· Original article ·

Prevalence of symptomatic dry eye disease among Chinese college students with associated risk factors

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大学生干眼症的流行病学调查及相关危险因 素分析

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摘要

目的:了解中国大学生干眼症患病状况,探讨干眼症发病的相关危险因素。

方法:横断面研究方法。以兰州大学医学院所有在读学生 作为研究对象,采用问卷调查方式对干眼症患病状况及相 关危险因素进行调查。干眼症诊断采用六项问卷形式,以 受检者经常或总是出现一个或一个以上症状作为干眼症 的诊断标准。干眼症阳性体征包括泪膜破裂时间(TBUT) ≤10s以及单眼或双眼角膜染色(FSS)计分≥1。采用多 因素 logistic 回归模型进行相关危险因素分析。

结果: 共1139名学生纳入本研究,应答率为84.37%,其 中男生475名,女生664名,年龄16~26岁。干眼症的患 病率为18.70%(95% *CI* = 16.59~20.81),阳性体征中 TBUT ≤10s的比例大约占47.67%(95% *CI* = 44.95~ 50.57),FSS≥1占了13.97%(95% *CI* = 11.95~15.99)。 多因素 Logistic 回归分析结果显示每日阅读时间≥4h (OR=1.58,95% *CI*=1.15~2.18)、每日电脑使用时间≥ 4h(OR=1.52,95% CI=1.02~2.25)以及长时间配戴眼镜(OR=1.54,95% CI=1.08~2.13)是干眼症发生的危险因素,不同性别、是否进行准分子手术、是否戴隐形眼镜之间干眼症患病率无显著性差异。

结论:中国大学生干眼症患病率较高,主要的危险因素包括每日阅读时间和电脑使用时间超过4h,以及长时间配戴眼镜。

关键词:大学生;干眼;患病率;危险因素;症状

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Abstract

• AIM: To obtain the prevalence and risk factors of symptomatic dry eye disease (SDED) among college students in China.

• METHODS: Population – based cross – sectional study. Students in Medical School of Lanzhou University were approached. A questionnaire was used to evaluate the prevalence of SDED and its risk factors. The diagnosis of SDED was based on reported symptoms and was established if the participants reported "often" or "all the time" once or more for 6 – item questionnaire. Positive tests included a tear-film breakup time (TBUT) \leq 10s and a fluorescein staining score (FSS) \geq 1. Demographic information and possible factors that may contribute to SDED were analyzed in a step – wise multivariate logistic regression modelto assess risk factors of SDED.

• RESULTS: There were 1139 participants (84. 37% response rate) have completed the questionnaire, 475 males and 664 females aged 16 - 26y. The prevalence of SDED was 18.70% [95% confidence interval (CI) = 16.59-20.81]. A TBUT of \leq 10s and a FSS \geq 1 were noted in 47.67% (95% CI=44.95-50.57) and 13.97% (95% CI=11.95-15.99) for all participants, respectively. The multivariate regression analysis revealed the following risk factors: daily reading time of \geq 4h (OR = 1.58,95% CI = 1.15-2.18), daily computer use of \geq 4h (OR = 1.52,95% CI = 1.02 - 2.25), and constant eyeglasses wearing (OR = 1.54,95% CI=1.08-2.13). The female gender, refractive surgery and contact lens (CLs) wearing were not risk factors for SDED in this analysis.

• CONCLUSION: The prevalence for SDED is high in Chinese college students. The risk factors include daily reading time of $\ge 4h$, daily computer use of $\ge 4h$ and constant eyeglasses wearing.

• KEYWORDS: college student; dry eye disease;

prevalence; risk factor;symptom DOI:10.3980/j.issn.1672-5123.2016.6.04

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INTRODUCTION

 \mathbf{D} ry eye disease (DED) is a common disorder characterized by eye discomfort, visual disturbance and tear-film instability; it could lead potential damage to the ocular surface^[1]. DED symptoms (*e. g.* dryness, ocular fatigue or visual difficulty) become common complaints as well as ocular surface diseases in daily ophthalmic practice worldwide and are reported more frequently than musculoskeletal pain and mental stress^[2]. It negatively influences daily activities and life quality^[3-4] and place a heavy burden on society through costs of care and treatment^[5].

A variety of factors, including environmental, occupational and personal factors, contribute to $DED^{[1]}$. Indoor pollutants, low humidity, high altitude, and visual display terminal (VDT) related work, senior age, female gender, smoking, contact lens (CLs) use, ocular surgeries and systemic medication are associated with $DED^{[6-10]}$. In addition, Zhang *et al*^[11] found that inadequate refractive correction is a strong risk factor for symptomatic dry eye disease (SDED). It is instructive to study the risk factors because reduced exposures to risk factors will alleviate the symptoms^[6,12]. Except for the difference in investigated population, factors including differences in questionnaire setting and diagnose criteria lead to significantly varying prevalence of DED from 3.9% to 52. 4% across different populations^[13-18].

Several population-based studies of DED have been carried out in China. Among elderly Chinese population in Taiwan^[19]. the prevalence of SDED was 33.7%; the prevalence in people living at high altitude were 50.1% and 52.4%, respectively, according to the Henan Eye Study (HES)^[10] and the Zeku Survey (ZES)^[20] (Qinghai Province, China). Li et $al^{[21]}$ reported a 9. 54% prevalence of SDED in outpatients in southeast China. It is worthy of noting that the prevalence of SDED in senior high school students was 23.7% in China^[11], being higher than those reported in senior population by some^[15,22-24] but not all studies^[14,18]. DED symptoms will interfere daily activities and restrain ability to perform various tasks requiring sustained visual concentration, forming a particularly severe problem for students. To date, prevalence of dry eye in different Chinese cohorts have been reported by previous studies; however, the college - aged group remains largely unknown. This study aims at examining the prevalence along with potential risk factors of SDED among college students.

SUBJECTS AND METHODS

Study Population This cross-sectional study was conducted between Sep. and Nov. 2011 in the Schools of Clinical

Medicine, Pharmacy, Stomatology and Public Health at Lanzhou University in Gansu Province, China. We obtained permissions by all deans and informed all students of these schools to take part in our survey. Students attending classes on the date of survey (n = 1350) were asked to fill out a questionnaire and received a series of eye examinations. We excluded those who had systemic diseases (*e. g.* rheumatoid arthritis, Sjögren syndrome or thyroid disease) and who did not complete the questionnaire. The final response rate was 84. 37% (1139 out of 1350). The study was carried out in agreement with the guidelines of the Declaration of Helsinki (2010) and was approved by the Institutional Review Board of Lanzhou University Second Hospital, Gansu Province, China. All participants provided written informed consent.

Questionnaires The questionnaire included basic demographic information (e. g. name, age, gender, and grade), a 6-item domain for SDED diagnosis, and potential SDED-related factors. A diagnosis of SDED was established if the subjects reported "often" or "all the time" for at least one of the following symptoms^[1,15-16,23-24]: 1) did you feel dry in the eyes? 2) did you feel a gritty or sandy sensation in the eyes? 3) did you feel the eyes ever having a burning sensation? 4) did your eves ever get stuck shut? 5) did you notice much crusting on your lashes? 6) did your eyes ever turn red? Multiple choices, which comprising none, sometimes (at least once in 2wk), often (at least once in 1wk), and all the time, followed each question. Potential risk factors included CLs use, refractive surgery, eye exercise, daily computer use time ($<4h vs \ge 4h$), daily reading time ($< 4h vs \ge 4h$), and frequency of eyeglasses wearing ("no", "intermittent", or "constant"). Four trained team members collected all the questionnaires.

Examination All participants underwent ocular examinations by five ophthalmologists from Lanzhou University Second Hospital. The examinations consisted of auto – refraction, visual acuity test, slit lamp examination of anterior segment and lens, corneal and conjunctival fluorescein staining (FSS), and tear–film breakup time test (TBUT). The participants were requested to remove CL at least 2h prior to the examinations and not to use artificial tears within 2h prior to the tests^[21].

The TBUT and FSS test were conducted following the instillation of one drop of sodium fluorescein solution (1%) in the lower conjunctival sac. Observations were aided with a slit-lamp with a cobalt-blue filter. Subjects were asked to blink several times and then hold eyes open. The time between the last blink and the appearance of first desiccation spot was recorded as the TBUT. TBUT $\leq 10s$ in one or both eyes was considered to be abnormal. The FSS test was performed after TBUT test with results graded as 0 (no staining), 1 (mild staining limited to less than one-third of the cornea), 2 (moderate staining of less than half of the cornea), or 3 (severe staining of half or more of the cornea).

Table 1 Baseline characteristics of 1139 participants								
Patient characteristics	Total subjects, $n^{a}(\%)$	M, $n^{a}(\%)$	F, $n^{a}(\%)$					
Age (a) ^b	20.97±1.38	21.08±1.36	20.89±1.38					
Gender								
Μ	475(41.70)	-	-					
F	664(58.30)	-	-					
Contact lens use								
No	1029(90.34)	450(94.74)	579(87.20)					
Yes	110(9.66)	25(5.26)	85(12.80)					
Refractive surgery								
No	1116(98.60)	465(98.73)	651(98.49)					
Yes	16(1.40)	6(1.27)	10(1.51)					
				1				

^aThe sum does not necessarily equal the sample size for all variables because of data missing;

 $^{\rm b} Values$ represent mean \pm standard deviation for age.

Table 2	Prevalence of symptoms and	tests for SDED in	1139	participants	with age a	ind gender
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Parameters	Tetal	SDED			TBUT≤10s	FSS≥1		
	Total	n	Percentage(95% CI)	n	Percentage(95% CI)	n	Percentage(95% CI)	
Age (a) ^b	-		20.97±1.36		20.97±1.43		20.96±1.35	
Prevalence	1139	213	18.70(16.59-20.81)	543	47.67(44.95-50.57)	159	13.97(11.95–15.99)	
Gender								
Μ	475	86	18.11(14.74–21.68)	202	42.53(38.11-47.15)	51	10.76(8.02-13.71)	
F	664	127	19.13(16.12-21.99)	341	51.36(47.74-55.12)	108	16.27(13.40-19.13)	
Р			0.66		0.003		0.008	

SDED: Symptomatic dry eye disease; TBUT: Tear film breakup time; FSS: Fluorescein staining.

Statistical Analysis The statistical analysis was performed with Statistical Analysis System Software (Version 8. 2, SAS Institute Inc. Cary, NC, USA). Categorical variables were analyzed using Chi–square test or trend test. Student's *t*-test was employed to analyze ages in different groups. Predisposing factors for SDED were examined by a step–wise multivariate logistic regression model. Factors with $P \leq 0.2$ in univariate analysis were involved in ensuing multivariate analysis. Results were reported as adjusted odds ratios (AORs) and 95% CIs. CL and refractive surgery history were both included in the multivariable analysis despite that P>0.2 because they are clearly important risk factors for DED^[7,24,27]. Statistical significance was set at P<0.05.

RESULTS

The overall participation response rate was 84. 37% (1139 out of 1350) including 475 males (41. 70%) and 664 females (58. 30%). The ages of participated subjects ranged from 16–26y (20. 97 in average with a standard deviation of 1. 38). Particularly, 16 (1. 40%) and 110 (9. 66%) participants had refractive surgery and CL wearing (Table 1), respectively.

Among the participants, SDED prevalence was found in 18.70% (95% CI = 16.59 - 20.81) of the subjects (Table 2), specifically, 18.11% (95% CI = 14.74 - 21.68) of males and 19.13% (95% CI = 16.12 - 21.99) of females (P = 0.66). TBUT abnormality was noted in 47.67% (95% CI = 44.95 - 50.57) and FSS abnormality 13.97% (95% CI = 11.95 - 15.99). SDED did not correlate with TBUT and FSS (Table 3).

Table 3 The correlations between signs and symptoms of DED

Signs	Tetal	SDED	Correlation		
	Total	Negative	Positive	F	Р
$TBUT\!\leqslant\!\!10s$	543	430(46.4)	113(53.1)	3.04	0.09
FSS≥1	159	122(13.2)	37(17.4)	2.52	0.13

SDED:Symptomatic dry eye disease; TBUT:Tear film breakup time; FSS: Fluorescein staining.

Table 4 delivers the frequency distributions of different DED. Dryness by different degree (sometimes, often or all the time) was the most commonly complained symptom with a prevalence of 64.27%. Totally, 445 participants (39.07%) reported to have experienced red eyes, which is the second most common symptom. By contrast, 12.03% participants suffer from crusting on eyelashes, indicating a lowest prevalence. Regarding the severe symptoms that bring continuous distortion (reported by "all the time"), dryness (0.44%) and red eyes (0.44%) are the most prevalent ones.

The risk factors associated with SDED are shown in Table 5. According to the univariate analysis, SDED was associated with the duration of reading time and frequency of wearing spectacles (P = 0.006, 0.01, respectively). Meanwhile adjusted multivariate analysis revealed significant association of SDED with daily reading time \geq 4h (AOR = 1.58,95% CI = 1.15-2.18) and constant eyeglasses wearing (AOR = 1.52, 95% CI = 1.08-2.13). On the other hand, the crude odds ratio for the association between daily computer using time \geq 4

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Table 4 Symptoms distrib	n, %			
Symptoms	None	Sometimes	Often	All the time
Dryness	407(35.73)	614(53.91)	113(9.92)	5(0.44)
Gritty or sandy sensation	749(65.76)	357(31.34)	30(2.63)	3(0.26)
Burning sensation	841(73.84)	268(23.53)	29(2.55)	1(0.09)
Red eyes	694(60.93)	394(34.59)	46(4.04)	5(0.44)
Crusting on lashes	1002(87.97)	124(10.89)	11(0.97)	2(0.18)
Get stuck shut	809(71.03)	283(24.85)	44(3.86)	3(0.26)

None: Less once in 3mo; Sometimes: At least once in 2wk; Often: At least once in 1wk.

Table 5 Risk factors for SDED

	Non	Non-DED		SDED		OD(050) CI	AOD(050) CI) ^a	
Risk factors	n	%	n	%	P	OR(95% CI)	AUR (95% CI)	
Age (a)	20.9	7±1.36	20.98	8±1.38	0.94 ^b	-	_	
Gender								
М	389	81.89	86	18.11	-	1	1	
F	537	80.87	127	19.13	0.66	1.07(0.79,1.45)	1.02(0.73,1.38)	
Time of wearing eyeglasses								
No	173	84.80	31	15.20	-	1	1	
Intermittent ^d	390	83.33	78	16.67	-	0.90(0.57,1.41)	1.53(0.96,2.43)	
Constant ^e	369	77.73	104	22.27	0.01 [°]	0.63(0.40,0.97)	1.52(1.08,2.13)	
Contact lens use								
No	839	81.44	191	18.56	-	1	1	
Yes	88	80.00	22	20.00	0.71	1.10(0.67,1.80)	0.90(0.53,1.51)	
Refractive surgery								
No	907	81.27	209	18.73	-	1	1	
Yes	12	75.00	4	25.00	0.52	1.46(0.46,4.53)	1.87(0.57,6.09)	
Eye exercises								
No	843	81.61	190	18.39	-	1	-	
Yes	78	78.79	21	21.21	0.49	1.19(0.72,1.98)	-	
Time of reading $(h/d)^{f}$								
<4	448	84.69	81	15.31	-	1	1	
≥4	469	78.30	130	11.52	0.006	1.53(1.13,2.08)	1.58(1.15,2.18)	
Time of computer using (h/d)								
<4	778	82.07	170	17.93	-	1	1	
≥4	137	76.54	42	23.46	0.08	1.40(0.96, 2.06)	1.52(1.02, 2.25)	

SDED: Symptomatic dry eye disease; OR: Odds ratio; AOR: Adjusted odds ratio; CI: Confidence interval; "Odds ratio was adjusted for sex, contact lens use, refractive surgery and all of the associated factors identified in the univariate analyses (P < 0.2); "The P value of t-test is given; "The P value of trend test is given; "Intermittent wearing eyeglasses: wearing glasses just for having classes, reading, watching TV or using computers;" Constant eyeglasses wearing: wearing glasses all the time except sleeping;" Time of reading: limited to traditional reading, excluding VDT reading.

hand SDED was insignificant (P=0.08, OR=1.40, 95% CI= 0.96-2.06). However, we found a borderline association between SDED and the daily computer using time $\geq 4h$ (AOR= 1.52,95% CI = 1.02-2.25) after multivariate adjustment analysis. In addition, gender and eye exercises were not the risk factors of SDED. Significant correlation between SDED with CL wearing (AOR = 0.90, 95% CI = 0.53-1.51) or refractive surgery (AOR = 1.87, 95% CI = 0.57-6.09) was unproven because of the limited sample size.

DISCUSSION

DED is a worldwide multifactorial disorder influencing daily activities and life quality. Limited study regarding the

prevalence of DED in college – aged population has been carried out. In this population – based cross – sectional association study, a 18. 70% prevalence of SDED among college students has been observed along with risk factors of daily reading time \geq 4h, daily computer using time \geq 4h and constant eyeglasses wearing. Note that significant associations of SDED with gender, refractive surgery history or CL use haven't been validated with this study, differing from some other previous reports^[3,7,27].

Prevalence of SDED varied significantly in different populationbased studies because of the utilizations of different questionnaires, objective tests and definitions on dry eye. HES and ZES showed high prevalence (50.1% and 52.4%. respectively) of dry eye syndrome in people with age $\geq 40y$ at high altitude in China^[10,20]. All the subjects in HES and ZES studies lived at altitude \geq 3000m with dry and cold climate, as well as with strong solar infrared light and ultraviolet radiation, which are also factors contributing to high SDED prevalence^[28-29]. Prevalence of SDED adjusted for age was 27.5% in Indonesia^[30]. The Salisbury Eye Evaluation Study found that 14.6% of the participants with an average age of 73. 5y suffered from SDED^[26]. Previous studies reported prevalence of 7.8% in females and 4.7% in males with ages ≥50y in the United States^[15,22], of 11.0% in a Spanish population with ages $\geq 40y^{[31]}$, and of 9.5% in a Singapore population with ages $\leq 25y^{[13]}$. Additionally, a survey covering 963 people with age \geq 73y from French exhibited a 29.6% prevalence of $\text{DED}^{[18]}$.

Because of the narrow age interval (16-26y) in our study, the association of SDED with age, which is considered as a risk factor according to previous investigations ^[15,32-34], has not been validated herein.

Gender difference does not constitute a risk factor for SDED in this study, showing agreement with some previous reports^[10-11,17]. Note that exceptions where gender difference is considered as a risk factor for SDED have been reported as well^[4,7,18,21]. Many previous studies suggested the high prevalence in female results from the sex hormones^[13,32,35]. The hormonal variations are related to the tendency to have dry eye symptoms in female. In addition, menopause in aged women may contribute to the emergence or aggravation of DED as a consequence of overall hormonal imbalances^[36]. In this study, the female group did have higher prevalence of SDED, but statistically significant difference in gender – specific prevalence was not observed. One possible reason may be that the female participants were young and were unlikely to suffer from imbalance in sex hormones.

In our study, abnormal TBUT and FSS results were noted in 47.67% and 13.97% of the participants, respectively. Many of the participants (51.36% in female and 42.53% in male) did not have a stable tear - film and sustain TBUT abnormality. The abnormality rates were higher than several previously reported results^[10,20]. The TBUT and FSS abnormalities rate were 37.7% and 6.0% in HES, and 35. 3% and 5.8% in ZES. Moreover, a study on VDT workers showed amuch higher rate of TBUT $\leq 5s$ at 74.6% ^[6]. TBUT. which describes the stability of tear film on the ocular surface. is capable of measuring evaporation problems in DED accurately^[37]. Previous studies showed that VDT use increased the proportion of incomplete blinks and accelerated the evaporation of tear film^[6,38]. In our study, although 15. 88% participants declare to possess daily computer uses over 4h, yet the rest participants as well experience certain daily computer uses, constituting a potential reason for high prevalence rate of TBUT.

Recent studies suggested that SDED is not correlated to clinical tests [14,39-41]; our findings agreed well with these

previous studies, even though HES study found the correlations between SDED and tests^[10]. The poor correlation between tests and symptoms might be due to wide variation in the sensation of symptoms and variable disease process^[40]. Further research is needed to develop methods of testing or refining existing tests to provide accurate, objective measures for DED.

This study showed an association of SDED with daily reading duration $\ge 4h$, computer use duration $\ge 4h$ and constant eyeglasses wearing after adjusting other factors.

Prolonged visually stressful activities (e.g. viewing computer, watching television, driving, and reading) will cause and aggravate SDED^[42-44]. Specifically, the daily VDT use $\geq 4h$ is a risk factor for SDED^[45-46], and the daily duration of VDT use is linearly related to SDED^[2], the rate of SDED increases with increasing exposure to VDTs^[6,47,48]. With the widespread use of mobile devices, computers and smart phones, VDT exposure is increasing in the general population (particularly in college students) instead of VDT workers merely. Logaraj et $al^{[46]}$ reported 31. 2% rate of SDED in students with more frequent computer use (engineering major) vs 17.4% in students with less computer use (medical students). Prolonged blinking intervals while gazing in VDT users lead to excessive evaporation of tear fluid and further higher prevalence of SDED. Several studies reported that blink rate significantly reduces during reading^[49-50], which in part explain the correlation between computer use and SDED, as well as between reading and SDED in this study.

We also explored the relation between SDED and frequency of eveglasses wearing. Our results revealed that participants reporting "constant eyeglasses wearing" had significant higher prevalence (22. 27%) for SDED than those who reporting "no" and "occasionally" (15. 20% and 16. 67%, respectively). Nichols *et al*^[51] found that a spectacle wearing</sup>is a risk factor for SDED (OR = 2.06, 95% CI = 1.12 - 3. 80). Logaraj et $al^{[46]}$ also reported higher rate of ocular symptoms in people wearing eyeglasses. Several factors may possibly explain such findings. First, it is possible that spectacles wearers tend to be more aware of their ocular health and status and thus may offer over-estimated results than an individual not requiring refractive correction. Second, inadequate refractive correction may play an important role in enlarging the prevalence of SDED^[11,52-54]. Further study is still necessary to determine the relation between inadequate refractive correction and SDED.

The CLs use^[7,24,55] and refractive surgery^[56-58] are validated as two risk factors for SDED. Refractive surgery tends to break tear film^[59], and decrease corneal sensitivity and aqueous tear production^[57]. However, due to the low rates of CLs use (only 9. 60% vs 37. 8% among Japanese students^[45]) and refractive surgery (1. 4%), our statistical analyses did not provide sufficient proof for determining these two factors.

In this study, all participants were students from medical – related majors and may thereafter run healthier lifestyle than students from other majors, which may introduce a population-

selection bias. The threshold for categorizing daily reading duration or computer-use time was set as a certain value (4h herein). However, it may suffer from potential deviation because a direct cut actually hides the fact that bilateral values are similar, *e. g.* 3. 9h does not exhibit significant difference from 4. 1h. Moreover, the use of artificial tears was not included in our survey because of the complicated accompanied problem: artificial tears with various functions are provided by the drugstore, does the user choose a suitable one? Artificial tear should be used according to certain professional advice (*e. g.* specification or prescription); does the use adopt regular proper dosage?

In summary, this study discovers a high prevalence of SDED among college students. Meanwhile, the risk factors involve VDT use, prolonged reading duration and constant spectacles wearing. Based on these results, we recommend college students decrease VDT use and have proper breaks during reading and studying. The recommendations also apply to those who share similar environment and life style with college students.

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