



REVIEW ON THE PREVALENCE OF DRY EYE DISEASE

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Abstract: Dry eye disease (DED) is a multifactorial disease of the tears and ocular surface that is associated with hyperosmolarity of tear film which in turn leads to inflammation and damage of the ocular surface that accompanied with ocular symptoms of discomfort, fatigue and disturbance in vision. The burden of DED to the patient is not negligible. It may result from dysfunction of a superficial lipid layer, a middle aqueous layer, an innermost mucin layer, either singly or in combination.

Prevalence of DED varies country to country, from Asian region to Western region around the world, with a range of between 4.34 –93.2%. Various population-based studies have been done to find out the prevalence and the magnitude of the problem. The variation of the prevalence rate depending on which study is cited, how the disease is diagnosed, and which population is surveyed. Disparities in epidemiological information could arise from age difference, gender characteristics, occupational dissimilarity, risk factors, and differences in etiological factors, which can vary significantly among studies. Studies confirmed that prevalence increases with age and women have a higher prevalence of DED than men. Different occupation and geographic area also attributed risk factors of DED. Different questionnaires used to evaluate symptoms and its impact of our daily life.

Generally, DED patients may experience ocular discomfort, including burning sensation, foreign body sensation, grittiness, itching and watering. Others may complain of dryness, ocular fatigue, photophobia, visual disturbance and also sometimes redness. Symptom assessment is a key component of clinical dry eye diagnosis. The prevalence of symptoms was higher and more variable than signs. Several diagnostic tests have been used to assess the quantity; quality and functioning of various layers of tear film and diagnose of Dry Eye Disease. tests like Meibomian Gland Dysfunction test, Tear Film Breakup Time test, Fluorescein staining test, Rose Bengal staining test, Lissamine Green test and Schirmer's test are commonly used in clinical practice.

DED is not only limited to signs and symptoms, some of the studies included in this review reported various diseases, several type of medication, environmental factors, in fact age and sex having associations with DED. Studies suggest that DED can have a considerable impact on visual function, daily activities, social and physical functioning, workplace productivity, and direct and indirect costs of the disease, with a substantial effect on sense of well-being that limits important daily activities and leads to a significantly reduced quality of life. Subjects with dry eye are more likely to develop problems carrying out professional work, using a computer, reading newspaper, watching TV and driving.

Future research should establish the prevalence of disease of varying severity, the incidence in different populations and elucidate the impact of climate, environment and socioeconomic factors. More studies have to done in future to explicate the correlation of dry eye symptoms and signs as in this study we are not discuss about the strong relationship between two.

Method of Literature Search:

A systemic literature review was performed using PubMed and Google Scholar database to collect the studies oriented to dry eye. Mainly focused on the prevalence of dry eye in different region worldwide. The search strategy was not limited by year of publication.

Index Terms – Dry Eye Disease (DED), Prevalence, Tear film, Questionnaire, Etiological risk factors, Quality of life.

I. INTRODUCTION

Dry eye is most common economic burden worldwide and most significantly increasing clinical problem in developing countries. The term “dry eye” can be attributed to the Swedish Ophthalmologist Henrik Sjogren, who described the triad of dry eye, dry mouth, joints pains in the year 1993 [1].

In 2007, the International Dry Eye Workshop (DEWS) defined “Dry eye disease is a multifactorial disease of tear film and ocular surface that results in symptoms of discomfort, visual disturbance, and tears instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface” [2]. According to the recent official report of the International Dry Eye Workshop (DEWS 2017), that based on summary of the findings of current research, DED was defined as “Dry eye disease is a multifactorial disease of the tears and ocular surface that is associated with hyperosmolarity of tear film which in turn leads to inflammation and damage of the ocular surface that accompanied with ocular symptoms of discomfort, fatigue and disturbance in vision” [3].

Additionally, DED can be categorized as episodic or chronic. Episodic dry eye occurs when environmental or visual tasks with reduced blinking overwhelm the stability of the tear and produce symptomatic dry eye. Chronic dry eye, although aggravated by the same environmental conditions, persists continuously with symptoms and possible damage to the ocular surface [4]. DES is also called Keratoconjunctivitis sicca (KCS), keratitis sicca, sicca syndrome, xerosis, xerophthalmia, dry eye disease, ocular surface disease, or dysfunctional tear syndrome, simply dry eyes, or dysfunctional lacrimal functional unit. Dry eye disease is characterized by instability or abnormality in the precocular tear film that can be due to

1) insufficient amount of tear production which is called aqueous production deficient dry eye disease

2) poor quality of tear film, which results in increased evaporation of the tears, is called evaporative dry eye disease. Meibomian gland dysfunction (MGD) is the most common cause of evaporative dry eye disease.

The precocular tear film, classically, is a three-layered structure consisting, from posterior to anterior, of the mucous, the aqueous and the lipid layers [5], either single or in combination. For some people, the cause of dry eyes is decreased tear production. For others it's increased tear evaporation and an imbalance in the makeup of tears. The deficiency of aqueous component of tear film is known as Keratoconjunctivitis Sicca. Xerophthalmia occurs when the xerotic process spreads over the cornea, mainly caused by vitamin A deficiency. It can be a component of systemic disease including Sjogren's syndrome, lupus, and Stevens-Johnson syndrome. In addition, factors such as contact lens wear and adverse environmental exposure such as arid environments, windy conditions, or visual tasking can (computer vision syndrome) exacerbate the symptoms of dry eye [1]. Patients with dry eye disease may experience a bunch of symptoms such as dryness, irritation, foreign body sensation, photophobia, eye fatigue/ felling sleepy, discharge, redness, watering, grittiness, heaviness, pain, visual disturbance etc. which hamper their daily activities as well as quality of life. Patients may complain of symptoms of dry eye in the presence or absence of signs of the disease [6]. DED can be assessed based on a combination of symptoms and signs. However, several studies reported poor correlation between DED symptoms and signs [3].

Symptom-based Dry eye assessment were evaluated by using different types of validated questionnaire that include questions allow for the monitoring of dryness symptoms and their frequency and or their severity over time [3]. Examples of these questionnaires include: Ocular Surface Disease Index (OSDI), Dry Eye Questionnaire (DEQ), McMonnies Questionnaire, Impact of Dry Eye on Everyday Life (IDEEL), Dry Eye Epidemiology Project (DEEP), Standard Patient Evaluation of Eye Dryness (SPEED), Women's Health Study (WHS) Questionnaire etc.

Objective Dry eye assessment were performed by the patients underwent different types of comprehensive examination test like, Schirmer's test, Tear Film Breakup Time (TBUT), assessment of Meibomian Gland Dysfunction (MGD), assessment of the ocular surface through corneal and conjunctival staining by Fluorescein, Rose Bengal, Lissamine Green etc.

Dry eye is recognized as a growing public health problem and one of the most frequent reasons for visiting an ophthalmologist in middle and old age people [7].

II. PURPOSE OF THE STUDY

Dry eye disease (DED) is most growing public health problem and common conditions seen by eye care practitioners. Current trends of industrialization, urbanization, and modernization could result in a shift to other forms of DED. Many studies conclude the prevalence rate of DED particular into a region. But dry eye is not limited with a region, it becomes an economic burden worldwide day by day. In this modern technological generation, most of population engaged with various kind of electronic devices. In fact, now a day's children use mobile phones for paying games rather than to go outside and so many organizations used to teach children through online classes. For that reason, children connected with mobile phones or computer for a long period of time. Not only young age group, DED also affects in older age group. The retired persons are also kept themselves to watching television, using computer for banking or playing games or for their personal work. Because of that, they all are facing the problems like redness, heaviness, burning sensation, grittiness, tiredness, blur vision etc. which hamper their daily life. Due to a wide variety of presentations and symptoms, it often frustrates the ophthalmologists as well as patients. From this study we gather knowledge regarding the problems related to dry eye and summarize knowledge on the prevalence and incidence of DED from well-designed population studies.

Herein, a review the epidemiology of DED in these geographic areas, prevalence rate, highlighting potential causes and risk factors of DED while presenting information on diagnostic tools of DED that could useful to clinicians and think about the solution faster.

III. DEMOGRAPHICS OF DRY EYE DISEASE

The prevalence of DED is greatly influenced by geographic location, climatic conditions, and lifestyle of the people [8], and the tear film and ocular surface society dry eye workshop II epidemiology report stated globally prevalence of dry eye ranges from 5 to 50% [9].

This is probably because of two factors: First, the geographical location of the study population and secondly, there is no standardization of the selected population, dry eye questionnaires, objective tests and dry eye diagnostic criteria [10].

1. Dry Eye Prevalence in Asian & Western Countries:

In general, it was reported that prevalence of DED more prevalent in Asian countries compared to Western countries. Reported prevalence of dry eye in the literature is diverse ranging between 7.8% in one study from western world to 93.2% in one study from Asia [11],[12]. Asian studies on Dry Eye Disease showed that the prevalence of dry eye is higher than that in western population and ranged between 14.5% and 93.2%. Studies from India reported that the prevalence varies between 18.4% and 64% [13].

Table 1- Prevalence of Dry Eye in Different Population-based studies in Asian Countries:

SL NO	Authors	Place	Sample Size	Age (Year)	Diagnostic Criteria- Prevalence Rate %
1	Basak <i>et al.</i> , 2012 [10]	West Bengal, India	3023	>30	6 item questionnaire: one or more symptoms: often or all the time- 40.8%
2	Suresh <i>et al.</i> , 2018 [14]	Andhra Pradesh, India	100	>20	8 item questionnaire: one or more symptoms often (at least once a week) or all the times- 48%
3	Majumder <i>et al.</i> , 2016 [2]	Assam, India	200	21-60	Symptoms plus any one of abnormal Schirmer's 1 score, Tear film break up time, Tear meniscus height, Fluorescein, Rose Bengal or Lissamine green staining- 32.5%
4	Banik <i>et al.</i> , 2018 [1]	Eastern India	500	>20	Symptoms plus any one of abnormal Schirmer's 1 score, Tear film break up time, Tear meniscus height, Tear meniscus floaters, Fluorescein or Rose Bengal staining 52%
5	Chavhan <i>et al.</i> , 2019 [7]	Maharashtra, India	1562	>30	Ocular Surface Disease Index questionnaire- 24.7%
6	Gupta <i>et al.</i> , 2010 [15]	New Delhi, India	400	>40	McMonnies' & Ocular surface Disease Index questionnaires- 29.25%
7	Titiyal <i>et al.</i> , 2018 [8]	North India	15625	21-40	Ocular Surface Disease Index questionnaire- 32%
8	Sahai & Malik, 2005 [5]	Rajasthan, India	500	>20	13 point 'Dry Eye questionnaire': one symptom sometimes, often or all the time plus any one of abnormal Schirmer's score, tear film break up time or filaments- 18.4%
9	Baisoya <i>et al.</i> , 2016 [16]	Uttarakhand, India	503	Any age	6 item questionnaire: One or more symptoms: sometimes, often or all the time- 46.71%
10	Shah & Jani <i>et al.</i> , 2015 [6]		400	>40	8 symptoms contain IDEEL questionnaire & any one of abnormal Tear film break up time, Meibomian gland function using Fluorescein staining- 54.3%
11	Choudhary <i>et al.</i> , 2015 [17]	Madhya Pradesh, India	1178	21- >51	13 point 'Dry Eye questionnaire' plus any one of abnormal Schirmer's score, Tear film break up time, Rose Bengal test, and Lissamine green staining- 9.6%
12	Gupta, Ranjan <i>et al.</i> , 2014 [18]	Kanpur, India	728	20-59	Ocular Surface Disease Index questionnaire- 33.79%

13	Gupta, Prasad <i>et al.</i> , 2008 [19]	Leh, India	50	20- >60	McMonnies', Ocular Surface Disease Index & Schirmer's test- 20%
14	Adlakha <i>et al.</i> , 2017 [20]	Central India	150	45- >75	Ocular Surface Disease Index questionnaire plus any one of abnormal Schirmer's score, Tear film break up time, Meibomian gland function using Fluorescein or Rose Bengal staining- 34.66%
15	Behara <i>et al.</i> , 2017 [13]	Odisha, India	280	20-83	Symptoms plus any one of abnormal Schirmer's 2 score, Tear film break up time, Meibomian gland function using Fluorescein or Lissamine green staining- 66.4%
16	Lee <i>et al.</i> , 2002 [21]	Indonesia	1058	>21	6 item questionnaire: One or more often or all the time- 27.5%
17	Han <i>et al.</i> , 2011 [22]	Korea	657	> or = 65	6 item questionnaire: One or more often or all the time- 30.3%
18	Jie <i>et al.</i> , 2009 [23]	China	1957	>40	6 item questionnaire: One or more symptoms: Often or all the time- 21%
19	Lin <i>et al.</i> , 2003 [24]	Taiwan	1361	> or = 65	One or more symptoms: often or all the time- 33.7%
20	Yasir <i>et al.</i> , 2019 [25]	Saudi Arabia	320	>40	McCarty Symptom questionnaire- 35.9%
21	Alshamrani <i>et al.</i> , 2017 [26]	Al-Ahsa, Saudi Arabia	1858	16-78	6 item questionnaire: One or more symptoms: often or constantly- 32.1%
22	Bukhari <i>et al.</i> , 2009 [12]	Saudi Arabia	251	Any age	One or more symptoms: Often or all the time- 93.2%
23	Lekhanont <i>et al.</i> , 2006 [27]	Bangkok, Thailand	550	>40	One or more symptoms: Often or all the time- 34%
24	Jamaliah <i>et al.</i> , 2002 [28]	Malaysia	200	>20	One or more symptoms plus one abnormal sign (Tear film break up time or Phenol red thread)- 14.5%
25	Shanti <i>et al.</i> , 2020 [3]	Palestine	769	18-90	Ocular surface Disease Index questionnaire score \geq 13 & presence of any abnormal clinical sign of Schirmer 1 Score, Tear film break up time & Fluorescein corneal staining- 64%

Table 2- Prevalence of Dry Eye in Different Population-based studies in Western Countries:

SL NO	Authors	Place	Sample Size	Age (Year)	Diagnostic Criteria- Prevalence Rate %
1	Martinez <i>et al.</i> , 2016 [29]	Mexico	338	>16	Ocular Surface Disease Index- 43% and Dry Eye Questionnaire-5- 30%
2	Caffery <i>et al.</i> , 1997 [30]	Canada	13517	<10 ->80	One or more symptoms: often or all the time- 28.7%
3	McCarty <i>et al.</i> , 1998 [11]	Australia	926	40-97	Abnormal Rose Bengal test- 10.8% Abnormal Schirmer's test- 16.3% Low Tear film break up time- 8.6% Fluorescein staining- 1.5% Two or more signs- 7.4%
4	Chia <i>et al.</i> , 2003 [31]	Australia	1174	>50	At least one dry eye symptom with moderate to severe intensity- 16.6% Three or more symptoms regardless of severity- 15.3%
5	Schaumberg <i>et al.</i> , 2009 [32] PHS	United States (Men)	25444	>=50	Clinically diagnosed Dry eye disease or severe symptoms (both dryness and irritation constantly or often)- 4.3%
6	Schaumberg <i>et al.</i> , 2003 [33] WHS	United States (Women)	39876	45-84	Clinically diagnosed Dry eye disease or severe symptoms (both dryness and irritation constantly or often)- 7.8%
7	Schaumberg <i>et al.</i> , 2017 [34]	United States (Adults)	75000	>=18	Self-reported Dry eye disease and 8 symptoms contains Dry eye questionnaire- 6.8%
8	Viso <i>et al.</i> , 2011 [35]	Spain	654	40-96	One or more present: often or all the time- 11%
9	Moss <i>et al.</i> , 2000 [36]	United States	3722	48-91	Self-reported history of dry eye- 14.4%
10	Moss <i>et al.</i> , 2004 [37]	United States	2414	48-91	Self-reported history of dry eye- 13.3%
11	Moss <i>et al.</i> , 2008 [38]	United States	13599	43-86	Self-reported history of dry eye- 21.6%
12	Paulsen <i>et al.</i> , 2014 [39]	United States	3286	21-84	Self-report of frequency of symptoms and the intensity of those symptoms- 14.5%
13	Schein <i>et al.</i> , 1997 [40]	United States, Maryland	2420	65-84	6 item questionnaire: One or more present: Often or all the time- 14.6%
14	Bandein-Roche <i>et al.</i> ,1997 [41]	United States, Maryland	2520	65-84	6 item questionnaire: One or more Present: Often or all the time- 15%
15	Galor <i>et al.</i> , 2011 [42]	United States	16862	21-90	The period prevalence of DED- 12%
16	Hom <i>et al.</i> , 2005 [43]	Southern California	463	Any age	Single symptom variable of self-assessed ocular dryness- 43.6%

17	Vehof <i>et al.</i> , 2014 [44]	United Kingdom	3824	20-87	Questionnaire based prevalence of DED- 9.6% DED symptoms in past 3 months- 20.8%
18	Onwubiko <i>et al.</i> , 2014 [45]	Enugu, Nigeria	402	>18	Ocular Surface Disease Index questionnaire & one of any abnormal Schirmer's score or Tear film break up time- 19.2%
19	Gillan <i>et al.</i> , 2009 [46]	South Africa	112	18-80	Ocular Surface Disease Index questionnaire- 64%
20	Mostafa <i>et al.</i> , 2016 [47]	Southern Egypt	3128	18-75	Ocular Surface Disease Index & one of any abnormal Schirmer score, Tear film break up time and Corneal/Conjunctival staining- 22.8%
21	Matel <i>et al.</i> , 2013 [48]	France	963	>73	Self-reported dry eye confirmed by use of artificial tears and/or OSDI >22- 21.9%
22	Jonas <i>et al.</i> , 2018 [49]	Russia	5361	>40	5 item questionnaire: Rarely or sometimes feeling dry eyes- 15.9% & frequently or always feeling dry eyes- 3.2%
23	Posa <i>et al.</i> , 2014 [50]	Germany	170	>40	Symptoms related dry eye- 65%

2. Dry Eye Prevalence in Sex & Age Groups:

Epidemiologic studies showed that the disease is more prevalent among women (particularly post menopause) and elderly population [3]. The prevalence of dry eye increases with age. Prevalence varied from 8.4% in less than 60 years to 19.0% in those older than 80 years [36]. It is estimated that nearly 75% of people over 65 will experience dry eye syndrome [1].

A population-based study in West Bengal published in 2012 found the prevalence dry eye is 48.3% over the age of 71 years and females were more affected than males (52.1% versus 28.7% respectively) [10].

A study in New Delhi revealed that compared with the younger patients, those aged ≥ 80 years were more likely to have OSDI questionnaire that were indicative of dry eye (41.2%), and the women investigated were more likely to have dry eye (as indicated by OSDI questionnaire) than the men (27% versus 12%) [15].

A study conducted in Bihar showed that the prevalence of dry eye increased progressively with age having a peak in the age group >70 years (11.4%) and the prevalence of dry eye was found to be higher in females (31.2%) than in males (20.8%) [1].

A clinical population-based study in Assam found the prevalence of dry eye was 32.5% and there is a relative peak in the dry eye prevalence in the age group of 51-60 years (39.13%) which is consistent with the findings in other dry eye studies. The study also found that the DED affects more in females than males the ratio was 35.83% $>$ 27.50% [2].

Reliable epidemiological studies from the large Women's Health Study and Physician's Health Study indicate that the prevalence of symptomatic dry eye in the United States is about 7% in women and 4% in men over the age of 50 years [33],[32].

The prevalence of DED is approximately 7.4% in Australia, with significant increase of prevalence in older patients and a significant decrease of tear production in women 50 to 59 years of age [4].

Few studies are there, which stated a controversial result in the sex and age variations.

An observational study showed the prevalence of DED in North India to be 32%, DED was more in males (65.3% males, 34.7% females) and in patients between 21 and 40 years of age (52.1%) [8].

Uttarakhand study found that prevalence of dry eye was maximum (66.37%) in the age group of 21 to 40 years in males (48.8%) [16].

In Indonesia, dry eye prevalence is approximately 27.5%, and 40–49 year age group reported most dry eye symptoms (37.6%), although a significant increase in dry eye symptoms was found with increasing age. The prevalence of dry eye was 1.4 times higher for men than for women (32.7% $>$ 22.8%) [21].

Andhra Pradesh study found that male had more prevalence of dry eye than female which is contrast to the most of the previous studies and the ratio was male 57.14% $>$ females 36.36%. In their study also, dry eye prevalence increased progressively with age, ≥ 80 year age group had highest prevalence of 90% [14].

3. Dry Eye Prevalence in Rural-Urban & Occupational Group:

Indian society is broadly on the basis of urban, rural and tribal societies taking into account their socio-economic characteristics and geographical locations. Urban society is formed with the establishment of industries, offices, educational institutions, training centers and the services sector. In the urban areas, individuals are mostly engaged in non-agricultural occupations and they adopt a western way of life. Rural societies are the societies that are residing in rural areas, where agriculture is stated to be the primary occupation. In rural areas too there have been certain progressions and developments. There has been development of schools, medical and health care centers and measures have been implemented for leading to the advancement and progress of the rural communities, as in India over 70% of the population reside in rural areas. The tribal communities are found all over the country. Tribals live in isolation and they have their own cultures, traditions, religions, norms, values and lifestyles. They have their own languages and in most cases are dependent upon the natural resources to sustain their living conditions [51].

Many research works had two arms, the rural and the urban arm. This was help to get accurate demographic profile and more detailing about the life style of the population. Environmental factors play an important etiological role in dry eye. Dry eye interferes with daily activities and work productivity and is related to an overall reduction in the quality of life [52].

In the study of West Bengal, which included those above 40 years, has a dry eye prevalence (by study criteria) of 40% in the rural group and 55% in the urban group. 68% of those with dry eye in the rural population are males, whereas 55% of those with dry eye in the urban population are males. The much higher percentage of males can be attributed to the fact that majority of the males (73%) with dry eye in the rural group are farmers, who spend long hours in the sun. 86% of the females with dry eye in the rural group were post-menopausal as compared to 54% in the urban group [53].

Study in North India found that majority of patients belonged to the urban areas (65.02%) as compared to a rural background (34.98%) and patients involved in desk jobs with computer use were more predisposed to develop DED [8].

In Bihar study, the prevalence of dry eye was highest in the farmers (24%) followed by housewife (12.4%) and higher dry eye prevalence in rural residents (36%) than in urban dwellers (16%). The increased rural prevalence in the study population was a consequence of the exposure of the rural residents, largely farmers, and manual laborers to sunlight and wind [1].

Choudhary et al. documented that farmers/laborers (33.4%) were most affected followed by factory workers (16.6%), office workers/shop keepers (14.9%), homemakers/ students (13.2%), others with high exposure (12.3%), and those with low exposure (11; 9.6%) and most of the patients (60.5%) belonged to rural background [17].

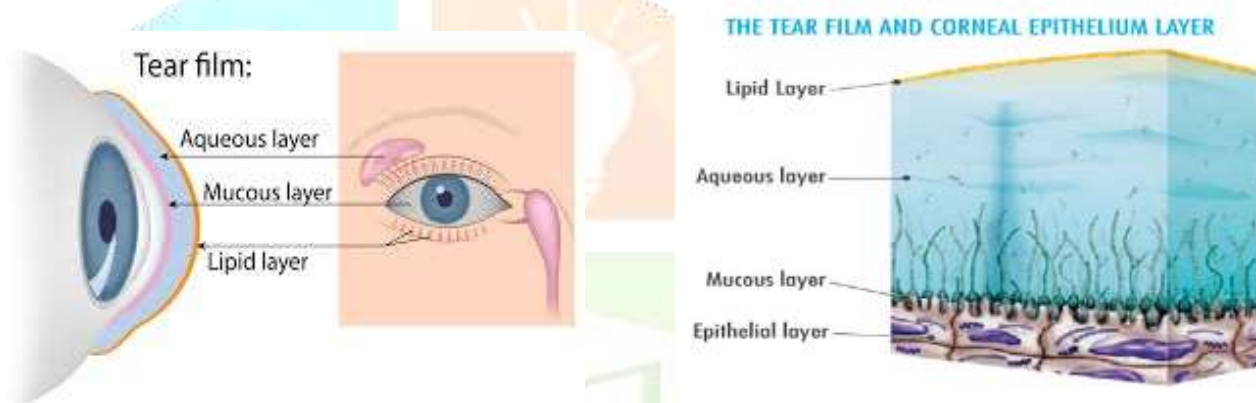
Sahai and Malik (2005) also found increased prevalence of dry eye in rural residents (41.8%) than urban (58.2%), and in farmers and laborers (25.3%) [5].

But this sort of variation observed very less in case of Western countries except one study in Russia (2018) [49] found urban region mostly feel the dry eye.

IV. TEAR FILM COMPOSITION

The eyes produce tears all the time, not only when we yawn or experience emotion. Healthy eyes are constantly covered with a fluid, known as a tear film. It is designed to remain stable between each blink.

The tear film composed of three main layers.



[54]

[55]

1) Mucin layer: 0.02 to 0.05 μ m, thinnest layer produced by conjunctival goblet cells.

- Composition of mucin layer: Mucin, Proteins, Water and Electrolytes.
- This layer maintains tear film stability and the mucus helps the overlying watery layer to spread evenly over the eye [56].

2) The middle layer is Aqueous layer: 8 μ m, thickest layer produced by the glands of upper lids and the accessory tear glands and contains essentially a very dilute saltwater solution.

- Composition of aqueous layer: Water, Proteins and Electrolytes (Na, K, Cl⁻, Mg²⁺, Cu²⁺, Hco₃).
- Deficiency of this layer may cause hypo secretive dry eye.
- This layer supplies the atmospheric oxygen to the avascular corneal epithelium, keeps the eye moist and helps in the removal of any dust, debris, or foreign particles [56].

3) The superficial layer is Lipid layer: 0.1 μ m, very thin layer of the tear film produced by the meibomian glands, sebaceous gland of Zeis & Moll glands (oil glands in the eyelids).

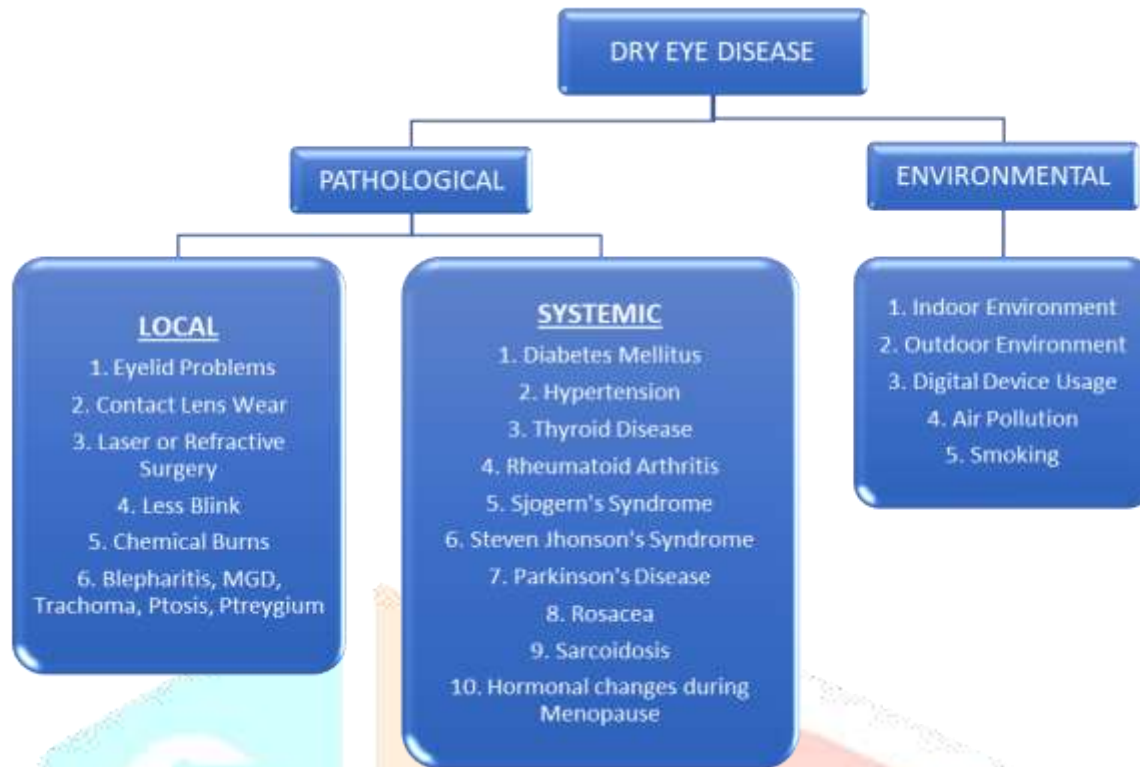
- Composition of lipid layer: Wax monoesters and 60-70% of Sterol ester.
- Others: Diglycerides, monoglycerides, free fatty acids, sterols, polar lipids, hydrocarbons.
- Dysfunction of this layer may cause evaporative dry eye.
- This layer prevents excessive evaporation of the watery layer beneath it [56].

Tears are made of water, fatty oils, protein, electrolytes such as K, Na, and Cl in higher concentration than blood, immunoglobulins, mucins, cytokines, lysozymes, lactoferrin to fight off bacteria, and growth factors.

Osmolarity of tears is 309 mOsm/liter. Average pH of the tears is 7.25 and refractive index of the tear film is 1.336 [56].

The mixture helps keep the surface of the eyes smooth & clear, prevents the eyes from becoming dry, helps to protect eyes from infection and enables clear vision. The tear glands produce fewer tears, the tear film can become unstable. It can break down quickly, creating dry spots on the surface of the eyes.

V. CAUSES OF DRY EYE DISEASE



Dry eye is caused by decreased tear production, excessive tear evaporation, and an abnormality in the production of mucus or lipids normally found in the tear layer, or a combination of these.

Common causes of poor production of tears by the lacrimal gland glands include:

1) Aging, 2) Various autoimmune diseases, such as primary Sjogren's syndrome, diabetes, rheumatoid arthritis, scleroderma, thyroid disease, lupus or vitamin A deficiency, 3) Certain medications, including antihistamines, decongestants, hormone replacement therapy, antidepressants, drugs for birth control, high blood pressure, acne and Parkinson's disease, 4) Laser eye surgery, Refractive eye surgery.

Evaporative loss of the watery tear layer is usually a result of an insufficient overlying lipid layer. Common causes of excessive tear evaporation include:

1) Outdoor environment: Excessive sun exposure, high temperature, high altitudes, exposure to high wind velocity, 2) Indoor environment: Low relative humidity, occurring either as part of natural variation at different geographic locations or in special circumstances created by air conditioning, air travel, or other artificial environments, 3) Less or frequent blinking, when working at a computer or using a smartphone or other portable digital device, 4) Eyelid problems, such as ectropion, entropion, lagophthalmos, ptosis etc.

Non-inflamed obstructive meibomian gland dysfunction is another major cause of lipid tear deficiency or evaporative dry eye and has recently attracted attention as a cause of ocular discomfort. Meibomian gland dysfunction (MGD) the supply of normal lipid, which leads to increased tear evaporation decreased tear stability, loss of lubrication, and damage to the ocular surface epithelium resulting in dry eye [14].

In the West Bengal study [10], the prevalence of MGD was 31.1%, in Bangkok study [27], prevalence of MGD was 46.2%; in Shihpai Eye study [24], it was 38.8%; in Japanese study [57], it was 61.9% and in Beijing Eye study [23], it was 69.3%.

VI. SIGNS AND SYMPTOMS OF DRY EYE DISEASE

Some population-based studies [9],[35],[44],[48] reported on a combination of symptoms and signs, with an overall prevalence ranging from 8.7 to 30.1%, however very different criteria were applied in each of the studies. In the Asian studies, the overall prevalence of disease based on symptom report ranged between 14.4 and 24.4% [9],[58]. There is considerable variation in the prevalence of DED diagnosed using clinical signs only. Some studies report a single clinical sign and others a combination of tear stability, tear production and ocular surface damage signs. Positive signs were if one or both eyes revealed any abnormal score of these tests like tear-film breakup time of <10 seconds, Schirmer's 1 test score of <5 mm in 5 min, fluorescein score of >1, or the existence of meibomian gland disease which was diagnosed when telangiectasia at the lid margin or plugging of the gland orifices was present grade 1. Prevalence of a tear breakup time (TBUT) of <10 seconds in one or both eyes varied between studies from 15.6 to 85.6%, of a Schirmer test score of <5 mm from 19.9 to 37%, and of a fluorescein score of >1 from 5.8 to 77% [9],[22], [35],[48]. Screening of patients in the preclinical phase when symptomatic without any sign of dry eye is important for its early detection [16]. But the use of symptoms alone will result in missing a significant percentage of dry eye patients so combined approach with symptoms and signs of dry eye is important tool for diagnosis of dry eye [5].

Table 3- Common Dry Eye Signs & Symptoms in Different Population-based studies in Asian Countries:

SL NO	Authors	Symptoms (%)	Signs (%)
1	Basak <i>et al.</i> , 2012 [10]	Burning: 15.9%, Fb sensation: 15.1%, Dryness: 6.8%, Discomfort: 6.1%	MGD: 31.1%, TBUT<10 seconds: 34.3%, Schirmer-1 test <5mm in 5min: 32.2%, Rose Bengal staining test (Van Bijsterveld score: 4 or more): 10.9%
2	Banik <i>et al.</i> , 2018 [1]	Itching: 80%, Burning sensation: 24.62%, Redness: 16.92%, Fb sensation, Blurring of vision: 15.38%	Not Specified
3	Sahai & Malik, 2005 [5]	Reduction of vision: 55.6%, Watering: 24.4%, Ocular pain: 19.4%	Not Specified
4	Shah & Jani <i>et al.</i> , 2015 [6]	Watering: 41%, Itching: 19.8%, Heaviness: 15.2%, Burning: 14.7%	Not Specified
5	Chavhan <i>et al.</i> , 2019 [7]	Uncomfortable in windy conditions: 53%, Gritty eyes: 52.7%, Problem in watching TV: 34.8%, Uncomfortable in low humidity area: 29.7%	MGD: 13.8%, TBUT <10 seconds: 23.1%, Schirmer 1 test <5mm in 5min: 5.2%, Lissamine green staining test (Van Bijsterveld score: 3 or more): 7.8%
6	Suresh <i>et al.</i> , 2018 [14]	Dry eye feeling & sensation: 100%, Red eye: 81.25%, Watering: 72.92%	Not Specified
7	Lee <i>et al.</i> , 2002 [21]	Burning: 59.1%, Grittiness & Redness: 0.9%	Not Specified
8	Choudhary <i>et al.</i> , 2015 [17]	Foreign body sensation:84.2%, Photophobia: 37.7%, Mucous discharge: 35%, Burning & Ocular fatigue:30.7%	Conjunctival congestion & Mucous thread: 100%, Ulcer/ Opacity: 41.2%, Superficial vascularization: 29.8%, Circumcillary congestion: 22.8%
9	Behara <i>et al.</i> , 2017 [13]	Itching: 43.55%, Watering: 36.56%, Fb sensation: 36.02%, Ocular pain: 29.57%	Not Specified
10	Alshamrani <i>et al.</i> , 2017 [26]	Grittiness:21.3%, Burning: 20.9%, Redness: 17.8%, Crusts: 14.9%	Not Specified
11	Jamaliah <i>et al.</i> , 2002 [28]	Visual disturbance: 11%, Grittiness: 9.5%, Increased sensitivity: 9%, Dryness: 5.5%	TBUT <8 seconds: 39%, Schirmer 1 test <5mm in 5min: 13%, PRT test <10mm: 4.51%, Diminishes tear film: 25%

Abbreviations: MGD- Meibomian gland dysfunction, TBUT- Tear film break up time, PRT- Phenol red thread

Table 4- Common Dry Eye Signs & Symptoms in Different Population-based studies in Asian Countries:

SL NO	Authors	Symptoms (%)	Signs (%)
1	Martinez <i>et al.</i> , 2016 [29]	Not Specified	MGD: 68%, Schirmer 1 test <5mm in 5min: 22%, TBUT <94%, Corneal staining >2: 11%
2	McCarty <i>et al.</i> , 1998 [11]	Not Specified	Schirmer test <8mm: 16.3%, TBUT <8 seconds: 8.6%, Rose Bengal staining test: 10.8%, Fluorescein staining test: 1.5%
3	Schaumberg <i>et al.</i> , 2009 [32]	Dryness: 0.8% constantly, 3.6% often; Irritation: 0.5% constantly, 4.1% often	Not Specified
4	Schaumberg <i>et al.</i> , 2003 [33]	Dryness: 1% constantly, 5.7% often; Irritation: 0.6% constantly, 5.7% often	Not Specified
5	Schaumberg <i>et al.</i> , 2017 [34]	Itching: 60%, Gritty sensation: 48%, Foreign body sensation: 46%, Blurred vision: 44%, Redness: 42%, Light sensitivity: 32%, Pain: 19%	Not Specified
6	Schein <i>et al.</i> , 1997 [40]	Not Specified	Schirmer test <5mm: 2.2%, Rose Bengal test score >5: 2%
7	Bandeem-Roche <i>et al.</i> , 1997 [41]	Gritty eyes, Burning, Dryness, Redness, Crust and Shut	Not Specified
8	Hom <i>et al.</i> , 2005 [43]	Dryness, Mild: 16.4%, Moderate: 6.2%, Severe: 2.3%	Not Specified
9	Mostafa <i>et al.</i> , 2016 [47]	Discomfort in windy conditions: 85%, Sore painful eyes: 60%, Gritty sensation: 60%, Blurred vision: 44%	TBUT <10 seconds: 44.7%, Schirmer 1 test <10mm: 39.3%, Fluorescein staining test (score >1): 30.6%, MGD: 18.5%
10	Matel <i>et al.</i> , 2013 [48]	Painful/sore eye: 74%, Sensitivity to light: 67.5%, Gritty sensation: 65%, Blurred vision and poor vision: 43.2% and 42.7%	TBUT <5 seconds: 44.9%
11	Posa <i>et al.</i> , 2014 [50]	Dry eye feeling: rarely or sometimes: 15.9%, frequently or always: 3.2%	Not Specified

Abbreviations: MGD- Meibomian gland dysfunction, TBUT- Tear film break up time.

Symptom assessment is a key component of diagnosis of clinical dry eye and may provide a more integrated view of clinical condition over time [16].

For assessment of the dry eye symptoms using various types of validated Dry eye questionnaires which include questions regarding dry eye symptoms. When a respondent indicated the presence of a symptom, he or she was asked to indicate whether the symptom was experienced rarely, sometimes, often, or all the time. Various types of questionnaire listed in the table 5.

[9] Table 5:

SL NO	Name of Questionnaire	Description	Utility	Category	No of Items	Domains Sampled	Recall Frequency
1	OSDI	Ocular Surface Disease Index	Clinical studies	Symptoms and HRQL	12		1 week
2	McMonnies	Key questions in a dry eye history	Clinical studies	Symptoms and risk factors	15	1) Symptoms; 2) Environment; 3) Review of systems	Not specified
3	IDEEL	Impact of Dry Eye on Everyday Life	Epidemiological and clinical studies	Symptoms and HRQL	57	1) Daily Activities 2) Treatment Satisfaction 3) Symptom Bother	2 weeks
4	WHS	Women's health study questionnaire	Epidemiological studies	Symptoms	3	1) Ocular symptoms 2) History of DED	Not specified
5	DEQ	Dry Eye Questionnaire	Epidemiological and clinical Studies	Symptoms and bother someness	21	1) Prevalence 2) frequency, diurnal severity and intrusiveness	Not specified
6	CANDEES	Canadian Dry Eye Epidemiology Study Questionnaire	Prevalence study	Symptoms	13	Symptoms severity, risk factors	Not specified
7	Melbourne VIP	Melbourne Visual Impairment Project	Epidemiological studies	Symptoms	6	Symptoms (severity)	Not specified
8	SEE	Salisbury Eye Evaluation	Prevalence Study	Symptoms	6	Symptoms (frequency)	Not specified
9	SPEED	Standard Patient Evaluation of Eye Dryness	Epidemiological studies, clinical practice	Symptoms	4	Symptoms (type, frequency, severity)	3 months
10	DEEP	Dry Eye Epidemiology Projects	Screening	Symptoms	19	Symptoms (frequency)	Not Specified

Abbreviation: HRQL: Health related quality of life.

Above all questionnaire, Canada Dry Eye Epidemiology Study (CANDEES), Melbourne visual impairment project, Salisbury eye evaluation (SEE) these are not yet validated. Most commonly used questionnaire is Ocular Surface Disease Index (OSDI) questionnaire.

Ocular surface disease index (OSDI) questionnaire contains 3 sections: section 1 is based on relative frequency of occurrence of each symptom (e.g., gritty feeling in eye, light sensitivity, and blurred vision etc.), section 2 includes questions indicating limitations on certain activities (reading, driving at night, watching television), and section 3 is based on effect of environmental conditions (wind, low humidity, and air conditioning) on eyes. The three sections have 5, 4, and 3 questions respectively. All items in the questionnaire have equal scores. Scores do not vary according to the item but according to the duration for which the symptom persists. All the 12 parameters of the OSDI questionnaire are graded on a scale of 0 to 4, where 0 indicates none of the time; 1 indicates some of the time; 2 indicates half the time; 3 indicates most of the time, and 4 indicates all the time. The total OSDI score can then be calculated on the basis of the following formula:

(Sum of severity for all questions answered) x (100)

$$\text{OSDI} = \frac{\text{Sum of severity for all questions answered} \times (100)}{\text{(Total \# no of questions answered)} \times (4)}$$

The OSDI score can range from 0 to 100. Dry eye symptoms were graded based on the OSDI score: normal (0–12), mild DED (13–22), moderate DED (23–32) and severe (33–100). Overall, the frequency of any DE symptoms was 78% by OSDI [29].

The presence of one or more dry eye signs revealed by diagnostic tests [12]. Several diagnostic tests have been used to assess the dry eye signs, the quality and quantity of tear film and functioning of the various layer of the tear film. Meibomian gland dysfunction, Tear-film breakup time, Schirmer test, Fluorescein, Rose Bengal, Lissamine green staining test of the cornea are commonly used diagnostic tests which perform in clinical practice.

Meibomian Gland Dysfunction (MGD): The condition of the meibomian gland was determined by observing the eyelashes, lid thickening, punctum, lid margins and meibomian orifices under a slit lamp examination. The patient was asked to look up and lower lid just below the margin was pressed against the globe with focusing over the meibomian gland orifices to see if it is blocked or open and type of material expressed out. Meibomian gland dysfunction defined as the presence of meibomian gland orifice plugging or lid margin telangiectasia. The presence of lid margin telangiectasia was recorded, and any meibomian gland obstruction was graded from Grade 0 to Grade 3.

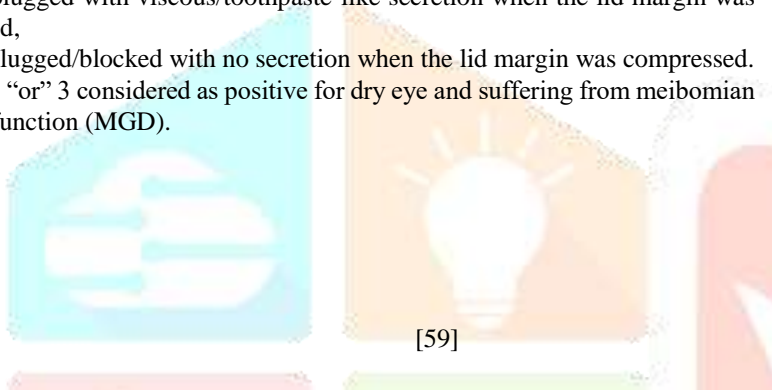
Grade 0: for no obstruction,

Grade 1: orifices plugged with serous secretion,

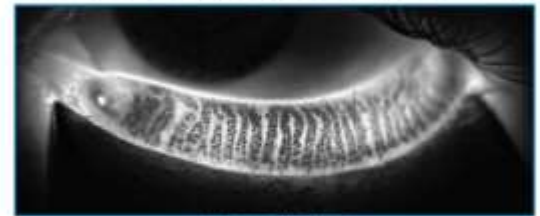
Grade 2: plugged with viscous/toothpaste-like secretion when the lid margin was compressed,

Grade 3: plugged/blocked with no secretion when the lid margin was compressed.

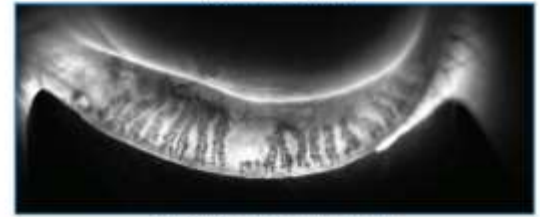
Grade of 2 “or” 3 considered as positive for dry eye and suffering from meibomian gland dysfunction (MGD).



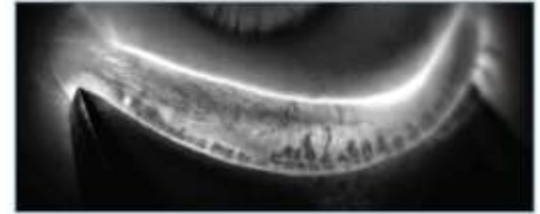
PROGRESSIVE MEIBOMIAN GLAND CHANGES



NO STRUCTURAL CHANGES

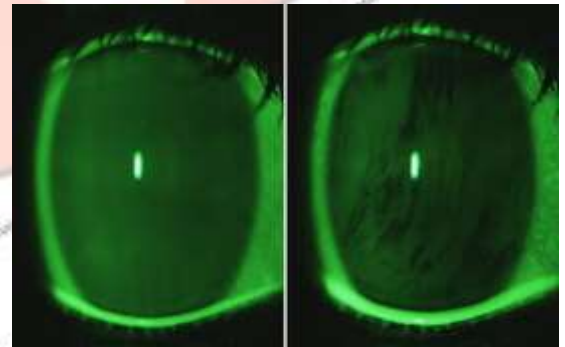


DUCT DILATION, TRUNCATION & DROP OUT



Tear Film Breakup Time (TBUT): The tear-film breakup time test was performed before the other dry eye tests to avoid any untoward interference. The test is performed with the patient seated at the slit lamp and all fans in the room switched off. A 2% fluorescein strip was moistened with normal saline or antibiotics drops and placed in the lateral one-third of lower lid in a non-anaesthetized eye. The patient cornea was focused by diffuse illumination using the cobalt blue light of the slit lamp and patient was asked to blink only once or twice to avoid pooling of fluorescein, following which the strip was removed. The time lapse between the last blink and the appearance of the first randomly distributed dark discontinuity in the fluorescein-stained tear film is the tear break up time. Values of less than 10 seconds were considered abnormal, indicative of tear film instability and dry eye.

[60]



Fluorescein staining test: A sterile, moist, dye-impregnated fluorescein paper strip is gently placed in the lower fornix of the junction of middle and lateral one-third. Fluorescein staining of the cornea was observed through a slit lamp with a cobalt-blue filter and was graded from Grade 0 to Grade 3.

Grade 0: no staining,

Grade 1: mild staining with a few disseminated stains, and limited to less than one third of the cornea,

Grade 2: moderate staining with a severity between grades 1 and 3, or

Grade 3: severe staining with confluent stains, and occupying half or more of the cornea.

Rose Bengal staining test: Rose Bengal strips were used by applying tear substitutes to the sterile dye-impregnated strips and touching the wet strip to the inferior palpebral conjunctiva. After 15 seconds, stained areas in the conjunctiva were examined with red-free filter on slit lamp. Results were evaluated using a grading system developed by Van Bijsterveld, in which the ocular surface was divided into three zones as Zone 1 if stains only cornea, Zone 2 if stains nasal bulbar conjunctiva and Zone 3 if stains temporal bulbar conjunctiva, each of which is graded 1-3 according to severity. Each eye was scored separately. Staining was graded on a four-tier scale for each area separately.

- Score: 0+ No staining, normal
- Score: 1+ Mild staining, few separated spots
- Score: 2+ Moderate staining, many separated spots
- Score: 3+ Extensive staining, confluent spots

Minimum score: 0, maximum score: 9, and positive dry eyes: >4.

Lissamine green staining test: Lissamine green staining was done next after washing the conjunctival sac and introducing wet Lissamine green strips. Test was performed and results were evaluated in the same way as Rose Bengal test. Van Bijsterveld scoring system was also used here to grade the staining.

Schirmer's 1 test: The Schirmer test was performed last, so that ocular irritation by the test strip would not interfere with other examination results. It is performed by folding 5 mm at the top end of a special Schirmer's test filter paper strip (Whatman filter paper no. 41 5x 35 mm) and placing it in the lower conjunctival sac of the open eye after instilling a drop of Proparacaine 0.5%. It is placed at the junction of outer one-third and medial two-thirds of the lower lid, left in place for 5 minutes or until 30 mm. of the strip becomes wet. The patient was advised to avoid squeezing the lids, looking up or moving eyes excessively. The patient was allowed to either blink normally or to close his or her eyes. The strip is removed from the eye after 5 minutes and the wet portion measured. Wetting of less than 5 mm was considered as positive Schirmer's test.



[61]

Schirmer's test positive was considered as Aqueous Tear Deficiency (ATD). Positive Rose Bengal and Lissamine Green staining test was considered as Mucin Layer Deficiency. Meibomian Gland Dysfunction was considered Lipid Layer Anomaly. Abnormal Tear film Break Up Time (TBUT) test value was considered Evaporative Tear Deficiency.

Maharashtra study found positive TBUT in 93.3% of dry eye patients, lipid layer deficiency (55.7%) is most common tear film abnormality followed by Mucin (31.6%) and aqueous layer deficiency (21.0%) in dry eye patients [7].

Adlakha *et al.*, 2017 [20] found the evaporative dry eye in postmenopausal women accounts for maximum contribution (46.15%), followed by mixed (40.38%) and minimum by aqueous deficient (13.46%).

VII. ETIOLOGICAL RISK FACTORS ASSOCIATED WITH DRY EYE DISEASE

A number of factors can increase the risk of dry eyes. These include:

- 1) Aging: DED can occur at any age, but it becomes increasingly more common later in life, especially after age of 50. Tear secretion decreases as the age increase.
- 2) Female sex particularly post-menopausal women: About 60% of menopausal women are affected by dry eyes. After menopause, the level of estrogen in the blood decreases [33],[44]. The reduction of naturally occurring estrogen as a possible reason for the occurrence of dry eye in menopausal women. Sex steroid receptors are present on the meibomian glands, which are the sebaceous glands on the eyelids responsible for producing the oil component of tears that prevents evaporation [62]. Androgen binding results in synthesis and secretion of lipids from these glands, while estrogens actually cause a decrease in lipid production [63]. For this reason, increased levels of estradiol are believed to be a risk factor for dry eye. Most common type of dry eye in post-menopausal women is of evaporative type possibly due to meibomian gland dysfunction and its decreased secretion due to atrophy of acinar cells (declined functioning of sebaceous glands) due to hormonal imbalance particularly androgen deficiency [20].
- 3) Contact lens wear: Though it can be difficult to determine the exact extent that contact lens wear contributes to dry eye problems, dry eye discomfort is a primary reason why people discontinue contact lens wear. It has been found previously that pre lens tear film thinning time was most strongly associated with dry eye followed by nominal contact lens water content and refractive index. This, together with poor lens wettability, could be a basis for a higher evaporative loss during contact lens wear and was attributed to potential changes in tear film lipid composition [13].
- 4) Computer use: When working at a computer or using a smartphone or other portable digital device, we tend to blink our eyes less fully or less frequently, which leads tear evaporation and increased risk of dry eye symptoms.
- 5) Smoking: Smoking has been linked to serious eye problems including macular degeneration, cataract, uveitis.
- 6) Indoor environment: Air conditioning, ceiling fans and forced air heating systems all can decrease indoor humidity and/or hasten tear evaporation, causing dry eye symptoms [8].
- 7) Outdoor environment: Air pollution, excessive sun exposure, high temperature, high altitudes, hot, dry or windy climates increase dry eye risks.
- 8) Health conditions: Certain systemic disease such diabetes, hypertension, thyroid associated disease, rheumatoid arthritis, Sjogren's syndrome, Steven Johnson's syndrome, Parkinson's disease, gout, connective tissue diseases etc. contribute to dry eye symptoms.
- 9) Eyelid problems: Blepharitis [12], Ptosis, Ectropion, Entropion, Lagophthalmos, which can be caused by aging or occur after cosmetic blepharoplasty or other causes- can cause severe dry eyes that can lead to a corneal ulcer if left untreated.
- 10) Vitamin A deficiency, 11) Alcohol and caffeine use, 12) Systemic and topical drugs and multivitamin use, 13) Pterygium or Pinguecula, 14) Meibomitis [41] and Meibomian Gland Dysfunction, 15) Hormone replacement therapy [31],[33], 16) Laser or Refractive eye surgery, 17) Sjogren syndrome.

Several studies divulge different risk factors such as, In the West Bengal study 2012 [10], regular use of anxiolytic and antidepressant medication was found to be a significant risk factor for the dry eye.

Another study in West Bengal [53] found environmental factors such as air pollution play an important role in dry eye disease and was seen in 45% respondents in the rural group and 64% in the urban group, which substantiates the effect of air pollution on dry eye disorders.

Chavhan et al. [7] found systemic risk factors associated with dry eye patients are hypertension (7.8%), diabetes mellitus (2.9%), thyroid disorder (2.6%), Sjogren's syndrome (1.6%), other connective tissue diseases (1.8%), Steven Johnson syndrome (0.5%), leprosy (0.3%), and tuberculosis (0.3%).

Madhya Pradesh study [17] demonstrated that dry eye was more prevalent in patients with more exposure to air pollution (33.3%), smoking (14.9%), sunlight (16.6%), and drugs (14.9%). These findings are consistent with observations of Moss et al. 2000 [36], Sahai and Malik [5]. Smoking predisposes the eye to tear film instability by its direct irritant action on the eye and represents a modifiable risk factor in dry eye concentration and drugs too may disrupt one or more components of the tear film causing it to become unstable.

In the Odisha study [13], 51.07% of dry eye subjects use systemic drugs and 13.9% of dry eye subjects use topical drugs. Many components of eye drop formulations can induce a toxic response from the ocular surface. The most common offenders are preservatives such as benzalkonium chloride, which causes surface epithelial cell damage and punctate epithelial keratitis. This interferes with ocular surface wetting.

Also, in the same study [13], 9.35% of dry eye subjects had diabetes mellitus and hypertension was seen in 25.8% of dry eye cases. The Beaver Dam Eye study 2000 [36] too showed similar associations. In addition, after controlling age and sex, the following factors were independently and significantly associated with dry eye: history of arthritis, smoking status, caffeine use, history of thyroid disease, history of gout, high-density lipoprotein cholesterol ration, diabetes and multivitamin use [31],[39].

Gupta et al. [64] in their study found that air pollution (24%) over a long period of time increases the prevalence of dry eye because it causes tear film abnormalities.

In Uttarakhand study [16], smoking and using topical drug have been suggested as risk factors for DED. 5.95% patients were smokers, exposure to tobacco smoke or cigarette smoke predisposes tear film instability by its direct irritant action on the eyes with eventual decrease TBUT by 30-40% and 5.53% of the patients used topical drugs off and on for minor ocular ailments. It has been seen that topical drugs with added preservatives may disrupt one or more components of the tear film leading to tear film instability.

In Indonesia study [21], pterygium in either eye and current smoking history was significantly associated with one or more of the six dry eye symptoms often or all the time.

In the Beijing study [23], the risk factors that contribute to the difference are assumed to include air pollution, workplace environment, and lifestyle in urban regions.

Lekhanont et al. [27] stated that positive associations with dry eye tests were found in subjects with pinguecula/pterygium [65] and MGD. Osaka study [66] identified Visual display terminal (VDT) use for more than 8 hours a day has been reported as a significant risk factor for DED, mainly attributed to the decrease in blink rate while using these devices, thereby hampering the uniform distribution of the tear film over the ocular surface. Titiyal et al. [8] study showed the similar associations, 89.98% of dry eye cases with 4 hours or more of Visual display terminal (VDT) usage had severe DED. As well, significant association of DED with contact lens usage as well as smoking. Contact lens usage may cause dry eye or aggravate preexisting DED [30]. Nearly 50% of contact lens users may complain of symptoms of dryness, discomfort, grittiness, irritation, burning, or foreign body sensation [30].

Hikichi et al [67] found the prevalence of dry eye in visual display terminal (VDT) users and contact lens (CL) wearers was significantly higher than in non-VDT users and non-CL wearers.

Schaumberg et al. 2009 [32] revealed that high blood pressure and benign prostatic hyperplasia were associated with a higher risk of DED. Use of antidepressants, antihypertensives, and medications to treat benign prostatic hyperplasia were also associated with increased risk of DED. Similar associations found by Matel et al. [48] & Galor et al. [42] Several medical conditions were found to increase DES risk including post-traumatic stress disorder, depression, thyroid disease and sleep apnea in the same study [42].

Moss et al. 2008 [38] & 2004 [37] found a marginally increased risk of DED associated with the use of diuretics (antihistamines, antianxiety drugs, antidepressants, oral steroids) but a decreased risk with the use of angiotensin-converting enzyme (ACE) inhibitors.

In Koumi study [58], a low body mass index (BMI), CL use and hypertension (HT) were risk factors for DED in men. Use of a VDT, CL use and myocardial infarction or angina were the risk factors whereas high BMI was a preventive factor for DED in women.

Alshamrani et al. 2017 [26] showed that female gender, older age (>56 years), current smoking and history of diabetes mellitus were significantly associated with DED.

Presence of glaucoma and use of topical glaucoma medication was significantly associated to DED in the study of Saudi Arabia [12].

Onwubiko et al. [45] reported older age, windy conditions and illiteracy are the predictors of DED. Gillan et al. [46] revealed that contact lens uses and oral contraceptives these two are the associated with DED.

VIII. IMPACT OF DRY EYE DISEASE

The currently validated dry eye specific questionnaires, the OSDI and the Impact of Dry Eye on Everyday Life (IDEEL) are frequently used to measure disease severity [39],[68]. The IDEEL, which is a 57-item questionnaire, comprises three modules: dry eye symptom bothersomeness; impact on daily life (including daily activities, emotional impact, and impact on work) and treatment satisfaction (both effectiveness and treatment related bother/inconvenience). There are two items related to visual disturbance that assess the extent to which the patient is affected by blurry vision and sensitivity to light, glare, and wind. The strength of the IDEEL is that it covers all relevant domains of DED and it also distinguishes the severity of DED [9].

Multifactorial dry eye disease is most prevalent condition due to diminished tear production or increased tear evaporation results ocular discomfort, fatigue and visual disturbance that interferes with quality of life (QoL). The available evidence suggests that DED has an adverse effect on overall QoL. It causes pain and irritation and affects ocular and general health and well-being, the perception of visual function, and visual performance [9],[39],[68]. Pain associated with DED can have psychological and physical impacts, while blurred vision may impose restrictions in daily life activities such as reading, driving, watching television, and operating smartphones [9]. Due to insufficiency of adequate tears, you may have an increased risk of eye infection, damage to the ocular surface. If left untreated, severe dry eyes may lead to eye inflammation, abrasion of the corneal surface, corneal ulcer and vision problems which decreased quality of life.

Studies suggest that DED can have a considerable impact on visual function, daily activities, social and physical functioning, workplace productivity, direct and indirect cost of the disease, and quality of life (QoL) [4]. A reduction in QoL is inevitable when the symptoms of dry eye occur, whether they are mild, transient irritations or persistent symptoms [4]. This symptomatic dry eye was associated with difficulty in performing vision-dependent tasks, independent of visual acuity and other factors [69].

Loretta et al. found that poorer visual acuity, rather than worse contrast sensitivity, drives visual symptoms and complaints in dry eye and greater tear film instability was associated with worse contrast sensitivity [70].

A study from Singapore with 3239 individuals aged >40 years showed that patients with symptomatic dry eye reported significantly more difficulty in performing vision related daily activities, independent of their visual activity. The specific activities that were navigating stairs, reading road signs, reading newspaper, cooking, recognizing friends, watching television, and driving at night [69].

Physicians' Health Study [32] and Women's Health Study [33] demonstrate that people with DED are significantly more likely than people without DED to report problems with reading, performing professional work, computer use, television watching, daytime driving, and nighttime driving.

Pooled data from the women's health study and the physicians' health study in the United States, with 690 participants (preponderance of female participants), showed that symptomatic dry eye was significantly associated with difficulty in reading, carrying out professional work, using a computer, watching television, and driving during the day and at night, after controlling for age, diabetes, hypertension, and other factors [71]. Prolonged use of electronic devices results reduced blinking. Visual function of dry eye patients becomes abnormal with ocular surface irregularity when the eye is kept open for 10-20 seconds [72]. Greater visual demands require in performing these daily activities and exposure to air-conditioning and low-humidity environments, which can result in instability and increased evaporation of the tear film leading to irregularity of the optical refracting surfaces. Studies have reported a significant reduction in the blinking rate associated with visual display terminal work [66],[73] reading [72], increased driving speed [72], which can further result in instability of the tear film.

IX. OBSERVATIONAL WORK

In the rural population I observed 53 individuals within the age group of 20 to 35 years. All the participants completed OSDI questionnaire and further going through objective tests after fill up their written consent. 40 females and 13 males were participated during my observation period. DED found more in females (23/40) than males (7/13).

Out of 53 participants, symptomatic dry eye detected in 30 patients. Of these, 12 patients had mild dry eye, 7 patients had moderate dry eye and 11 patients had severe dry eye.

The patients who were tested positive dry eye according to Ocular Surface Disease Index (OSDI) questionnaire where seen to be positive in both Schirmer's test and Tear film Break Up Time (TBUT) test.

According to the Schirmer's test, dry eye detected in 29 patients. Of these 15 patients had mild dry eye, 12 patients had moderate dry eye and 2 patients had severe dry eye. In case of Tear film Break Up Time (TBUT) test, it is shown that most of the participants had marginal to low score in break up timing. Under the slit lamp examination of corneal staining, I found grade 1 staining of cornea in 4 eyes and grade 2 in 2 eyes only. Left all had no stain marking.

In the urban population I observed 55 individuals within the age group of 20 to 35 years. All the participants administered OSDI questionnaire and further going through objective tests after fill up their written consent. 38 females and 17 males were participated during my observation period. DED found more in females (22/38) than males (8/17).

Out of 55 participants, symptomatic dry eye detected in 30 patients. Of these, 14 patients had mild dry eye, 10 patients had moderate dry eye and 6 patients had severe dry eye.

The patients who were tested positive dry eye according to Ocular Surface Disease Index (OSDI) questionnaire where seen to be responsive in Schirmer's test, and where seen to be unresponsive rather marginal positive when they were going through Tear film Break Up Time (TBUT) test.

According to the Schirmer's test, dry eye detected in 17 patients out of 55 participants. Of these 15 patients had mild to moderate dry eye and 2 patients had severe dry eye. In case of Tear film Break Up Time (TBUT) test, it is shown that most of the participants had normal score in break up timing. Only 15 patients had marginal score and 7 patients had low score in break up timing. Under the slit lamp examination, I was not found any fluorescein staining over cornea.

In conclusion, it was seen that females were more affected by DED than male. Females belongs to rural areas were more affected than urban areas. Because of illiteracy and unhygienic environment. Most of them were house wives/ students or laborers/ factory workers. Direct consequence of the overwhelming exposure of rural residents to sunlight, high temperature, and excessive wind were the risk factors for dry eye.

Schirmer's test score was most frequently positive in all Ocular Surface Disease Index (OSDI) questionnaire score ranges. So aqueous tear deficiency is commonly seen in all dry eye subjects followed by evaporative tear deficiency.

X. DISCUSSION

The prevalence of dry eye disease ranges from 4.34 to 93.2%. Prevalence appears to be higher in Asian than in Western population.

The prevalence of DED increases with age. Chavhan et al. [7] reported the prevalence of dry eye was increased significantly with age with relative peak in 6th decade (32.0%). Banik et al. [1] study reported similar trends with relative peak in 7th decade (11%). Sahai & Malik [5], reported similar trend but relative peak in 3rd decade (20.0%) while Gupta et al. [15] study reported peak in 8th decade (41.2%). Schaumberg et al. [32] reported men over 80 years or older more likely to have DED (7.7%) and Schaumberg et al. [33] reported prevalence increased with age from 5.7% among women <50 years old to 9.8% among women aged >75 years old.

Studies reported females had higher prevalence of DED compared to males. DED is mostly common in postmenopausal female compared to non-menopausal female. Chavhan et al. [7] reported dry eye is most common among postmenopausal female 69.6% (156/224) compared to non-menopausal female. Similarly, Jamaliah et al. [28] reported 51.3% (59/115) postmenopausal females with dry eye disorder, whereas Sahai & Malik [5], reported equal distribution of dry eye among both post and non-menopausal females (22.8%). Rural-urban & occupational variation also observed in so many studies. The variation manifest because of the life style in their particular environment or geographic area in the study population.

All of these factors, like age, sex, occupation, indoor and outdoor environments attributed risk factors of DED. There are so many other conditions like, various autoimmune disease, many systemic health conditions, various medication, different eyelid related problems, any

eye surgery; in fact, depression, anxiety, sleep apnea, stress, hormone replace therapy, contact lens usage, Vitamin A deficiency all of these are associated risk factors of DED.

Overall DED reflect a negative impact which hamper our vision and quality of life. DED create pain, irritation results visual disturbance and we are facing problems during reading, driving, cooking, watching televisive, computer use or any personal/ professional work etc. Prolonged use of electronic devices results less or frequent blinking which hamper visual performance, causing tear evaporation. Exposure to air-conditioning and low-humidity environments, which can result in instability and increased evaporation of the tear film leading to irregularity of the optical refracting surfaces. Inadequate tear insufficiency results eye infection. If it is not treating appropriate time, further it turns into eye inflammation, corneal abrasion, corneal ulcer etc. and all of these hamper daily activities.

Reduction in quality of life is inevitable when symptoms of dry eye occur. These symptoms range from mild transient irritation to persistent dryness, burning, itchiness, redness, pain, ocular fatigue, and visual disturbance. This study has considered the epidemiology of DED based on causes, diagnostic criteria, including symptoms and/or signs. The prevalence of symptoms was higher and more variable than signs.

Meibomian gland dysfunction is a major cause of lipid tear deficiency or evaporative dry eye. Poor production of tears by the lacrimal gland glands may be a result of age, hormonal changes, or various autoimmune diseases, such as primary Sjogren's syndrome, rheumatoid arthritis, or lupus. Evaporative loss of the watery tear layer is usually a result of an insufficient overlying lipid layer. Lipid layer deficiency is commonest type. Chavhan et al. [7] reported most of the dry eye patients are affected by lipid layer deficiency (55.7%) followed by mucin layer (31.6%) and aqueous layer deficiency (21.0%). However, in contrast to our study Rege et al. [74] reported prevalence of lipid layer deficiency as 14.5%, followed by aqueous layer (13.4%) and mucin layer deficiency (3.5%).

For the primary diagnosis of DED commonly used questionnaire is OSDI questionnaire which give strength in diagnosis. But all the symptomatic individuals are not clinically significant. Meibomian Gland Dysfunction (MGD), Tear film Break Up Time (TBUT), Schirmer's test, corneal and conjunctival staining with the help of Fluorescein, Rose Bengal, Lissamine green etc. helps to detect symptomatic subjects. TBUT was most frequent positive test. A rapid Tear film Break Up Time (TBUT) is seen in both aqueous tear deficiency as well as Meibomian gland dysfunction.

In conclusion, an accurate testing and differential diagnosis of dry eye which is crucial for medical management of DED. Therefore, the clinicians play challenging role in identification of symptoms of dry eye, selection of appropriate diagnostic tests and products, interpretation, and instructing patients on the proper use of medications. Current available therapies such as lubricants and anti-inflammatory drugs alleviate symptoms and reduce signs of DED.

This study may have some limitations. The exclusion of Sjogren's syndrome, contact lens wearers, post refractive surgery patients and patients with severe conjunctival and corneal disease etc. might underestimate the range of the prevalence of DED in this study. Correlation between signs and symptoms are imported in case diagnosis of DED. Future studies need to sort out this correlation. Limited studies recount the prevalence of DED of varying severity, incidence and treatment plan in different population, which enduring future desires in this field. This substantial economic burden of DED interconnected with the cost of the treatment. Recent economic burden and its treatment for treated or untreated DED this remains an important aspect for future research. Artificial tears remained the quintessential agent used in the treatment of dry eye with majority of the patients attaining relief from the discomforting symptoms of dry eye. Many pharmaceutical companies are working on other treatments options. The millions of people worldwide affected by DED are a major tear deficiency disorder, and which is often overlooked and under diagnosed. So, increased awareness in general population is the most important step for future which help to enhance quality of life.

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XIII. APPENDIX:

Ocular Surface Disease Index[®] (OSDI[®])²

Ask your patient the following 12 questions and mark (✓) the number in the box by that best represents each answer.

A. 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
1. Eyes that are sensitive to light?	4	3	2	1	0
2. Eyes that feel gritty?	4	3	2	1	0
3. Painful or sore eyes?	4	3	2	1	0
4. Blurred vision?	4	3	2	1	0
5. Poor vision?	4	3	2	1	0

B. Have problems with your eyes limited you in performing 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	
6. Reading?	4	3	2	1	0	N/A
7. Driving at night?	4	3	2	1	0	N/A
8. Working with a computer or bank machine (ATM)?	4	3	2	1	0	N/A
9. Watching TV?	4	3	2	1	0	N/A

C. Have your eyes feel uncomfortable in any of the following 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
10. Windy conditions?	4	3	2	1	0
11. Please or areas with low humidity (very dry?)	4	3	2	1	0
12. Areas that are air conditioned?	4	3	2	1	0

N/A
N/A
N/A

Scoring:

$$\text{OSDI} = \frac{(\text{Sum of severity for all questions answered}) \times (100)}{(\text{Total \# no of questions answered}) \times (4)}$$

Where the severity was graded on the scale of

- 0 = None of the time
- 1 = All of the time
- 2 = Most of the time
- 3 = Half of the time
- 4 = Some of the time

Do not include questions answered N/A

Results:

- 0-12 points: Normal
- 13-22 points: Mild Dry Eye
- 23-32 points: Moderate Dry Eye
- 33-100 points: Severe Dry Eye

Worksheet

Name:

Age:

Sex:

1. How long you used computer?

Ans:

2. Have you used contact lens?

Yes / No

- If yes then How long you used contact lens once a day?

Ans:

- Do you used contact lenses every day?

Yes / No / Occasionally

3. Do you have any systematic history like DM / HTN / Rheumatoid arthritis / Thyroid / Vit-A deficiency / Anti-depression?

4. Do you have any medical history like Parkinson's diseases / Sjogren syndrome / Gout?

5. Do you have any history of eye infections or any eyelid problems?

Yes / No

6. Do you smoke cigarettes / drink alcohol?

7. Have you had any eye operations like lens surgery / Lasik surgery / cosmetic surgery before?

8. If there is a pregnant woman then Does, she takes birth pills?

Yes / No

- Schirmer's Value: RE
LE
- TBUT Value: RE
LE
- Grades of Corneal Staining: RE
LE

