Original Article

Prevalence of dry eye, its categorization (Dry Eye Workshop II), and pathological correlation: A tertiary care study

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Purpose: To study the prevalence of dry eye disease (DED), further categorize using DEWS II protocol, grade squamous metaplasia in each group, and determine associated risk factors in a tertiary care hospital. **Methods:** This cross-sectional hospital-based study screened 897 patients ≥30 years via systematic random sampling. Patients with both symptoms and signs as defined by the Dry Eye Workshop II protocol were considered as DED, further categorized, and subjected to impression cytology. Categorical data were assessed using the Chi-square test. P value < 0.05 was considered statistically significant. **Results:** In total, 265 (of 897) patients were defined as DED based on the presence of symptoms (DEQ-5 ≥6) and at least one positive sign (fluorescein breakup time [FBUT] <10 s or OSS ≥4). DED prevalence was thus 29.5% with aqueous deficient dry eye (ADDE), evaporative dry eye (EDE), and mixed type seen in 92 (34.71%), 105 (39.62%), and 68 (25.7%) patients, respectively. The risk of developing dry eye was higher in the age above 60 years (33.74%) and in the third decade. Females, urban dwellers, diabetics, smokers, history of previous cataract surgery, and usage of visual display terminal devices were found to be significantly associated with risk factors of DED. Squamous metaplasia and goblet cell loss were more severe in mixed compared to EDE and ADDE. **Conclusion:** Hospital-based prevalence of DED is 29.5% with a preponderance of EDE (EDE 39.62%, ADDE 34.71%, and mixed 25.71%). A higher grade of squamous metaplasia was seen in the mixed type compared to other sub-types.

Key words: Categorization, DEWS II, dry eye, impression cytology, prevalence

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Dry eye disease (DED) is a multifactorial disease of ocular surface and tear film characterized by decreased tear production and/or excessive tear evaporation, which leads to increased osmolarity and loss of homeostasis of the tear film, inflammation of the ocular surface, and neurosensory abnormality. It thus results in an altered tear film and ocular surface, which leads to ocular irritation and visual disturbances. It is increasingly becoming a major concern because of discomforting symptoms and is often overlooked and frequently underdiagnosed. Patients of DED present with a myriad of symptoms, which include grittiness, burning, itching, foreign body sensations, redness, tiredness, watering, visual disturbances, limitations in performing daily activities, poor general health, and often depression.

The prevalence of dry eye ranges from 10.8% to 57.4% as documented by previous studies.[1-5] The clinical diagnosis of DED is difficult and remains a challenge due to its multifactorial etiopathogenesis, lack of specific symptoms, a poor association between signs and symptoms of dry eye, and lack of specific dry eye diagnostic tests. To aid in the clinical diagnosis of dry eye, Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop (DEWS) II, in 2017, proposed a new guideline for diagnosing dry eye.[6,7]

There are only a handful of studies[8-12] conducted describing the epidemiology of DED from the Indian subcontinent using different definitions and diagnostic criteria of dry eye, which may not be standardized. Thus, more studies need to be conducted in different geographical regions to expand the epidemiological study of DED using a standard and uniform dry eye diagnostic guideline. We determined the hospital-based prevalence of dry eye using the most recent diagnostic criteria as proposed by DEWS II and further sub-categorized DED into the aqueous deficient dry eye (ADDE), evaporative dry eye (EDE), and mixed types in a tertiary care hospital. We also graded squamous metaplasia in each group and determined the associated risk factor of DED.

Methods

This cross-sectional, hospital-based observational study was conducted for 1 year at the Regional Institute of Ophthalmology, which is a tertiary care referral center after taking permission from the Ethics Committee and the study adhered to the tenets of the Declaration of Helsinki.

Patients ≥30 years visiting the outpatient department were selected via systematic random sampling wherein the first patient was selected randomly and thereafter every sixth patient was included. In case the sixth patient met the exclusion

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criteria, then the next patient was included, and thereafter every sixth patient was selected. Patients <30 years, all cases of gross corneal/conjunctival pathologies, active ocular surface infection, contact lens users, use of any topical eye medications, systemic conditions such as Sjogren syndrome, and history of any intraocular or extraocular surgery (cataract surgery, refractive surgery) within past 12 months were excluded from the study.

After explaining the procedures, all patients included in the study signed informed consent and underwent a comprehensive history taking with an emphasis on history pertaining to the dry eye, which included a history of diabetes mellitus, smoking, history of cataract or refractive surgery, use of visual display terminals including television, smartphones, and laptops.

The primary objective of our study was to determine the hospital-based prevalence of DED based on DEWS II guidelines, sub-categorize DED patients into ADDE, EDE, and mixed types, and determine squamous metaplasia in each group. The secondary objective was to analyze the associated risk factors of DED.

After taking a detailed history, all patients were given dry eye questionnaire-5 (DEQ-5) in their local language. The objective tests were undertaken only in patients having DEQ-5 scores ≥6. The tests were carried out in the same room by a single examiner, with similar temperature and humidity for all patients. The objective tests performed included:

FBUT (fluorescein breakup time)

A fluorescein strip moistened with saline was applied to the inferior cul-de-sac and the patient was asked to blink a few times. Slit-lamp bio-microscopy using a broad beam with a cobalt blue filter was used to measure the time interval between the last blink to the appearance of the first random dry spot in the cornea. Value < 10 s was indicative of tear film instability.

Ocular surface staining (OSS)

After 2 to 3 min of application of fluorescein-impregnated strip moistened with saline, the resultant staining pattern was observed, under the cobalt-blue beam of a slit lamp, and graded according to Van Bijstervald Score (vBS). Punctate epithelial erosions (PEEs) that stain with dye were counted and scored as score 0-no dots, score 1-sparsely scattered dots, score 2-densely scattered dots, and score 3-confluent spots. The maximum possible score for each cornea was 3. Nasal and temporal conjunctival were graded separately using the above score with a maximum score of 3 for each area or a total maximum score of 6 for each eye. The total vBS for each eye was the summation of the corneal and nasal and bulbar conjunctival fluorescein score. Thus, the maximum possible score for each eye was 9, and a score of ≥4 was considered abnormal.

Any patient with a DEQ-5 score ≥6 and with at least one positive objective test of the two (FBUT, OSS) was labeled as a DED patient. Patients labeled as DED were further categorized into ADDE, EDE, and mixed type based on tear meniscus height (TMH), which was manually calculated using anterior segment-optical coherence tomography (AS-OCT) from inferior tear meniscus by joining corresponding points from upper corner-meniscus junction to lower eyelid meniscus junction at the lowest margin of the cornea with the help of calipers and meibomian gland status examination performed using a slit lamp. DED patients having Tear Meniscus Height (TMH) below 0.2 mm were labeled as ADDE, whereas DED patients were labeled as EDE based on meibomian gland expressibility and meibum quality was performed using slit-lamp examination, and patients falling in both above categories were labeled as mixed variety. After the categorization of DED patients into ADDE, EDE, and mixed types, those who gave consent were further subjected to conjunctival impression cytology.

Statistical analysis

The data were compiled and subjected to statistical analysis using IBM SPSS Statistics for Windows, Version 23.0. (Armonk, NY: IBM Corp). *P* (probability value) value of < 0.05 was considered statistically significant. Categorical variables were analyzed between groups using the Chi-square test.

Results

A total of 897 patients were screened over 1 year (August 2020 to July 2021), and their demographic profile is summarized in Table 1. Out of 897 patients, 495 patients were found to have a DEQ-5 score ≥6. Out of 495 patients, 265 patients were diagnosed as having DED. Thus, the hospital-based prevalence of DED in our study was 29.54%**.** Of DED patients, 92 (34.7%) patients had ADDE, 105 (39.6%) had EDE, and 68 (25.66%) had mixed types of dry eye. The demographic features of DED patients are elaborated on in Table 2.

The prevalence of DED was found significantly higher in females (33.0%) compared to males (26.59%) (*P* value 0.0359), in age group more than 60 years (33.74%), in urban dwellers (32.44%) compared to rural dwellers (23.74%) *P* value 0.0071).

The occupation was also found to have a significant impact on the development of dry eye in our study. To determine the relation of occupation with respect to dry eye, we divided the study group into a high-risk group and a low-risk group. The high-risk group ($n = 388$) included farmers, laborers, field workers, salesman, desk job workers/person >6 h screen time, and drivers. Low-risk group ($n = 509$) included teachers, retired/unemployed, housewives, and priests. We found dry eye to be more prevalent among the high-risk group (33.50%) compared to the low-risk group (26.52%) (*P* value 0.0231).

Diabetes (*P* value 0.00001), smoking (*P* value 0.0134), history

Table 1: Demographic profile of the study population

Demographic characteristics	Number of patients (%)
Age	
Third decade	235 (26.20%)
Fourth decade	210 (23.41%)
Fifth decade	209 (23.30%)
Elderly (>60 yrs)	243 (27.10%)
Sex	
Male	485 (54.07%)
Female	412 (45.93%)
Residency	
Urban	598 (66.67%)
Rural	299 (33.33%)
Occupation	
High risk	388 (43.26%)
Low risk	509 (56.74%)

of previous cataract surgery (*P* value 0.00001), and use of visual display terminal devices (VDT) (*P* value 0.00001) were found to be significantly associated risk factors of DED as elaborated in Table 3.

A total of 151 out of 265 DED patients gave consent for undergoing impression cytology due to the ongoing COVID-19 pandemic. Of 151 DED patients, a reduction in goblet cell loss was seen in all patients. Sixty-one (40.40%) patients showed absent/occasional goblet cells, 68 (45.03%) patients showed a moderate reduction of goblet cells, and 22 (14.57%) patients showed a mild reduction of goblet cells. In the ADDE group, 10 (37.03%) patients showed absent/occasional presence of goblet cells; in mixed type, 19 (52.80%) showed absent/occasional presence of goblet cells, whereas, in EDE, 32 (36.36%) showed absent/occasional presence of goblet cells. Thus, marked goblet cell reduction was seen in the mixed group, whereas moderate reduction of goblet cells was seen in EDE and ADDE groups. Moderate to severe loss of cell cohesion was seen in 51 (33.77%) and 41 (27.15%) patients, respectively, with the presence of keratinization in 64 (42.38%) patients. Different grades of squamous metaplasia were observed among the DED patients as depicted in Table 4. The mixed group showed higher grades (grades 2 and 3) of squamous metaplasia followed by the EDE group, whereas the ADDE type of DED showed grade 2 and grade 1 metaplasia.

Table 2: Demographic profile of dry eye patients

Demographic characteristics	Number of patients (%)
Age	
Third decade (*n*=235)	69 (29.36%)
Fourth decade (*n*=210)	56 (26.67%)
Fifth decade (*n*=209)	58 (27.75%)
Elderly (>60 yrs) (*n*=243)	82 (33.74%)
Sex	
Male (*n*=485)	136 (33%)
Female (*n*=412)	129 (26.59%)(*P*-0.0359)
Residency	
Urban (*n*=598)	194 (32.44%)
Rural (*n*=299)	71 (23.74%)(*P*-0.0071)
Occupation	
High risk (*n*=388)	130 (33.50%)
Low risk (*n*=509)	135 (26.52%)(*P*- 0.0231)

Table 3: Other factors in relation to dry eye in the study population

	DED positive cases (*n*=265)		DED negative (*n*=632)		*P*
	Number	%	Number	%	
Diabetes	37	13.96%	53	8.38%	0.00001
Smoking	35	13.20%	50	7.91%	0.0134
Cataract surgery (>12-month duration)	54	20.37%	60	9.49%	0.00001
VDT use	81	30.56%	102	16.14%	0.00001

Table 4: Grading of squamous metaplasia in different groups

Grade	ADDE (*n*=27)	EDE (*n*=88)	Mixed (*n*=36)
Grade 1	9 (33.33%)	16 (18.18%)	8 (22.22%)
Grade 2	13 (48.15%)	53 (60.23%)	11 (30.55%)
Grade 3	5 (18.51%)	19 (21.16%)	17 (47.22%)

Discussion

DED is a major healthcare problem affecting millions of people worldwide and one of the most frequent causes of visits to an ophthalmologist.[6] It affects the quality of life by causing disabling symptoms and signs.

Diagnosis of dry eye is complex because dry symptoms and signs do not always correlate with each other. TFOS DEWS II, in 2017, proposed a new guideline for diagnosing dry eye. According to DEWS II, "Any patient with the presence of both symptoms (DEQ-5 score ≥6) and signs (at least one positive objective test of the two [FBUT, OSS]) was labeled as DED patients."

Dry eye prevalence in India ranges from 18.4% to 54.3%.[7,8,12] The reasons for such a vast disparity in DED prevalence could be attributed to geographical variations, climatic conditions, the lifestyle of people, and lack of standard dry eye diagnostic criteria. The dry eye prevalence of our hospital-based study based on DEWS II guidelines was 29.54%, which falls within the above range. Other studies have also reported a higher DED prevalence such as Sahai and Malik,[11] Chavhan *et al*.,[13] Titiyal *et al*.,[10] Hikichi *et al*.,[1] Baisoya *et al*.[14] but none of the studies had used any standard DED diagnostic protocol, which our study has used for diagnosing DED. Of DED patients, EDE patients showed a higher preponderance.

Our study reflects an increase in the prevalence of dry eye in those above 60 years of age as a result of decreased tear secretion, increasing meibomian gland dysfunction, and thinning of the lipid layer with advancing age. The second peak was found in the age group of 30–40 years as this age group is more prone to the use of VDT devices with screen time of more than 6 h, which reduces the blink rate, increases exposure to the air conditioner, and is occupationally most active with increased exposure to air pollution and smoking.

As reported by previous studies,[8,9,11,13,15,16] our study also observed a higher prevalence of dry eye among females. Hormonal influences play an important role in the development of dry eye among females as sex hormones effects both the lacrimal and meibomian glands. Also, post-menopause, there occurs estrogen deficiency, which decreases tear production from the lacrimal gland resulting in dry eye.

Urban dwellers were found to be more prone to the development of the dry eye. This was consistent with the studies conducted by Chavhan *et al*.,[13] Donthineni *et al*.,[16] and Hikichi *et al*.,[1] which also documented a higher prevalence of dry eye in the urban population. This could be explained due to increased use of VDT devices and air conditioners among urban dwellers, and the presence of air pollution.

Increased exposure to environmental conditions such as sunlight, high temperatures, windy conditions, dirt, dust, and air pollution among farmers/laborers, field workers, salesmen, and drivers; and reduced blink rate hampering uniform tear film distribution among desk job workers with increased use of computers could be a possible explanation of increased dry eye prevalence among high-risk groups. These were comparable to studies conducted by Sahai and Malik,[11] Titiyal *et al*.,[10] and Chavhan *et al*.[13]

Diabetes mellitus has been recognized as one of the leading systemic risk factors for DED. Several studies have revealed a higher prevalence of DED in diabetic patients such as the Beaver Dam Eye study, which reported that 20% of dry eyes occurred in type 2 diabetic patients aged between 43 and 86 years, Hom and De Land[17] reported 53% of diabetic patients had a dry eye. Our study also observed diabetes to be a significant risk factor for DED. This could be attributed to chronic tear secretion deficiency, tear film dysfunction,[18,19] a significant decrease in the thickness of the lipid layer, stability of tear film, corneal sensitivity, and tear quantity[20] in diabetics. We also noted smoking to be a significant risk factor for DED, which has a harmful detrimental effect on the ocular surface and tear film stability.[21]

A significant association between the development of dry eye with a history of previous intraocular surgeries, particularly cataract surgery, was also observed in our study. Abnormal meibomian gland,[22] and thinning of the lipid layer[23] were reported as the cause of dry eye following cataract surgery. Another mechanism responsible for dry eye post cataract surgery could be damage to the corneal sensory nerve as a result of incision highlighted by other studies as well.[24]

One of the common extrinsic risk factors for the development of dry eye is the use of a digital screen (laptops, computers, smartphones, and tablets), which affects the blinking dynamics (reduction of both blink rate and blink completeness), leading to increased ocular surface dryness.[25,26] In the present era, the use of digital screen time increased significantly due to the COVID-19 pandemic, which made people stay at home and work, study, learn, and socialize virtually.[27] In our study, we found that people using digital screen time for more than 6 h were significantly associated with the development of dry eye as shown by reduced tear breakup time and increased ocular surface staining, which correlated with the OSAKA study[25] and JPHC-NEXT study.[26]

In this study, we also analyzed the potential of conjunctival impression cytology to differentiate among the different categories of dry eye patients. We observed a reduction in goblet cell loss in all dry eye patients with marked goblet cell reduction seen in the mixed group, whereas a moderate reduction of goblet cells was seen in EDE and ADDE groups. The mixed group showed a higher grade (grades 2 and 3) of squamous metaplasia followed by the EDE group and ADDE. However, no conclusive information could be drawn from the above observation due to the small sample size.

A major limitation of this study was that it was a hospital-based study, thus the study may not be representing the real picture at the community level. Secondly, the cross-sectional design, of the study restricts the ability to infer causality because only potential associations between DED and identified risk factors could be demonstrated. Thirdly, all cases of gross corneal/conjunctival pathologies, contact lens users, use of topical medications, and systemic conditions such as Sjogren syndrome were excluded from the study, thereby underestimating DED prevalence. Fourthly, due to the COVID-19 pandemic, impression cytology could not be performed in all dry eye subjects.

Conclusion

Hospital-based prevalence of DED in a tertiary care hospital is 29.5% with a preponderance of EDE. Thus, this study reflects a major burden of DED on routine outpatients. Our study also showed that age, sex, residency, and occupation have a significant impact on the development of DED. Reduction of goblet cells and different grades of squamous metaplasia were observed among DED patients. The mixed group showed a marked reduction in goblet cells and a higher grade (grades 2 and 3) of squamous metaplasia compared to other types.

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Conflicts of interest

There are no conflicts of interest.

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