# EVALUATION OF OCULAR SURFACE DISEASE AMONG CIGARETTE SMOKERS

**JASON ALLAN CHEAH SENG SOON**

DISSERTATION SUBMITTED IN
PARTIAL FULFILLMENT OF THE
REQUIREMENT FOR THE DEGREE OF
MASTER OF MEDICINES
(OPHTHALMOLOGY)


UNIVERSITI SAINS MALAYSIA
2023

# DISCLAIMER

I hereby certify that the work in this dissertation is my own except for the quotations and summaries which have been duly acknowledged.

Date: 20.05.2023

_____

Dr Jason Allan Cheah Seng Soon

P-UM0263/19

# ACKNOWLEDGEMENT

First and foremost, I would like to express my sincere thanks and gratitude to my supervisor Dr Julieana Muhammed, a senior lecturer who expertise in cornea and ocular surface disease in the Department of Ophthalmology and Visual Science, School of Medical Sciences, Universiti Sains Malaysia for her continuous support and guidance throughout my Master program journey and particularly in completing my dissertation.

My deepest appreciation to Dr. Jamalia Rahmat, a senior lecturer in the Department of Ophthalmology, Hospital Kuala Lumpur for her guidance as my co-supervisor in this dissertation. My earnest gratitude to Professor Dr. Hajjah Shatriah Ismail, head of department, and all the lecturers in the Department of Ophthalmology and Visual Science, School of Medical Sciences, Health Campus, Universiti Sains Malaysia for their advice and encouragement throughout my course.

I would like to thank my colleagues and staffs of the ophthalmology clinic for their kind assistance throughout my course as well as in completing my dissertation. My appreciation to Dr. Siti Azrin (lecturer of the Biostatistics and Research Methodology Unit, Universiti Sains Malaysia), for her invaluable advice and in the analysis of data.

Last but not the least, I will be forever thankful to have the support, encouragement, and unceasing love from my parents and siblings to achieve my ambition.

**PAGE**

**TABLE OF CONTENTS**

**List of Tables** **Page**

**List of Figures** **Page**

**Abbreviations**

| | |
|---|---|
| DED | Dry Eye Disease |
| DEWS | Dry eye workshop |
| HUSM | Hospital Universiti Sains Malaysia |
| MGD | Meibomian gland disease |
| OSD | Ocular Surface Disease |
| OSDI | Ocular Surface Disease Index |
| TBUT | Tears Break Up Time |
| TFOS | Tear film and ocular surface society |
| SD | Standard Deviation |

# Abstrak


**Pengenalan**

Penyakit permukaan mata mewakili spektrum gangguan yang menjejaskan permukaan mata dan penyakit mata kering adalah yang paling utama dalam kalangan penyakit permukaan mata. Asap tembakau muncul sebagai salah satu ancaman kesihatan awam di dunia masa kini, sama ada pendedahan secara langsung atau secara tidak langsung. Ini boleh membawa kepada penyakit okular seperti degenerasi makula yang berkaitan dengan usia, penyakit mata tiroid dan penyakit permukaan okular.

**Objektif**

Untuk menilai parameter penyakit permukaan okular di kalangan penghisap rokok.

**Methodologi**

Kajian keratan rentas telah dijalankan di klinik oftalmologi Hospital Kuala Lumpur dan Hospital Universiti Sains Malaysia daripada Disember 2020 hingga Jun 2022. Sampel dipilih dengan kaedah persampelan mudah . Peserta yang memenuhi kriteria inklusi akan dipilih. Peserta dibahagikan kepada kumpulan penghisap rokok dan kumpulan tidak

menghisap rokok. Para peserta daripada kedua-dua kumpulan kemudian menjalani sesi jawab soalan ‘ocular surface disease index (OSDI)’, ‘tears break up time (TBUT)’, ‘Schirmer test’ dan perwarnaan fluorescein pada kornea.

**Keputusan**

Seramai 160 peserta (80 mata dari pesakit penghisap rokok dan 80 mata dari pesakit tidak menghisap rokok) telah disertakan dan purata umur adalah 32.5 dan 30.78. Purata bacaan ‘TBUT’ dalam kumpulan penghisap rokok adalah lebih rendah (7.16 saat) daripada kumpulan tidak menghisap rokok (13.91) dan perbezaannya adalah ketara ($p<0.01$). Manakala purata skor ‘OSDI’ dan perwarnaan pendarfluor pada kornea adalah lebih tinggi dalam golongan penghisap rokok 8.35 vs 2.98 dan 1.43 vs 0.13, perbezaan ini juga adalah ketara ($p<0.01$). Purata ‘Schirmer test’ adalah lebih rendah dalam kumpulan penghisap rokok. Walau bagaimanapun, perbezaan ini tidak ketara. Apabila menilai perhubungan antara parameter mata kering dengan tempoh masa merokok, terdapat perhubungan positif yang ketara dalam skor ‘OSDI’ dan tanda pendarfluor pada kornea ($p<0.01$) dan perhubungan negatif yang ketara dalam ‘TBUT’ ($p<0.01$). Manakala terdapat perhubungan negatif yang ketara dalam ‘TBUT’ dengan bilangan rokok yang dihisap dalam sehari ($p<0.05$).

## Kesimpulan

Terdapat perbezaan yang signifikan di antara purata ‘TBUT’, ‘OSDI’ dan tanda fluorescein pada kornea antara kumpulan penghisap rokok dan kumpulan bukan penghisap rokok. Terdapat juga korelasi signifikan di antara tempoh dan bilangan asap rokok dengan parameter permukaan kornea terutama ‘TBUT’ dan perwarnaan fluorescein pada kornea. Oleh itu, perubahan gaya hidup dalam berhenti merokok dapat mengurangkan kejadian penyakit mata kering di samping mendidik dan menggalakkan perubahan tingkah laku penggunaan rokok di kalangan remaja dan dewasa muda.

# Abstract


## Introduction

Ocular surface disease (OSD) represents a spectrum of disorders that affect the surface of the eye and dry eye disease is the most common of the OSD. Tobacco smoke is emerging as one of the public health threats in the current world, whether direct or indirect exposure. This can lead to ocular disease such as age-related macular degeneration, thyroid eye disease and ocular surface disease.

## Objective

To evaluate the ocular surface disease parameters among cigarette smokers

## Methodology

A cross-sectional study was conducted in ophthalmology clinic of Hospital Kuala Lumpur and Hospital University Sains Malaysia from Dec 2020 till June 2022. The samples were selected with the convenience purposive sampling method. The participants who fulfilled the inclusion criteria were recruited. Participants were divided into cigarette smoker group and non-cigarette smoker group. The participants in both groups then undergo dry eye assessment such as Ocular Surface Disease Index (OSDI) score, Tear break up time (TBUT), cornea fluorescein staining and Schirmer

test.

**Result**

A total of 160 participants (80 eyes in cigarette smokers and 80 eyes in non-cigarette smokers group) with mean age of 32.50 in smoker and 30.78 in nonsmoker group were recruited. Mean TBUT was lower in the cigarette smoker group (7.16 sec) than the non cigarette smoker group (13.91 sec) and the difference was statistically significant ($p<0.01$). While the other mean ocular surface parameters which are statistically significant ($P<0.01$) were OSDI and cornea fluorescein staining in which cigarette group was 8.35 vs 2.98 and 1.43 vs 0.13. Mean Schirmer test was slightly lower in cigarette smoker group. However, this was not statistically different. When assessing the correlation between duration of smoking and ocular surface parameters (OSDI, TBUT, cornea fluorescein staining), there was a statistically significant positive correlation with OSDI score and cornea fluorescein staining ($p<0.01$) and a statistically significant negative correlation with TBUT ($p<0.01$). There was also statistical negative correlation between number of cigarettes smoked and TBUT ($P<0.05$).

**Conclusion**

There was a statistically significant difference in the mean TBUT, OSDI and cornea fluorescein staining between cigarette smoking group and non-cigarette smoking group. There was also statistically significant correlation between duration and

number of cigarette smokes with ocular surface parameters TBUT and cornea fluorescein staining. Therefore, lifestyle change in stopping cigarette smoking can reduce the occurrence of dry eye disease while educating and promoting a behaviour change on cigarette usage among the youths and young adults.

# Chapter 1

# INTRODUCTION

# 1. INTRODUCTION

## 1.1 Background Of Study

Ocular surface disease (OSD) represents a spectrum of disorders that affect the surface of the eyes. The ocular surface comprises the cornea, conjunctiva, eyelids and lacrimal glands and any disorders in these structures can be classified as an OSD. OSD is becoming more prevalent as people are living longer, but knowledge and awareness is limited. Prevalence of OSD is variable through different geographical area, and due to lack of understanding of symptoms, cases are often go undiagnosed or undertreated (Khanna, 2017).

OSD includes condition like Dry Eye Disease (DED), blepharitis, meibomian gland dysfunction (MGD) and so on. DED is one of the most common OSD with incidence ranging from 5.7% to 21.6% (Uchino et al., 2011, Zhang et al., 2012). Symptoms of dry eye and OSD include sensation of dryness, redness, tearing, irritation, burning, foreign body sensation, light sensitivity, and intermittent blurred vision. If left untreated, this can severely affect eyesight and quality of life, and in severe cases lead to blindness.

The dryness of the eye can be detected using combination of different tests to measure of quantity and quality of tears. For example, Schirmer test, tear meniscus height, tear osmolarity, and tear break up time (TBUT). Beside examination, ocular surface disease index (OSDI) is also a good tool in quantify DED (Agrawal et al., 2018).

Tobacco epidemic is the one of the biggest public health threats in current world, killing more than 8 million people a year around the world (Thomas et al., 2012). According to World Health Organization (WHO), there are 1.1 billion of tobacco users in 2015. More

than 7 million of deaths are results of direct tobacco use while remaining 1 million are result of non-smokers being exposed to second-hand smoke. Tobacco use contributes to poverty by diverting household spending from basic needs such as food and shelter to tobacco. The economic costs of tobacco use are substantial and include significant health care costs for treating the disease.

Seven thousands of chemical compounds have been extracted from tobacco namely hydrocarbons, aldehydes, nitrosamines, methanol, carbon monoxide and heavy metals have been extracted. Such chemicals are toxic to eye in acute or chronic exposure (Masmali et al., 2016). This can lead to either ischemia or oxidative mechanism in the eye. The few common causes of eye disorder cause by cigarettes are thyroid eye disease, age related macular degeneration, ischemic optic neuropathy. Tobacco smokes contains fumes, chemical and is toxic to sensitive conjunctival mucosa and leading to conjunctival irritation, lacrimation, and discomfort. It is believed that tear film lipid layer minimise the evaporation of aqueous component of the tear film physiologic state however the negative impact of cigarette smoking in lipid layer is the main cause of deterioration (Agrawal et al., 2018). All this can leads to OSD and DED (Yoon et al., 2005).

## 1.2 Ocular Surface Disease (OSD)

Ocular surface is the interface between the functioning eye and our environment. Anatomically it comprises of palpebral and bulbar conjunctival epithelium, the corneoscleral limbus, the corneal epithelium, and the tear film. Adnexal structures including the anterior lamellae of the eyelids, eyelashes, meibomian glands, and the lacrimal system serve as functional protection to the ocular surface.

The ocular surface functions to maintain optical clarity of the cornea, serves as a refractive surface for accurate projection of light through the ocular media, and provides protection of the structures of the eye against microbes, trauma, and toxins. Compromise the integrity of any one of these protective functions from trauma or disease can lead to various forms of corneal and conjunctival dysfunction including from a mild corneal abrasion to severe stem cell loss, decreased vision, and blindness in the most severe disease.

Disorders of the ocular surface include a variety of conditions. Some of the more common conditions encountered in practice include dry eye disease, blepharitis, ocular allergies and pterygia. In addition, less common but more challenging conditions include limbal stem cell deficiency, and ocular surface disease (OSD) from systemic disease

Though the prevalence of OSD is quite high, unfortunately, cases often go undiagnosed or undertreated, due to a lack of understanding of symptoms, and inaccurate evaluation (Khanna, 2017). OSD includes conditions like DED including aqueous deficiency and mucin deficiency, blepharitis and MGD, allergic eye diseases (AED), chemical and thermal burns and so on (Khanna, 2017).

## 1.3 Classification Of OSD

The different disorders of ocular surface are divided by anatomical involvement as well as its pathophysiology.

### 1.3.1 Eyelids and Eyelashes

If the eyelid margin is not opposed to the corneal surface, significant ocular surface inflammation and mechanical trauma can occur. Flaws in the lid–lash complex, which can lead to instability of the ocular surface are myriad but fall into two basic groups. One group leads to a mechanical rubbing and irritation of the ocular surface and the other is related to poor closure resulting in desiccation of the tissue.

### 1.3.2 Lid Margin and Meibomian Glands

Blepharitis is a broad term used to describe inflammation of the lid as a whole. Anterior blepharitis is defined as inflammation of the lid margin anterior to the grey line and centered on the lashes. Marginal blepharitis refers to inflammation of the lid margin and includes both anterior and posterior blepharitis. Posterior blepharitis describes inflammation of the posterior lid margin Meibomian gland disease is used to describe a broad range of meibomian gland disorders, including neoplasia, congenital disease, and MGD. MGD is defined as a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion. It may result in alteration of the tear film, symptoms of eye irritation, clinically apparent inflammation, and ocular surface disease.

### 1.3.3 Tear Film and Dry Eye Syndrome

The Asia Dry Eye Society classification report suggest definition, diagnostic criteria and classification system should be practical and simple enough to be integrated into daily practice (Tsubota et al., 2020). DED can be broadly categorized into aqueous deficient dry eye and evaporative dry eye. Aqueous deficiency occurs due to reduction on aqueous production from lacrimal glands. It account for a tenth of DED (Findlay and Reid, 2018). Evaporative dry eye disease occurs due to excessive tear evaporation resulting in deficient tear film lipid layer. It is the most common form of DED (Findlay and Reid, 2018).

Differentiation of the subtype is important to classify the disease. However, TFOS DEWS mentioned that DED is a spectrum of disease, involving both evaporative and aqueous deficient subtypes, with overlapping of the pathophysiological entities. Identification of the main etiology is deemed most useful in guiding and deciding on treatment plans.

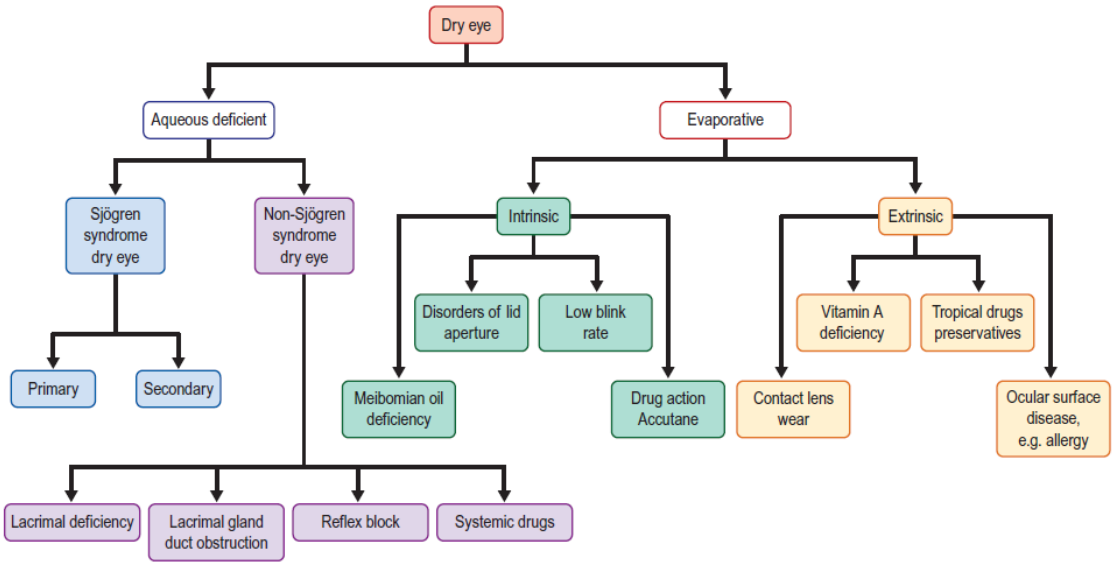


Figure 1 Classification of Dry Eye Disease (Edward J. Holland, 2013)

### 1.3.3.1 Evaporative Dry Eye Diseases

Evaporative dry eye comprises of over 85% of DED. It occurs due to excessive tear loss from ocular surface as a result of deficient or abnormal lipid layer in the tear film, in presence of normal lacrimal secretory function. Causes include meibomian gland dysfunction and blepharitis (Findlay and Reid, 2018). The causes can be divided into intrinsic and extrinsic. In evaporative dry eye, excessive evaporation of the tear film layer leads to ocular surface damage, triggering the ocular inflammatory cascade. This results in corneal epithelial injury which stimulates sensorial corneal nerve endings leading to symptoms of discomfort, increased blinking and compensatory reflex lacrimal tear secretion. Loss of normal mucin layer which is the innermost part of tear film layer that normally adhere on the corneal epithelial cells contributes to gritty and foreign body sensation by increasing frictional resistance between lids and globe. In severe cases, vision may also be compromised. As a result of these signs and symptoms, patients' ocular health, general well-being and quality of life may be greatly affected.

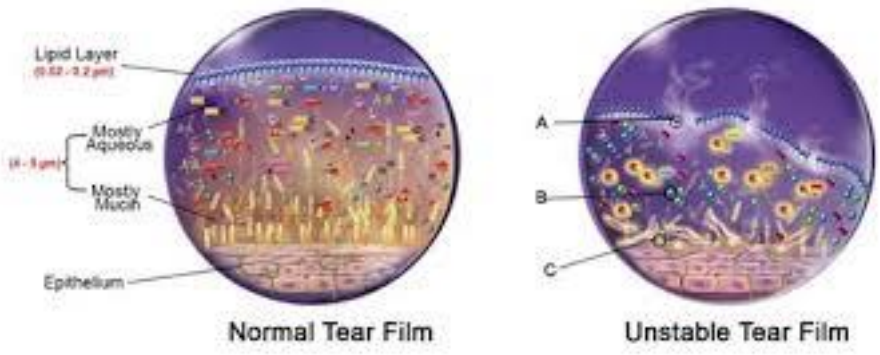


Figure 2: Illustration of unstable tear film (Edward J. Holland, 2013)

### 1.3.3.2 Prevelance Of DED

Global epidemiological studies have shown a prevalence of DED ranging from five to 50% (Stapleton et al., 2017). The National Health and Wellness Survey showed 6.8% of the United States adult population being diagnosed with DED (Farrand et al., 2017). In Asia, China reported prevalence of 17.0 %, (Liu et al., 2014) Indonesia reported 27.5% (Lee et al., 2002) and India had the highest with 29.3% of dry eye prevalence (Gupta et al.,2010).

### 1.3.3.3 Mechanism and risk factor of DED

There are several risk factors that leads to the development of DED (Figure 2). The most obvious factors associated with DED are increasing age, female gender and hormonal changes. Connective tissue disease is associated with more severe forms of DED, e.g. Sjögren's syndrome and graft-versus-host disease. Dry eye disease occurs with greater frequency in women, particularly in the menopausal and postmenopausal years. Table 1 listed the risk factors of DED according to most consistent evidence with well conducted study published, suggestive evidence which inconclusive information from peer reviewed publications or inconclusive information, and unclear evidence implies directly conflicting information in peer reviewed publications or inconclusive information (2007).

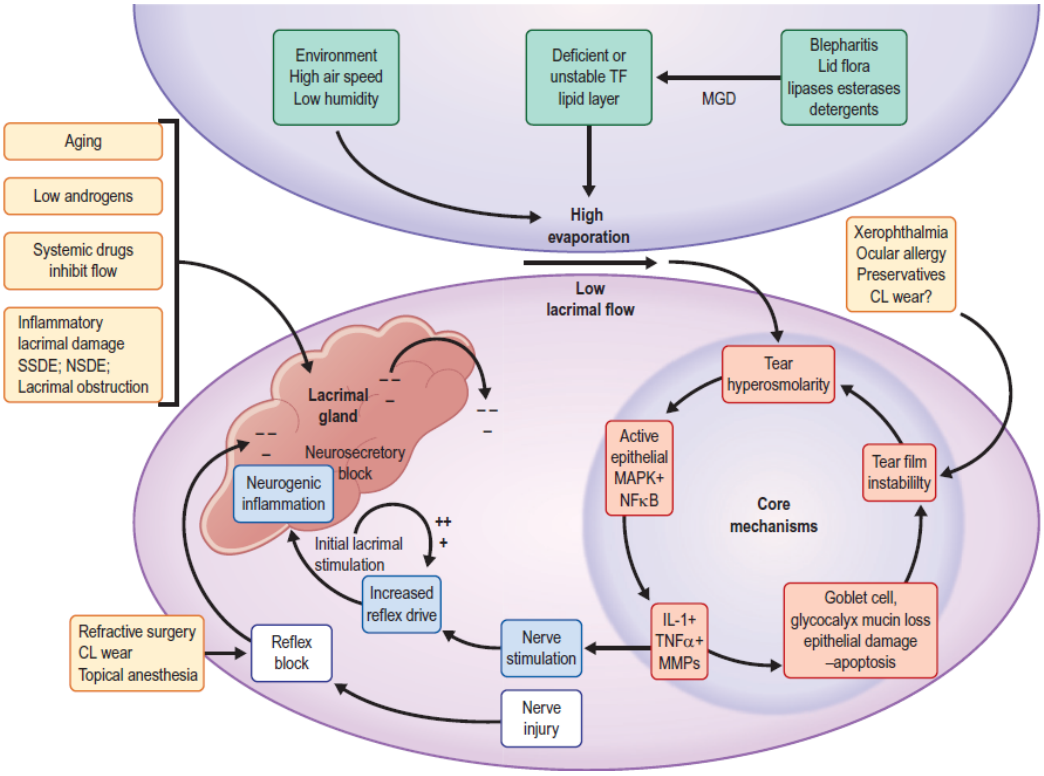


Figure 3: Mechanism of Dry Eye Disease (2007)

| **Most consistently** | **Suggestive** | **Unclear** |
|---|---|---|
| Older age | Asian race | Cigarette smoking |
| Female sex | Medications | Hispanic ethnicity |
| Postmenopausal estrogen therapy | Tricyclic antidepressants | Anticholigernic |
| Omega 3 and omega 6 fatty acids deficiency | Selective serotonin reuptake inhibitors | Anxiolytics |
| Connective tissue disease | Diuretics | Alcohol |
| LASIK and refractive excimer laser surgery | Beta blockers | Pregnancy |
| Vitamin A deficiency | Diabetes mellitus | Oral contraceptives |

Table 1 Risk factors of DED (2007)

#### 1.3.3.4 Pathophysiology of DED

Although there are numerous risk factors for the development of dry eye disease, the final common expression of the pathophysiology includes tear film hyperosmolarity and instability.

Tear hyperosmolarity is considered the central mechanism in DED, leading to inflammation at the ocular surface with resulting tissue damage and symptoms (2007). The hyperosmolar state is the result of either an insufficient secretion of fluid from the lacrimal glands (low aqueous flow) and/or excessive evaporation of the tear film. Normal tear osmolarity averages around 295 mOsmol/L which is isotonic with blood. Tear osmolarity over the ocular surface is greater than that in other tear compartments (e.g. the menisci), because of the larger surface area of the interpalpebral space, allowing for evaporative water loss between blinks (Edward J. Holland, 2013).

Hyperosmolarity affects the ocular surface in multiple ways. Hyperosmolarity initiates a cascade of inflammatory events mediated by at least two separate pathways, leading to the recruitment and activation of inflammatory cells on the ocular surface and the production of inflammatory cytokines and chemokines. Associated with these changes is an increase in surface cell death, changes in mucin production and a loss of lubrication between the lid and the ocular surface (Edward J. Holland, 2013).

Tear film instability results from disturbances in the mucin cover of the cornea and are responsible for the rapid break-up. Tear break-up can occur over areas of corneal irregularity and are more rapid and extensive (Edward J. Holland, 2013).

### 1.3.4 Conjunctiva

The conjunctiva has a relatively simple histological structure that limits the response to inflammatory stimuli to five morphologic responses: papillary, follicular, membranous/pseudomembranous, cicatrizing, and granulomatous. If the conjunctivitis involves only the epithelium and is short-lived, normal conjunctival anatomy and function will return once the inflammation has resolved. The end result of severe and chronic inflammation is irreversible changes, such as goblet cell damage and deficiency. Because goblet cells secrete mucin, which helps the aqueous tears coat the hydrophobic ocular surface, their loss will result in tear film abnormalities. Chronic conjunctival inflammation may lead to changes in the substantia propria of the conjunctiva, resulting in subepithelial fibrosis (Lindquist, 2005)

### 1.3.5 Corneal Epithelium

The corneal epithelium is continuous with the conjunctival epithelium, and both are composed of nonkeratinized, stratified, squamous epithelium cells, however, it is susceptible to desiccation if not properly protected by the lids and tear film. Some conditions not mentioned, that involve the cornea epithelium, include pterygium, corneal adhesion disorders, neurotrophic keratopathy, ocular surface neoplasias, and filamentary keratitis. The above-mentioned condition can lead to DED (Edward J. Holland, 2013).

### 1.3.6 Limbal Stem Cell Deficiency

Problems with the limbal stem cell population result in a decrease in the ability of the corneal epithelium to repopulate itself. Most cases of stem cell deficiency are acquired; however, congenital causes include aniridia, dominantly inherited keratitis, and ectodermal dysplasia. Acquired cases include chemical/thermal injury, contact lens use,

Stevens–Johnson syndrome, ocular cicatricial pemphigoid, and rheumatoid arthritis (Edward J. Holland, 2013).

### 1.4 Diagnostic Assessment of OSD

In regard to evaporative dry eye, diagnosis is usually made through history, ocular and systemic examination. There are particular diagnostic tools which assesses the specific components of evaporative dry eye. Cornea and conjunctival fluorescein staining determines the presence of OSD. The increased shedding of cornea and conjunctival cells, results in loss of protective glycocalyx barrier. This area of epithelial loss is readily visible using fluorescein strips places on the cornea and conjunctival against cobalt blue light at the slit lamp. Similarly, TBUT allows the assessment of tear film stability using fluorescein strips and cobalt blue light at the slit lamp. It is known that TBUT is reduced in DED. A validated questionnaire Ocular Surface Disease Index (OSDI) used clinically to discriminate between normal, mild to moderate, and severe dry eye based in score (Ramli et al., 2015, Agrawal et al., 2018). It has been used in many clinical trials and easy to use in clinics.

Newer additional diagnostic tests are impression cytology, tears osmolarity analysis, matrix metalloproteinase-9 analysis, rapid antigen detection for various ocular infectious diseases, and comprehensive analysis of the tear film and lipid. Other additional advanced diagnostic tools include confocal microscopy, optical coherence tomography (OCT) of the anterior segment, and Scheimpflug imaging of the cornea. The new device such as confocal microscopy evaluate ocular surface at the cellular level.

### 1.4.1 Slit Lamp Examination

The slit lamp examination is a crucial part of the process when evaluating any ophthalmologic patient and is no different for the individual with ocular surface disease. Careful, systematic examination from the outside to the inside of the eye should be performed every time. Care should be taken to specifically evaluate the condition of the meibomian glands and the entire conjunctival surface, including the palpebral areas, looking for inflammation and scarring.

### 1.4.2 Tear Break Up Time (TBUT)

The tear break-up time (TBUT) is defined as the time interval between a complete blink and the first appearance of a dry spot in the tear film after fluorescein administration (Lemp, 1973). It is believed that this represents an unstable tear film, whereby the mucous layer may rupture, allowing the aqueous to come in contact with exposed epithelium. More than 10 seconds defined as normal and values less than 10 seconds as abnormal.

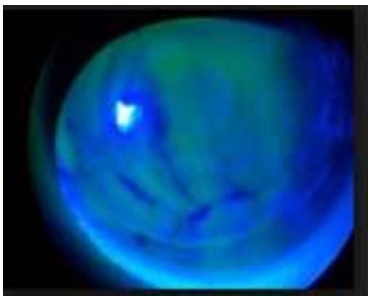

Figure 4: Abnormal TBUT

### 1.4.3 Corneal Fluorescein Staining

Many available dyes in market but the common one is fluorescein. The presence of corneal staining can be defined as more than one dot of fluorescein staining over the corneal surface. Punctate staining was recorded using an Oxford grading scheme that was dependent on the of staining in each eye. The staining area was graded by log-linear increase in number of dots on a numerical scale of 0–5, Grade 0 = 1–9 dots (Absent); Grade I = 10–31 dots (Minimal); Grade II = 32–99 dots (Mild); Grade III = 100–315 dots (Moderate); Grade IV = 315 dots (Marked); Grade V = 315+ (Severe) (Bron et al., 2003)

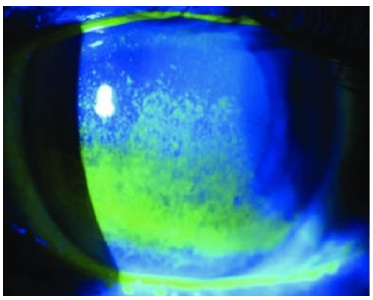

Figure 5 Cornea Fluorescein Staining

| Panel | Grade | Verbal description |
|---|---|---|
| A | 0 | Absent |
| B | I | Minimal |
| C | II | Mild |
| D | III | Moderate |
| E | IV | Marked |
| >E | V | Severe |

Figure 6: Oxford Grading Of Cornea Fluorescein Staining (Chien et al., 2017)

### 1.4.4 Schirmer Test

Schirmer test is the most common and Schirmer scores, representing the length of wetting (in mm) on the strip, are routinely used as a key diagnostic criterion for dry eye. The test involves the insertion of a small piece of filter paper into the lower fornix of the eye. There are two variations of the Schirmer test: Schirmer I measures total tear secretion (basal and reflex). Schirmer II is a measure of reflex secretion only and involves nasal stimulation following insertion of the strip. A variation of the Schirmer I that may allow measurement of basal secretion involves the application of topical anaesthetic prior to strip insertion. Although performing the Schirmer I with anaesthetic may provide a more accurate picture of basal secretion, the utility and overall effectiveness of anaesthetic administration in conjunction with the Schirmer is controversial.


Figure 7: Schirmer Strip Test

### 1.4.5 Patient Questionnaire

The Ocular Surface Disease Index (OSDI) is a questionnaire that has been validated to discriminate between normal, mild to moderate, and severe dry eye disease as defined by the physician's assessment and a composite disease severity score. It has been demonstrated to have the necessary psychometric properties to be used as an end point in clinical trials, and as such, it could be an important tool for in-office support for the diagnosis of ocular surface disease that is easy to administer. (Appendix B)

## 1.5 Management of DED

### 1.5.1 Treatment of Ocular Surface Disorders

Managing OSD is challenging even for experienced clinician. Presentation is complex and overlapping, but fortunately it can still be managed effectively by medical or surgical treatment. Generally, management comprises of the following:

### 1.5.2 Eliminate exacerbating factors

Many topical drops have preservative, therefore the use of preservative free will benefit patient and reduce irritancy on ocular surface. Other than that, any known allergy should be avoided.

### 1.5.3 Lubricants

A normal physiological tear film is essential in protecting ocular surface. Lubricant or so-called tear substitute not only wets the cornea but also dilutes surface irritants. There are many examples of lubricants that made up of basic substance hyaluronate, carmellose, hypromellose, polyvinyl alcohol, and paraffin. Lubricants with lipids are also available.

Other alternative lubricants such as autologous serum is expansive and not readily available.

### 1.5.4 Control Inflammation

As we know that inflammatory process is involved in the pathophysiology of the disease, by giving anti-inflammatory will aid in preserving ocular surface. The choice of steroids and frequency depends on cases. More potent steroid used in severe allergic cases and weak steroids are used in mild cases. Cyclosporin topical drops has also shown to benefit patient in the long run, and not acute setting. They are effective in controlling the inflammation without having the side effects of steroids.

### 1.5.5 Management Of Persistent Corneal Epithelial Defect

Therapeutic contact lens can be applied once infection has been ruled out or treated. Many available such as hydrogel, silicone, and others. Severe cases may need the use of rigid gas permeable scleral contact lens to prevent excessive evaporation.

### 1.5.6 Surgical Management

This are reserved for cases that failed medical therapy or it is due to other form of ocular disease. In patient with aqueous deficient dry eye, puncta plug or permanent occlusion will alleviate patient symptoms. Apart from that those who had persistence epithelial defect may benefit from temporary tarsorrhaphy and is indicated in patient who is unconscious and bed bound.

## 1.6 Effect of Cigarette Smoking

Tobacco use kills more than five million people per year and is responsible for one in 10 adult deaths. Among the five greatest risk factors for mortality, smoking is the single most preventable cause of death. It is estimated that tobacco use will kill more than eight million people per year by 2030 (Thomas et al., 2012).

Cigarettes contain many toxic chemicals such as hydrocarbons, aldehydes, nitrosamines, methanol, carbon monoxide, and heavy metals. Such chemicals can cause permanent damage to proteins, lipids, and nucleic acids (Masmali et al., 2016).

Ocular surface is highly sensitive to air borne chemical fumes and irrigative gas and its persistent exposure may lead to ocular surface damage and dry eye syndrome (Agrawal et al., 2018). The conjunctival mucosa is highly sensitive to airborne chemicals, fumes, and irritative gases that originate in tobacco smoke, leading to conjunctival redness, excessive lacrimation and discomfort due to stimulation of the conjunctival-free nerve endings (Yoon et al., 2005, Moss et al., 2000).

## 1.7 Cigarette Smoking and Its Effect on OSD

Pathogenesis of dry eye including chronic inflammation of the ocular surface, decreased sensitivity of cornea and conjunctiva, reduction of production and/or stability of tears, and epithelial damage (Xu et al., 2016). In another study, the eye irritation scores and indices of smokers were statistically higher than those of nonsmokers (Agrawal et al., 2018). Avunduk et al., (1997) determined a deterioration of projections and loss of microvilli, which are important for stabilizing the tear film in conjunctiva exposed to tobacco smoke. It was found that there is decrease of goblet cells in smokers than that of control group causing damage to the mucin layer lead to unstable tear film (Agrawal et al., 2018). Despite the multifactorial aetiology of these ocular syndromes, smoking is an independent risk factor that has dose-response effects. It causes morphological and functional changes to the lens and retina due to its atherosclerotic and thrombotic effects on the ocular capillaries. Smoking also enhances the generation of free radicals and decreases the levels of antioxidants in the blood circulation, aqueous humour, and ocular tissue (Cheng et al., 2000).

## 1.8 Rationale

Cigarette smoke is a well-known, significant source of toxic minerals and heavy metals, including more than 4000 toxic chemical substances. Direct contact with the ocular surface from its toxic and irritative contents leads to chronic inflammation of the ocular surface, decreased sensitivity of cornea and conjunctiva, reduction of production and/or stability of tears, and epithelial damage.

Despite the availability of important epidemiological data on hazardous effects of cigarette smoke, there are surprisingly only a few studies related to the alterations of the ocular surface and tear functions in cigarette smokers.

There have been insufficient studies to determine the specific effects of smoking on tear film and ocular surface including cornea and conjunctiva although cigarette smoking is known to cause conjunctival irritation. The relationship between smoking and dry eye has not been studied extensively, but for those with dry eye, smoking is a significant irritant that leads to symptoms such as scratchiness, foreign body sensation, burning of the eyes and grittiness.

In this study, we aim to prove the effects of long-term exposure to cigarette smoke on the precorneal tear film and ocular surface health of in chronic healthy smokers and compared the results with those of non-smoker subjects due to its direct contact with irritative, toxic content and heavy metals of cigarettes. This study will provide new insight to medical world about the association of tobacco uses and severity of OSD. These findings will contribute to the management of OSD by modifying the relevant associated lifestyles. This study can be used as a reference data for other studies. Furthermore, it

will provide an evidence-based information to educate and promote a behaviour change on cigarette usage among the youths and young adults.

# Chapter 2

# STUDY OBJECTIVES

## 2.1 Research Questions

1. Do cigarette smokers have lower OSDI score, lower tear film break up, more corneal fluorescein staining, and lower Schirmer score compared to non-smokers?

2. What is the correlation between the duration of cigarettes smoking and OSD parameters (OSDI score, tear film break up, corneal fluorescein staining and Schirmer score)?

3. What is the correlation between the mean number of cigarette sticks smoked with OSD parameters (OSDI score, tear film break up, corneal fluorescein staining and Schirmer score)?

## 2.2 Research Hypothesis

1. Cigarette smokers have lower OSDI score, lower tear film break up, positive corneal fluorescein staining and lower Schirmer score compared to non-smokers.

2. There is a significant correlation between the duration of cigarette smoking and OSD parameters (OSDI score, tear film break up, corneal fluorescein staining and Schirmer score).

3. There is a significant correlation between the mean number of cigarette sticks smoked and OSD parameters (OSDI score, tear film break up, corneal fluorescein staining and Schirmer score).

## 2.3 General Objective

To evaluate the ocular surface disorder among cigarettes smokers.

## 2.4 Specific Objectives

1. To compare the mean ocular surface disease parameters (OSDI score, tear film break up, corneal fluorescein staining and Schirmer score) between smokers and non-smokers.

2. To correlate between the durations of cigarette smoking and OSD parameters (OSDI score, tear film break up, corneal fluorescein staining and Schirmer score).

3. To correlate between the mean number of cigarette sticks smoked with OSD parameters (OSDI score, tear film break up, corneal fluorescein staining and Schirmer score).