	0	0	0	-	-	-	-
128	DM	5.5	11	14	16	16	5	9	0	0	0	0	0	0	-	-	-	-
129	DM	0	16	18	20	20	3	5	0	0	0	0	0	0	-	-	-	-

130	DM	30.5	4	4	6	5	7	4	0	0	0	0	0	0	-	-	-	-
131	DM	28.1	15	15	18	19	8	5	0	0	0	0	0	0	-	-	-	-
132	DM	5.5	18	18	12	10	7	9	0	0	0	0	0	0	-	-	-	-
133	DM	5.5	15	15	10	10	10	10	0	0	0	0	0	0	-	-	-	-
134	DM	5.5	15	15	6	6	10	10	0	0	0	0	0	0	-	-	-	-
135	DM	16.6	15	15	8	8	4	4	0	0	0	0	0	0	Mild	Mild	0	0
136	DM	37.5	20	25	11	12	10	10	0	0	0	0	0	0	-	-	-	-
137	DM	13.8	24	25	14	14	10	10	0	0	1	1	16	16	-	-	4	4
138	DM	28.1	25	20	11	11	10	10	8	8	0	0	0	0	-	-	-	0
139	DM	16.6	15	15	8	8	4	4	0	0	0	0	0	0	MILD	MILD	-	-
140	DM	8.3	15	15	6	6	10	10	0	0	0	0	0	0	-	-	-	-