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Prevalence of dry eye in people over 50 years old in Beichen district, Tianjin city: a cross-sectional population-based survey

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Abstract

Background A cross-sectional population-based survey in the Beichen district of Tianjin was conducted to estimate the prevalence of dry eye disease (DED) among the population over 50 years old with Dry Eye Workshop (DEWS) II and Chinese expert consensus (CEC) criteria.

Methods A total of 5791 subjects over 50 years old were enrolled. Ocular surface disease index (OSDI) questionnaire, lipid layer thickness (LLT), partial blink ratio (PBR), fluorescein tear film breakup time (FBUT), Schirmer I test (SIT), fluorescein staining, meibomian gland dropout, meibomian gland expression scores (MES) and quantity scores (MQS) was assessed. Additionally, basic information, weight, disease history, living habits, anxiety, and depression condition were collected.

Results According to the CEC, the prevalence of DED was 39.0%, whereas 44.0% based on DEWS II. The prevalence of DED increased with age and was substantially greater among women (41.1%, 95% CI, 39.5–42.6%) than males (35.1%, 95% CI, 33.1–37.2%) ($p < 0.001$). Furthermore, the severity of DED was more severe in women ($p = 0.006$). The associated risk factors were age, female, depression, smoking, insomnia, and glaucoma. On the other hand, 53.6% of these populations were diagnosed as asymptomatic DED, and the morbidity was higher in males ($p = 0.007$).

Conclusions The prevalence of DED in China was relatively high, which was associated with aging, female (sex), depression, smoking and sleep problems. Hence, it is crucial for clinicians and caregivers to be aware of the existence of asymptomatic DED within the susceptible population.

Keywords Prevalence, Dry eye disease, Risk factors, Sex, Sleep disorders

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Introduction

Dry eye disease (DED) is a chronic ocular surface disease caused by multiple factors. The unstable tear film or imbalance of the ocular surface microenvironment is caused by abnormal tear quality, quantity, and dynamics. It can be accompanied by ocular surface inflammatory reaction, tissue damage, and nerve abnormality, resulting in various ocular discomfort symptoms and/or visual dysfunction [1]. DED can cause a variety of eye symptoms, such as pain, itching, photophobia, fatigue, burning, foreign body sensation, and visual impairment [2, 3], therefore, has a significant impact on the mental state, quality of life, and work efficiency of patients. In China, the average annual economic loss of each dry eye patient due to treatment was estimated to be 465.54 ± 303.08 USD [4].

In recent years, factors such as environmental pollution and the popularity of smartphones and computers has been reported to worsen the prevalence of DED [5]. However, it has also been suggested that due to differences in demographic characteristics and the DED diagnostic criteria or tests used in the study, the prevalence of DED can be biased [6]. According to the 2017 Dry Eye Workshop (DEWS) II, the prevalence of DED worldwide was 5–50%. In the United States, Dana et al. [7] analyzed the United States Health Care System and found that prevalence of DED in the United States was 5.28%. Cafery et al. [8] investigated the population of Ontario and found that the prevalence of DED was 22.0%. However, the prevalence of DED in Asia was the highest and had become an independent risk factor for DED [9]. Sherry et al. [10]. found that the prevalence of DED in people over 18 years old was 36.4% in Lebanon. In India, the prevalence of DED in rural areas was 34.98%, while in urban areas, 65.02% [11]. A survey in Japan showed that the prevalence of DED in people aged 40–74 was 48.2% [12]. Meta-analysis showed the prevalence of DED in China was 13.55% according to the literature published from 1990 to 2016 [3], especially the prevalence reached 52.4% in Tibet [13].

DED is a multifactorial disease, and senility is one of the most important contributing factor. Bakkar et al. [14]. and Wang et al. [15]. found that the prevalence of DED increased with age. Dana R et al. [7] reported that the prevalence of DED increased from 0.02% at the age of 2–17 to 11.66% of the population over 50 years old through the analysis of the data from the United States Health Care System. In addition to the region and age, sex is also an important factor. Bikbov et al. [16]. Reported that the prevalence of DED in females was higher in Russia. Moreover, DED has been related to video terminal usage, diabetes, sleep disorders, anxiety and depression, abnormal lipid metabolism, the use of contact lenses, eye surgery and other factors [12, 17–22]. However, there is

a paucity of epidemiological studies on DED from China and the study data usually consists of outpatients. Hence, the objective of this investigation was to examine the frequency and determinants of DED among individuals aged 50 and above, not receiving clinical treatment.

Methods

Study population

The data was from the Beichen Eye Study. Beichen Eye Disease was an epidemiological survey of eye diseases based on community population by Tianjin Medical University Eye Hospital from December 2019 to February 2022. Beichen District, located in the north of the central of Tianjin, is in the transition stage from rural to urban, with small population flow, which meets the basic requirements of epidemiological investigation. This study obtained the ethical approval from the Ethics Committee of the Tianjin Medical University Eye Hospital (Ethics approval number: 2019ky-22). All subjects signed the informed consent form. The Beichen District has 16 streets (towns) and a multi-stage random sampling method was adopted. Four streets (towns) were randomly selected at the first stage and then 12 villages (neighborhood communities) with 8,218 residents were randomly selected. The list of sampling frame was obtained from the Beichen District Health Commission and neighborhood committees. Recruitment information was released to selected villages through leaflets and promotional videos and residents contacted by phones to confirm whether they qualified for enrolment. Individuals had to be aged 50 years of age or older, and to have been a resident at least 6 months in the target neighborhood community to be eligible for inclusion in the study. Exclusion Criteria: (1) Those who had moved from their residing address, had not lived there for more than 6 months, life expectancy less than 3 months or had severe mental illness, not contactable (after three unsuccessful phone calls); (2) Any eye disease diagnosed as affecting tear quality, tear volume or tear production, such as eyelid entropion, ectropion, ptosis, eyelid dyskinesia and conjunctivitis; (3) History of eye surgery or retinal laser photocoagulation within the past 6 months; (4) Systemic diseases outside the study; (5) Long-term oral or topical use of antibiotics or dry eye disease related drugs. A total of 5791 subjects were included in the study. Written informed consent was obtained from each participant. The present research adhered to the tenets of the Declaration of Helsinki.

Questionnaire

The information was collected by three trained investigators. The questionnaire include: (1) Basic information: name, sex, age, education level and occupation; (2) Disease history: hypertension, diabetes, abnormal lipid

metabolism, cardiovascular and cerebrovascular diseases, and eye diseases; (3) Life habits: The daily behaviors such as using video terminals, smoking, drinking and sleeping. (4) Anxiety and depression questionnaire. (5) Ocular Surface Disease Index (OSDI) questionnaire. The OSDI score was defined as normal (0–12 points), mild (13–22 points), moderate (23–32 points), or severe (33–100 points) [23, 24].

Comparison between the diagnostic criteria

According to the Chinese expert consensus (CEC) on DED [1, 25], the diagnostic criteria for DED are: (1) The patient complained one of the subjective symptoms, such as dryness sensation, foreign body sensation, burning sensation, fatigue, discomfort, redness of eyes, visual fluctuation, etc., the China Dry Eye Questionnaire ≥ 7 points or the OSDI ≥ 13 points; At the same time, fluorescein tear film breakup time (FBUT) ≤ 5 s or noninvasive breakup time (NIBUT) < 10 s, or Schirmer I test (without anesthesia) ≤ 5 mm/5min can be diagnosed DED. (2) The patient has symptoms related to DED, the China Dry Eye Questionnaire ≥ 7 points or the OSDI questionnaire ≥ 13 points; At the same time, FBUT > 5 s and ≤ 10 s or NIBUT = 10~12s, Schirmer I test (without anesthesia) > 5 mm/5min and ≤ 10 mm/5min, need to use fluorescein sodium staining to check the corneal and conjunctiva. Positive staining (≥ 5 points) can diagnose DED. Dry Eye Workshop (DEWS) II states that, symptoms and at least one positive result (NIBUT or FBUT < 10 s, Osmolarity ≥ 308 mOsm/L in either eye or interocular different > 8 mOsm/L, ocular surface staining > 5 corneal spots or > 9 conjunctival spots or lid margin ≥ 2 mm length & $\geq 25\%$ width) should also constitute the diagnosis of DED [26]. Participants were assessed using both DED diagnosis criteria and compared (CEC and DEWS II). In addition, we defined asymptomatic DED as a population with the OSDI score < 13 but clinical signs that meet the Chinese DED criteria [27].

Examinations

Systemic examinations

The examination of height, weight, waistline, hipline and blood pressure of the study populations was performed. In addition, routine blood test, blood sugar, glycosylated hemoglobin (HbA1c), lipid metabolism and hepatic and renal functions of each participant were tested by venous blood collection.

Ocular examinations

Lipid layer thickness (LLT) of tear film and partial blink ratio (PBR) were measured by LipiView® II Ocular Surface Interferometer (TearScience, Inc. NC, USA). In addition, we used LipiView Interferometer to take photos of the meibomian gland (separate measurement over the upper

lid and lower lid) of each participant, and scored the meibomian gland dropout according to the photos: 0 point, no meibomian gland dropout; 1 point, meibomian gland dropout ratio $< 1/3$; 2 points, the meibomian gland dropout ratio is $1/3-2/3$; 3 points, meibomian gland dropout ratio $> 2/3$. Subsequently, FBUT and corneal were examined using fluorescein staining with slit lamp examination. In a nutshell, the Fluorescein Sodium Ophthalmic Strips (Tianjin Jingming New Technological Development Co.,Ltd) was soaked with normal saline and then gently coated on the conjunctival sac. It is evenly distributed in the cornea by multiple blinks. Cobalt blue light of slit-lamp biological microscope was used for observation [28]. The expressibility of meibum was observed with the Meibomian Gland Evaluator (separate measurement over the upper lid and lower lid). There are 5 glands at each position, and a total of 15 glands were observed. Three positions were detected on each eyelid of the participant: Nasal, middle and temporal. 0 point, all glands expressible; 1 point, 3–4 glands expressible; 2 points, 1–2 glands expressible; 3 points, no glands expressible. At the same time, the characteristics of its secretion were also scored. The scoring standard is: 0, clear liquid; 1 point, cloudy liquid; 2 points, cloudy particulate fluid; 3 points, inspissated, like toothpaste. The upper and lower lids of each eye were also detected and recorded. Finally, Schirmer I test was used to detect the basic tear secretion (Fig. 1).

Data analysis

All data were analyzed using the Statistical Package for Social Sciences (SPSS) software (SPSS for windows version 24.0; SPSS Inc, USA). The values conforming to the normal distribution are expressed by the mean \pm standard deviation, and the data not conforming to the normal distribution are expressed by the median (interquartile interval). Chi-square test was used to test the difference of prevalence among groups. Wilcoxon (Mann-Whitney) rank sum test was used for data that did not conform to the normal distribution. Chi-square test and logistic regression model were used to analyze the related factors of DED. P values < 0.05 were considered statistically significant.

Results

A total of 5791 volunteers were assessed in this study, with median age of 63 (range: 58, 67). Of these, 2056 comprised of males (35.5%), with a median age of 64 (range: 59, 68) and 3735 females (64.5%), with a median age of 62 (range: 57, 67). The population of individuals between the ages of 60 and 69 was 2896, accounting for 50.0% of the total, 1959 individuals (33.8%) were aged 50–59 and 936 individuals (16.2%) were aged 70 and above. Junior high school degree held the highest proportion of subjects, 2518 (43.5%), in relation to their educational attainment.

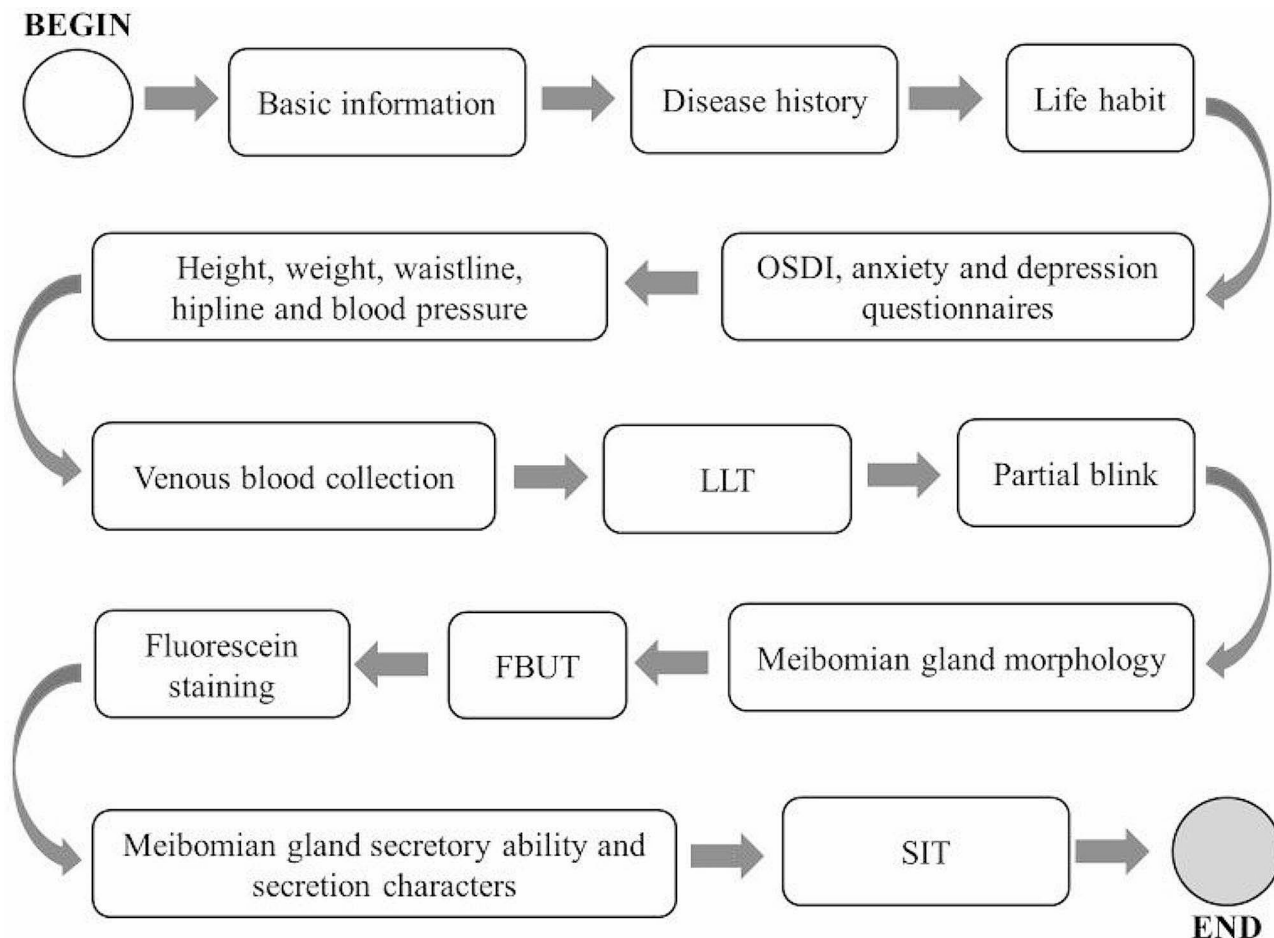


Fig. 1 Examination flowing chart
 OSDI: Ocular Surface Disease Index questionnaire; LLT: Lipid layer thickness; FBUT: fluorescein tear film breakup time; SIT: Schirmer I test

With regard to weight distribution, the study population comprised of 4229 individuals (74.2%) who were classified as overweight or obese. (Table 1).

Based on the CEC for DED, the study found that 2256 individuals had DED, resulting in a prevalence rate of 39.0%. When applying the DEWS II diagnostic criterion, we observed that 2547 patients had DED, with a prevalence rate of 44.0%. This prevalence rate was significantly greater than that determined by the CEC ($p < 0.001$) (Table 2).

The following data analysis was based on the CEC for DED. Prevalence was highest among aged 70 and above (42.4%; 95% CI, 39.2-45.6%) and lowest among those aged 50–59 years (35.8%; 95% CI, 33.7-37.9%). Prevalence among those aged 60–69 years was 40.0% (95% CI, 38.2–41.8%). The prevalence of dry eye increased with age, and the prevalence of DED among those aged 50–59 years was significantly lower than among those aged 60–69 years ($p = 0.01$) and aged 70 and above ($p = 0.002$), while the prevalence of DED among those aged 60–69 years

and aged 70 and above had no significant statistical difference ($p = 0.556$) (Table 3).

In terms of sex, the number of male patients with dry eye was 722, accounting for 35.1% (95% CI, 33.1-37.2%) of the male subjects (2056) in this study, whereas the number of female dry eye patients was 1534, reaching 41.1% (95%CI, 39.5-42.6%) of the female subjects (3735). The prevalence of female was significantly higher than that of male ($p < 0.001$) (Fig. 2). After comparing the prevalence of DED in different sexes of each age group, it was found that the prevalence of DED in female of all age was higher than that in male, but there was no statistically significant difference among those aged 50–59 years ($p = 0.077$), and the difference was the largest among those aged 60–69 years ($p < 0.001$) (Fig. 3).

According to the OSDI scores, study population with DED were divided into mild, moderate and severe. After comparing the prevalence of DED severity among sexes and ages (Table 4), it was found that the prevalence of severe DED in females were significantly higher than that

Table 1 Demographic characteristics of study populations

Demographic Characteristics	Number(%)	
Age, years	Male	Female
50–59	553(26.9)	1406(37.6)
60–69	1095(53.3)	1801(48.2)
≥ 70	408(19.8)	528(14.1)
Qualifications		
Unschooling	239(4.1)	
Literacy class	21(0.4)	
Primary school	1235(21.3)	
Junior high	2518(43.5)	
Senior high	1075(18.3)	
Polytechnic school	283(4.9)	
College	284(4.9)	
Bachelor Degree	131(2.3)	
Postgraduate	3(0.1)	
BMI		
Underweight	52(0.9*)	
Normal	1421(24.9*)	
Overweight	2595(45.5*)	
Obese	1634(28.7*)	

*: The height and weight of 89 subjects were not measured due to inconvenient movement and other reasons, which was shown as an effective percentage.

Table 2 Prevalence of DED in different criteria

DED criteria	DED (n)	Non-DED (n)	Prevalence (%)	p
CEC	2256	3535	39.0	< 0.001
DEWS II	2547	3244	44.0	

DED: Dry eye disease; CEC: Chinese expert consensus; DEWS II: Dry Eye Workshop II

Table 3 Prevalence of DED in study population among different ages groups

Age, years	Study participants (N=5,791) N1(%) vs. N2(%)	χ ²	p
50–59 vs. 60–69	701(35.8)vs 1,158(40.0)	8.735	0.010
50–59 vs. ≥ 70	701(35.8)vs 397(42.4)	11.829	0.002
60–69 vs. ≥ 70	1,158(40.0)vs 397(42.4)	1.730	0.556

N: Represented the number of DED in each age group

*: DED in this age group/Total population in this age group*100%

in males (p=0.006), however, there was no statistically significant difference in other groups (P>0.05).

Ocular surface symptoms and sign

Compared with non-DED populations, FBUT, Schirmer I test, PBR and meibomian gland expressibility of DED population were significantly worse (p<0.05). The mean LLT, meibomian gland morphology and secretion characteristics scores were not significant difference (Table 5).

Risk factors for DED

Logistic regression analysis was performed on the possible influencing factors of DED, and the analysis results are shown in Table 6. Increasing age, female, depression,

smoking, insomnia, and glaucoma were strongly associated with DED, while mobile phone use was negatively associated with DED. Compared to non- depressed populations, mild and moderately severe depressed populations were more prone to DED (p<0.05). The number of volunteers with sleep disorder suffering from DED was found to be 1188, accounting for 52.7% of the total number of DED participants. There was a statistically significant association between sleep disorder and DED (p<0.001). The proportion of smokers in DED populations (20.5%) was higher than that in non-DED populations (19.5%), and the difference was obvious (p=0.002). In the blood test results of participants in this study, the prevalence of DED with high cholesterol was lower than that of normal cholesterol (Table 6).

Asymptomatic DED

Furthermore, the study identified 3105 of the participants had asymptomatic DED, resulting in the prevalence of 53.6%. Among them, the number of asymptomatic males with DED were found to be 1151, accounting for 56.0% (95% CI, 53.8 -58.1%) of males in this study; 1954 female, accounting for 52.3% of the females in this study (95%CI, 50.7-53.9%). The incidence of asymptomatic DED in male was found to be higher than that in female, with statistically significant difference (p=0.007) (Fig. 4).

In terms of age, the number of asymptomatic DED patients in 50–59 years old was 1106, accounting for 56.5% (95% CI, 54.3 -58.7%) of the participants in this age group. On the contrary, the lowest morbidity of asymptomatic DED was 48.6% (95% CI, 45.4 -51.8%) among

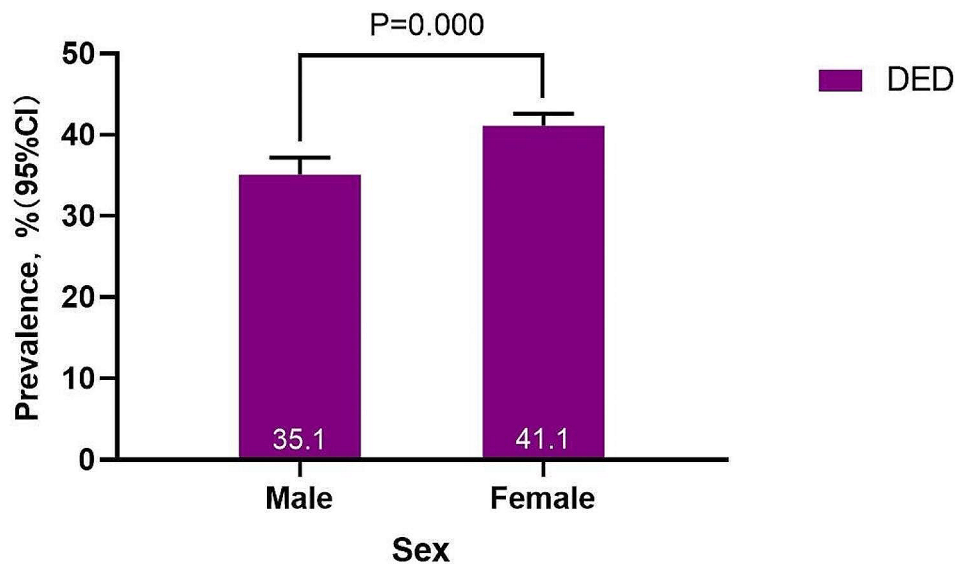


Fig. 2 Prevalence of DED among sexes

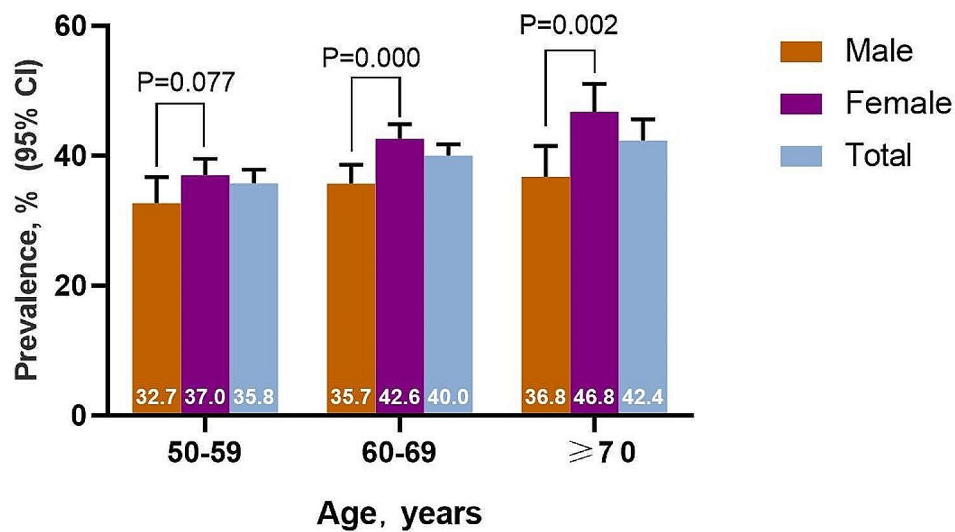


Fig. 3 Prevalence of DED in various age groups, categorized by sex. In 50–59 age group, there is no significant difference between male and female. However, the prevalence of DED was notably greater in females than in males within the age groups of 60–69 years and over 70 years

Table 4 Prevalence of varying severity of DED in different sexes and ages

DED degrees	Sex			p	Age			p
	Male	Female			50–59	60–69	≥ 70	
Mild (%)	334 (46.3)	665 (43.4)	0.194	304 (43.3)	515 (44.5)	180 (45.3)	0.804	
Moderate (%)	213 (29.5)	411 (26.7)	0.180	203 (29.0)	315 (27.2)	106 (26.7)	0.639	
Severe (%)	175 (24.2)	458 (29.9)	0.006	194 (27.7)	328 (28.3)	111 (28.0)	0.954	

Table 5 Comparison of ocular surface parameters between DED and Non-DED

Ocular Surface Parameters	Non-DED (n=7276)	DED (n=4306)	Z	p
FBUT/ [s, M(IQR)]	3.33(3.00)	3.33(1.67)	-7.126	0.000
SIT/ [mm, M(IQR)]	7.00(8.00)	6.00(7.00)	-1.431	0.000
LLT/ [nm, M(IQR)]	74.0(37.00)	73.0(40.00)	-0.776	0.504
PBR/ [%, M(IQR)]	0.83(0.50)	0.80(0.57)	-2.528	0.000
Meibomian gland dropout _{av} */ [M(IQR)]	2.00(0.50)	2.00(1.00)	-2.019	0.992
MES _{av} */ [M(IQR)]	4.50(3.00)	4.50(2.50)	-1.053	0.000
MQS _{av} */ [M(IQR)]	1.00(0.50)	1.00(0.50)	-1.347	0.069

FBUT: fluorescein tear film breakup time; SIT: Schirmer I test; LLT: lipid layer thickness; PBR: partial blink ratio; MES: meibomian gland expression scores; MQS: meibomian gland quantity scores

*av: Average value of two eyes

those aged 70 and above. There were statistically significant differences in the prevalence rates among different age groups (Table 7).

Discussion

This study was the community-based epidemiological survey of DED in Beichen District, Northern China. According to the CEC diagnostic criteria for DED, the analysis found that the prevalence of DED was 39.0%, coinciding to the worldwide prevalence of DED (5–50%) according to the DEWS II in 2017 [9]. When we used DEWS II diagnostic criteria, the prevalence of DED was 44.0% in our study, which was significantly higher than CEC criteria. A major challenge in the epidemiological study of DED is that there are no specific or universal diagnostic criteria that is utilized by various regions and populations [9]. Compared to the DEWS II criteria, CEC diagnoses fewer cases. Research has showed that there is a good concordance between the CEC and the Asian Dry Eye Society diagnostic criteria was (97.2%) [29]. A large amount of evidence suggests that the probability of DED in Asian people was 1.5–2.2 times that of western population [9]. This disparity in the prevalence could be related to the diagnostic criteria utilized by publications as most Asian publications tends to follow the criteria laid out by DEWS. However, research also suggests that the prevalence of DED could be regional as the prevalence of DED in India was found to be 32%–64% in Palestine [30] and Inner Mongolia, China, was found to have a prevalence rate of 34.5% [31]. Nevertheless, while the effect of diagnostic criteria and regions on the prevalence of DED can be further explored, it is important monitor and address the high prevalence of DED among communities.

Another possible explanation for the high occurrence seen in this research might be the advanced age of the participants. Previous studies have consistently shown a strong correlation between dry eye disease (DED) and older age. DEWS II, a comprehensive report on DED, also noted a progressive rise in DED prevalence among those aged 50 and above [9] which is consistent with the results

of this study. In addition, a large DED survey conducted by Dana et al. [7] found that the prevalence of DED increased from 0.20% aged 2–17 to 11.66% aged over 50, which also confirmed that the prevalence of DED aged over 50 was higher. Our research revealed substantial variations in the occurrence of DED among individuals over the age of 50 at various age intervals. Furthermore, there was a notable correlation between age and the likelihood of developing DED, with the risk increasing as age advanced. However, there was no notable disparity in the intensity of DED across different age groups.

We observed that the incidence and intensity of DED were greater in females compared to males. The DEWS II confirms that there is a significant difference in the occurrence of DED across sexes in individuals aged 50 years and older. Furthermore, sex was found to be an independent risk factor for DED in our study [9]. In addition, studies by Wang et al. [15], Dana et al. [7], and Bikbov et al. [32], have reported the higher risk of DED in elderly female population due to the decline in estrogen and progesterone secretion [3, 33]. Furthermore, females have been reported to have a higher susceptibility to immunological illnesses compared to males, including Sjogren's syndrome, systemic lupus erythematosus, thyroid disease, and rheumatoid arthritis, all of which may also contribute to DED [34].

Upon examination of the risk factors, DED correlated with sleep disorders, smoking, depression, glaucoma, mobile phone use, and television viewing or video game playing on a television screen. Increasingly, researchers are focusing on the connection between sleep disturbances and DED. A large, community-based study in Hangzhou, China showed a strong positive association between sleep disorders and higher severity of DED [35]. Similar to previous studies, our research also found that 1188 people with DED had sleep disorders, accounting for 52.7% of the total number of DED, which has obvious statistical significance in logistic regression analysis. Depression can also affect DED, which is similar to sleep disorders. It was reported that patients with depression

Table 6 Correlation analysis of factors for DED

Risk factor	Population count		Population %		p	OR (95%CI)
	DED (n = 2256)	Non-DED (n = 3535)	DED (39.0%)	Non-DED (61.0%)		
Age, years						
50–59	701	1258	35.8	64.2	Ref	Ref
60–69	1158	1738	40.0	60.0	0.04	1.196(1.058–1.352)
≥70	397	539	42.4	57.6	0.01	1.346(1.137–1.593)
Sex						
Male	722	1334	35.1	64.9	Ref	Ref
Female	1534	2201	41.1	58.9	0.000	1.304(1.133–1.502)
Level of education						
High and above	676	1580	30.0	70.0	Ref	Ref
Junior high and below	1100	2435	31.1	68.9	0.779	0.983(0.873–1.108)
BMI						
Normal	565	856	39.8	60.2	Ref	Ref
Underweight	28	24	53.8	46.2	0.082	1.652(0.939–2.909)
Overweight	1005	1590	38.7	61.3	0.964	0.997(0.870–1.142)
Adiposity	621	1013	38.0	62.0	0.710	0.972(0.834–1.131)
Depressed						
NO	2101	3413	93.1	96.5	Ref	Ref
Mild	120	99	5.3	2.8	0.000	1.675(1.266–2.216)
Moderate	21	15	0.9	0.4	0.079	1.852(0.932–3.679)
Moderately severe	13	5	0.6	0.1	0.019	3.480(1.231–9.843)
Severe	1	3	0.04	0.08	0.424	0.395(0.041–3.842)
Habits						
Smoke	463	691	20.5	19.5	0.002	1.276(1.096–1.485)
Drink	397	720	17.6	20.3	0.393	0.932(0.793–1.095)
Sleep disorders	1188	1514	52.7	42.8	0.000	1.392(1.245–1.557)
Afternoon nap	1181	1822	52.3	51.5	0.465	1.041(0.934–1.161)
Use mobile phone	2105	3360	93.3	95.0	0.027	0.767(0.607–0.970)
Read book or newspaper	-	-	-	-	0.862	1.003(0.968–1.039)
Play computer	-	-	-	-	0.244	0.957(0.889–1.030)
Watch TV or play games	-	-	-	-	0.008	0.962(0.934–0.990)
Diagnosis						
Pterygium	55	86	2.4	2.4	0.959	0.991(0.696–1.411)
Glaucoma	55	47	2.4	1.3	0.014	1.659(1.110–2.479)
Hypertension	1067	1551	47.3	43.9	0.058	1.116(0.996–1.251)
Diabetes mellitus	500	766	22.2	21.7	0.783	0.981(0.858–1.122)
Blood data						
Glucose	-	-	-	-	0.644	0.981(0.905–1.064)
HbA1c	-	-	-	-	0.938	0.995(0.869–1.139)
Triglyceride	-	-	-	-	0.386	0.991(0.971–1.012)
Cholesterol	-	-	-	-	0.033	0.768(0.602–0.980)
LDL	-	-	-	-	0.073	1.337(0.973–1.837)
HDL	-	-	-	-	0.566	1.153(0.710–1.872)

often have sleep disorders [36, 37]. He et al. [19] conducted a study on 321 DED patients from the Tianjin Medical University Eye Hospital and found that there was a significant correlation between DED and depression, and sleep disorders was the mediator between DED and depression; Coincidentally, the study by Liu et al. [38] also found that depression is closely related to DED, and sleep

disorders was associated with anxiety and depression in patients aged 41 to 65. Therefore, according to previous studies, the impact of depression on DED is likely to be achieved through sleep disorders. Conversely, the quality of life decreased with DED can lead to anxiety, depression, sleep disorders and other conditions. Compared to other irritant eye diseases (such as chronic conjunctivitis,

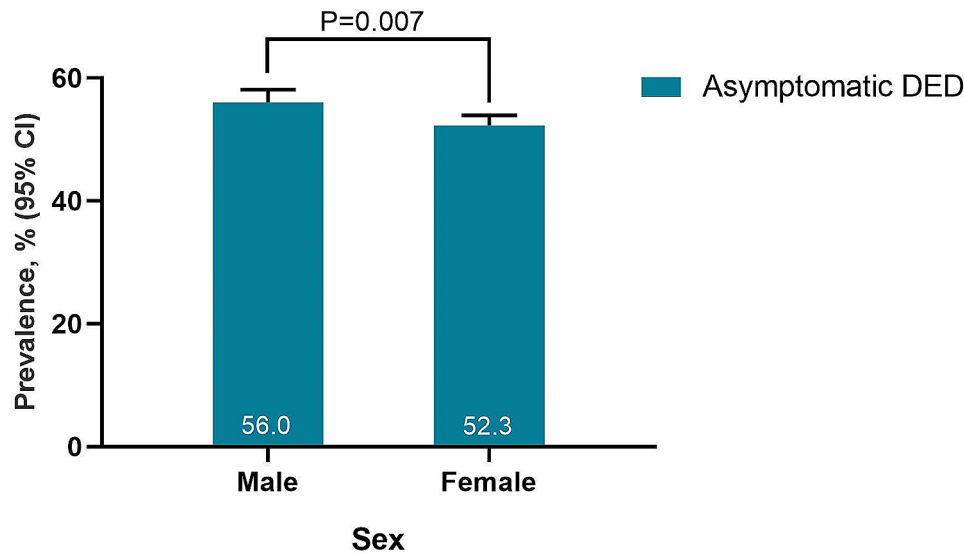


Fig. 4 Comparison of the prevalence of DED among sexes. Compare the prevalence of asymptomatic DED in different sexes. The number of asymptomatic DED in male was 1151 (56.0%, 95% CI 53.8%–58.1%); in female was 1954 (52.3%, 95% CI 50.7–53.9%). The prevalence of DED in male was significantly higher than that in female ($p=0.007$)

Table 7 Prevalence of asymptomatic DED in study populations among different ages

Age, years	Study participants (N=5,791) N1(%) vs. N2(%)	χ^2	p
50–59 vs. 60–69	1,106 (56.5) vs. 1,544 (53.3)	4.655	0.031
50–59 vs. ≥ 70	1,106 (56.5) vs. 455 (48.6)	15.694	0.000
60–69 vs. ≥ 70	1,544 (53.3) vs. 455 (48.6)	6.272	0.012

*: Asymptomatic DED in this age group/Total population in this age group*100%

allergic conjunctivitis, etc.), DED can cause more severe sleep disorders [39]. In summary, DED, sleep disorders, and depression interact with each other. The occurrence of one disease may lead to the occurrence or exacerbation of the other two diseases. In a large registry study, 52.6% (10,338/19,665) of glaucoma patients were diagnosed with DED [40]. Similar to the findings in the general population, DED in patients with glaucoma is more prevalent in the elderly population. And it was more common in women (56.9%) than men (45.7%) [41]. Similar to these studies, our study also found that glaucoma is a significant risk factor for DED. The increased prevalence of DED in patients with glaucoma is often associated with the use of anti-glaucoma drugs. In a large study of glaucoma patients (N=10,325), the odds of DED were found to increase with the number of drugs used (OR=1.23, 2 drugs; OR=1.63, 3 drugs; OR=2.60, containing 4 drugs) [42]. Together, these findings suggest that it is particularly important to evaluate DED in patients with glaucoma.

Interestingly, we found a decrease in the prevalence of DED among elderly people who use smartphone and watch or play game on TV. In contrast, extensive

cross-sectional analysis found that the use of video terminals can lead to an increase in the prevalence of DED. Nguyen et al.'s research even suggested that using visual display terminal (VDT) and other sedentary activities can increase the incidence of DED [43]. We speculate that this may be related to the age of the study population. Most of the study population is students or staff, with a younger age, this article focused on middle-aged and elderly people over 50 years old. This may be due to the fact that older people spend less time and frequency using electronic devices than younger people. In China and other low- and middle-income countries, especially in rural areas, a digital divide between older and younger people is still prevalent [44]. Older people's inability to afford Internet access or related devices, or their lack of knowledge and skills to use these technologies make a significant difference in the frequency of their use of electronic devices compared with younger generations [45]. In addition, having severe DED significantly affects visual quality, and this population may be less likely to choose to use VDT [46], resulting in a lower prevalence of DED among older adults who use VDT. We need more mechanistic research to determine the impact of VDT on the population aged 50 and above.

Research had found that dyslipidemia, especially hypercholesterolemia, could increase the melting point of meibomian gland lipid, which could not be squeezed from the meibomian gland, leading to DED [20]. However, there were different results in different cross-sectional studies: Vehof et al. [47]. found no significant correlation between DED and dyslipidemia; Rathnakumar et al. [20]. found that the increased prevalence of DED was related to hypercholesterolemia in female; Through a survey of

2272 middle-aged people in South Korea, Choi et al. [48] found that dyslipidemia was more likely to lead to an increase in the prevalence of DED in male. This study differs from previous studies in that the increase in total cholesterol leads to a decrease in the prevalence of DED, while the rest of the blood results have no significant correlation with DED.

Patients exhibiting signs of ocular surface disease but reporting no symptoms of discomfort was called asymptomatic DED, which was mentioned in DEWS II [26]. We observed that the prevalence of asymptomatic DED was 53.6%. Surprisingly, the condition of asymptomatic DED is opposite to that of DED. The prevalence of asymptomatic DED in male was higher than that in female, and the younger the age, the higher the incidence of asymptomatic DED. The mismatch between symptoms and signs is a common situation and a dilemma in DED research [49–51]. For example, it is quite common to encounter a patient with severe symptoms but lacking evidence of staining. Similarly, a patient may be asymptomatic but present with obstructed meibomian glands, short breakup time, and high osmolality [52]. There are several studies that show that people with chronic pain syndromes, atopic disorders, known allergies, antihistamine use, osteoarthritis, depression, and antidepressant use will have more symptoms of DED than signs [50]. In our study, there are possible reasons why the signs of DED outweigh the symptoms in men. First, there are sex differences in sensitivity of the ocular surface. Several studies conducted in different settings have shown increased corneal or conjunctival sensitivity in women [53, 54]. Second, sex differences in general pain sensitivity may play a role. Compared to women, men show less negative pain responses (i.e., increased threshold and tolerance to pain) [55]. Ocular pain was the common complaint among DED patients in outpatient [56, 57], but long-standing DED were likely to cause corneal nerve damage [50]. Corneal sensitivity reduced can mask discomfort symptoms [50]. These asymptomatic DED study populations were at risk of developing manifest DED with time or provocation, for example following ophthalmic surgery [22] should attract our more attention.

In conclusion, the prevalence of DED can vary with the diagnostic assessment criteria used. The prevalence of DED among individuals aged 50 and above was found to be 39.0%. It increased with age and was overall higher in female. Elderly women had the highest prevalence of DED and impacted their visual quality. In addition, depression, smoking and sleep disorders also increased the risk of DED. On the other hand, the prevalence of asymptomatic DED was 53.6% and male were more susceptible, this should prompt clinicians and caregivers to be vigilant in order to minimize the likelihood of developing clinical DED.

Abbreviations

DED	Dry eye disease
DEWS	Dry Eye Workshop
CEC	Chinese expert consensus
OSDI	Ocular Surface Disease Index questionnaire
LLT	Lipid layer thickness
FBUT	Fluorescein tear film breakup time
SIT	Schirmer I test
MES	Meibomian gland expression scores
MQS	Meibomian quantity scores
FBUT	Fluorescein tear film breakup time
NIBUT	Noninvasive breakup time
PBR	Partial blink ratio
VDT	Visual display terminal

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Author contributions

L.C: data collection, written first draft of the manuscript. Q.G: analyze the data and assemble it, assist in writing and revising manuscripts. E.E.P: performed formal analysis of data, reviewed and edit manuscript. F.L, Z.Z, Z.F: assist in the collection of some clinical data. Y.H, R.Y, H.L, X.L: made intellectual contributions to conceptualization of the work. C.Z: contribute to conceptualization of work, designed experiments, supervised work, funding, reviewed and edited manuscript; S.Z: conceptualization, critical revision of manuscript, funding, management, and supervision. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study obtained the ethical approval from the Ethics Committee of the Tianjin Medical University Eye Hospital (Ethics approval number: 2019ky-22). All subjects signed the informed consent form.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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