Original Article

Low ambient temperature correlates with the severity of dry eye symptoms

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Abstract:

PURPOSE: The symptoms of dry eye disease (DED) are influenced by environmental factors, but the effect of ambient temperature is less certain. Our purpose was to investigate the relationship between the severity of DED symptoms and the ambient temperature.

MATERIALS AND METHODS: This retrospective study reviewed the symptom scores, including ocular surface disease index (OSDI) and standardized patient evaluation of eye dryness (SPEED), as well as tear film parameters of first-time DED patients between June 2018 and June 2019. The contribution of tear film parameters and environmental factors, including ambient temperature, humidity, wind speed, and the concentration of air pollutants, to the severity of dry eye symptoms was evaluated by univariate and multivariate linear regression analyses.

RESULTS: There were 351 patients included aged 52.8 ± 13.6 years, and 257 (73.2%) were female. The average tear film break-up time, Schirmer test value, and lipid layer thickness were 2.6 ± 0.7 s, 5.5 ± 4.3 mm, and 64.1 ± 6.0 µm, respectively. The average OSDI and SPEED were 41.8 ± 19.8 and 12.1 ± 5.1, respectively. In winter, the patients reported higher OSDI and SPEED. Both scores were significantly correlated with low ambient temperature. Regression analysis showed that low ambient temperature and Schirmer test value contributed to higher OSDI, while low ambient temperature and younger age contributed to higher SPEED.

CONCLUSION: Low ambient temperature plays a significant role in DED symptom severity.

Keywords:

Dry eye disease, ocular surface disease index, standardized patient evaluation of eye dryness, temperature

Introduction

Dry eye disease (DED) is a common ocular disease in the modern world, with a prevalence of 5%–50%.[1] It is characterized with unstable tear film, a hallmark sign of DED, which leads to ocular surface inflammation and subsequent injury.[2] The resulting symptoms may not only lead to ocular discomfort and visual disturbance but also impact patients' quality of life.[3]

Several risk factors of DED have been identified, such as aging, female sex, Asian race, meibomian gland dysfunction, and Sjögren syndrome.[1] In addition to these patient-specific risk factors, environmental factors also play a significant role in contributing to DED prevalence and its severity. For example, low relative humidity has been shown to increase tear evaporation and ocular discomfort.[4] Wind exposure also increases dry eye prevalence.[5] Furthermore, several air pollutants, including PM2.5 and ozone, are associated with DED and ocular surface inflammation.[6,7]

Among the environmental factors, the role of ambient temperature is less certain. A previous study found that the prevalence of DED is higher in winter and spring.[8] However, other studies found that temperature is positively correlated with DED incidence, and higher

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temperature is associated with increased tear evaporation rate.[9,10] Concerning the complex nature of DED and high inconsistency between signs and symptoms,[11] we analyzed the symptoms quantitated by ocular surface disease index (OSDI) and standard patient evaluation of eye dryness (SPEED) questionnaires and correlated the scores with environmental factors, including meteorological parameters. This result may shed light on the effect of ambient temperature on DED symptoms.

Materials and Methods

Study population

This retrospective study adhered to the tenets of the Declaration of Helsinki and was approved by the Research Ethics Review Committee of the Far Eastern Memorial Hospital, New Taipei City, Taiwan. Waiver of informed consent was also approved by the Committee, as this study was based on the retrospective review of the clinical data (approval number: 107163-E). Data of first-time DED patients from June 2018 to June 2019 were included for analysis. To evaluate the influence of environmental factors at different time points on DED symptoms, only patients living in four adjacent districts to Far Eastern Memorial Hospital (Banqiao, Tucheng, Xinzhuang, and Shulin Districts, New Taipei City, Taiwan) were included to avoid confounding by geographical factors. The diagnosis of DED was based on the definition by the Asia Dry Eye Society if the patients presented with both dry eye symptoms and unstable tear film.[2] Dry eye symptoms were assessed by OSDI and those with OSDI ≧ 13 were considered to have DED symptoms.[12] Tear film stability was assessed by tear film break-up time (TBUT), and the cutoff value was ≤ 5 s for DED diagnosis. Exclusion criteria included (1) history of ocular surgery, ocular trauma, or ocular infection within 3 months; (2) active use of topical or systemic medications that may interfere with tear film stability, including artificial tears, antiglaucoma agents, antihistamines, and antipsychotics; (3) contact lens wearing within 1 week; (4) autoimmune diseases such as Sicca syndrome, systemic lupus erythematosus, rheumatoid arthritis, and Steven–Johnson syndrome.

Clinical examination

The symptoms of DED patients were assessed by OSDI as aforementioned. SPEED questionnaire was also used to evaluate symptom severity, which is better correlated with DED caused by meibomian gland dysfunction.[13] All patients completed OSDI and SPEED questionnaires were subjected to routine DED evaluation as follows. TBUT was evaluated by instilling 2 μl of 0.5% fluorescein into the lower fornix, and the interval between the last blink and the first TBUT was recorded. Lipid layer thickness (LLT) and meibomian gland morphology were evaluated using the LipiView II

interferometer (TearScience Inc., Morrisville, NC, USA). The amount of expressible meibomian glands (MGE) was recorded after applying the standardized diagnostic expression instrument (TearScience Inc., Morrisville, NC, USA) on the lid margin. Aqueous tear secretion was evaluated using the Schirmer test II with topical anesthetics measured at 5 min using a standard 35 mm × 5 mm tear test strip (EagleVision, Katena Products, USA). Only the data from the right eye were included for statistical analysis.

Meteorological parameters

To evaluate the correlation between the severity of DED symptoms and environmental factors, daily mean temperature, relative humidity, and wind speed from monitor stations of the aforementioned districts were acquired from the database of Central Weather Bureau, Taiwan (www.cwb.gov.tw). The daily average parameters from the four districts were used to correlate with each patient's symptoms on the visit date. To further explore the correlation between dry eye symptoms and air pollutants, the daily average concentration of air pollutants, including PM10, PM2.5, SO_2, O_3, CO, CH_4, NO, NO_2, total hydrocarbon (THC), nonmethane hydrocarbon, and the air quality index, was collected from the database of Environmental Protection Administration, Executive Yuan, Taiwan (www.epa.gov.tw).

Statistical analysis

Statistical analysis was performed using SPSS for Windows (version 19.0, SPSS Inc., Chicago, Illinois, USA). Analysis of variance (ANOVA) with Bonferroni *post hoc* test was used to test the difference between groups. Pearson's correlation analysis and linear regression analysis were performed to explore the correlation between the severity of dry eye symptoms and environmental factors. Results were considered statistically significant if $P < 0.05$.

Results

During the study period, we collected data from 351 patients. The mean age was 52.8 ± 13.6 years, and the percentage of female was 73.2% [Table 1]. The mean TBUT was 2.6 ± 0.7 s, indicating unstable tear film in these patients. Mean OSDI and SPEED scores of the whole study group were 41.8 ± 19.8 and 12.1 ± 5.1, respectively. The mean OSDI of female and male was 42.74 ± 19.80 and 39.08 ± 19.40 ($P = 0.12$), while the mean SPEED scores were 12.07 ± 4.90 and 12.11 ± 5.71 ($P = 0.94$), respectively. Other tear film characteristics are summarized in Table 1.

To evaluate the potential influence of environmental factors on the severity of DED symptoms, we arbitrarily divided the patients into four groups according to the

seasons of visit. First-time DED patients visiting dry eye clinic in winter reported significantly higher OSDI and SPEED scores compared with those in other seasons, especially in summer [Figure 1a and b]. When plotting the symptom severity against the temperature, there was a trend of increasing OSDI or SPEED score with decreasing ambient temperature [Figure 1c and d]. Linear correlation analysis also showed that both OSDI and SPEED scores were negatively correlated with the ambient temperature [Figure 2a and b]. These results imply that DED symptoms were worse in winter, and low ambient temperature may be one of the contributing factors.

In addition to low ambient temperature, relative humidity and wind speed also influence the prevalence, signs, and symptoms of DED.[14] Furthermore, air quality is usually deteriorated during winter months in Taiwan.[15] Previous studies also showed that air pollutants were associated with DED and ocular surface inflammation.[6,16] Therefore, aggravated DED symptoms may be, in fact, caused by other meteorological factors and air pollution in winter, instead of low ambient temperature. To explore the correlation between symptom severity and air pollution as well as other meteorological factors, we first performed univariate linear regression analysis and identified Schirmer value, temperature, CO, NO_2, THC, and CH_4 to be correlated with OSDI [Table 2]. Further, multivariate regression analysis was performed by selecting Schirmer value, temperature, and one of the air pollutants as variables due to high collinearity among the air pollutants [Table 3]. Although Schirmer value and temperature remained negatively correlated with OSDI, the effect of air pollutants became insignificant after adjusting the confounding effect [Table 4]. As for SPEED score, it was negatively correlated with age and temperature and was positively correlated with PM2.5, CO, NO_2, THC, and CH_4 by univariate analysis [Table 5]. Multivariate analysis showed that age and temperature remained negatively correlated with SPEED, while the effect of other air pollutants became insignificant [Table 6]. Both OSDI and SPEED scores were not affected by the indicators of tear film stability, including TBUT, LLT, and MGE [Tables 2 and 5].
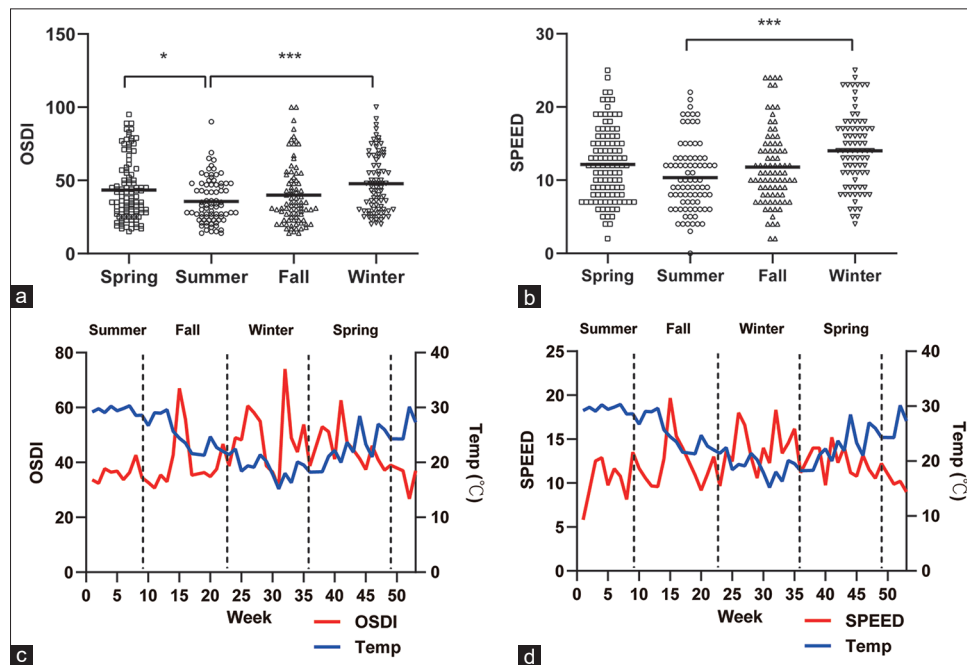
Discussion

Environmental factors consistently associated with DED include pollution, low humidity, and sick building

Table 1: Patient demographics (*n*=351)

Variables	Mean±SD (range)
Age (years)	52.8±13.6 (19-82)
Sex: Female (%)	257/351 (73.2)
OSDI	41.8±19.8 (13-100)
SPEED	12.1±5.1 (2-23)
TBUT (s)	2.6±0.7 (1-5)
Schirmer (mm)	5.5±4.3 (0-34)
Lipid layer thickness (μm)	64.1±6.0 (49-78)
Meibomian glands expressible	8.1±3.7 (0-24)

TBUT=Tear film break-up time, OSDI=Ocular surface disease index, SPEED=Standardized patient evaluation of eye dryness, SD=Standard deviation

Figure 1: Seasonal change of dry eye disease symptoms. (a and b) Seasonal change of OSDI and SPEED scores from June 2018 to June 2019. Spring: March to May; summer: June to August; fall: September to November; winter: December to February. *P < 0.05, ***P < 0.001 by ANOVA with Bonferroni *post hoc* test. (c and d) Change in OSDI and SPEED scores relative to ambient temperature. Average symptom scores versus ambient temperature per week were plotted for curve smoothing.
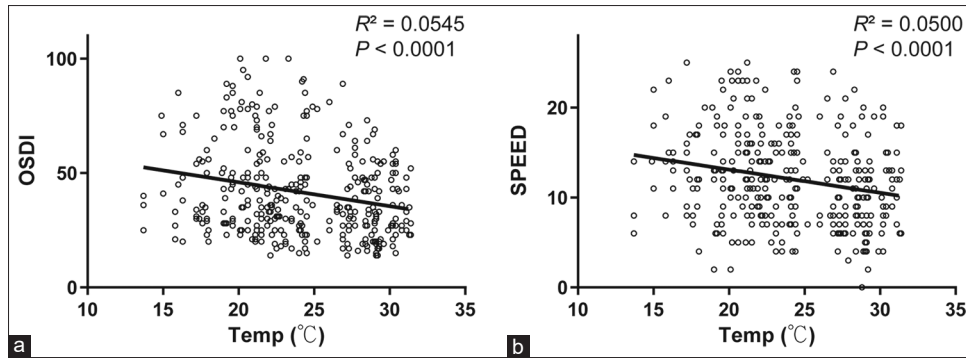
Figure 2: Low ambient temperature is associated with higher OSDI and SPEED scores. (a and b) Scatter plots of OSDI and SPEED scores of each patient versus ambient temperature of the visiting date.

Table 2: Univariate linear regression analysis between OSDI and the variables

Variables	β	95% CI	P
Age	0.0395	−0.03257-0.1116	0.2816
Sex	−0.00184	−0.004191-0.0005122	0.1249
TBUT	0.0007	−0.003139-0.004453	0.7337
LLT	−0.1578	−0.3170-0.001420	0.0521
MGE	−0.0018	−0.02167-0.01802	0.8563
Schirmer	−0.0357	−0.05878--0.01269	0.0025
Temp	−0.0523	−0.07523--0.02937	<0.001
RH	0.0436	−0.002713-0.08990	0.0649
Wind	−0.0002	−0.003304-0.002805	0.8724
PM10	−0.0401	−0.1162-0.03600	0.3009
PM2.5	0.0195	−0.01693-0.05583	0.2937
AQI	0.0215	−0.07828-0.1213	0.6716
SO_2	−0.0016	−0.01034-0.007228	0.7277
CO	0.1092	0.02909-0.1892	0.0077
O_3	0.0104	−0.04391-0.06479	0.7058
NO	0.0131	−0.004322-0.03051	0.1401
NO_2	0.0411	0.01122-0.07105	0.0072
THC	0.0093	0.0009608-0.01767	0.029
NMHC	0.0003	−0.0002610-0.0008045	0.3165
CH_4	0.0066	0.002861-0.01028	<0.001

TBUT=Tear film break-up time, LLT=Lipid layer thickness, MGE=Meibomian glands expressible, Temp=Ambient temperature, RH=Relative humidity, Wind=Wind speed, AQI=Air quality index, THC=Total hydrocarbon, NMHC=Nonmethane hydrocarbon, CI=Confidence interval

syndrome according to the DEWS II report.[1] In this study, we found that the mean OSDI and SPEED scores were higher in winter, and both scores were significantly correlated with low ambient temperature. Multivariate analysis showed that OSDI was negatively correlated with Schirmer value and temperature, while SPEED score was negatively correlated with age and temperature. Compared with OSDI, SPEED score is considered to be better correlated with DED caused by meibomian gland dysfunction.[13] In our previous study, we also found that SPEED score is higher in younger age group, while the difference in OSDI scores among age groups was borderline.[17] Therefore, different questionnaires may better reflect symptom severity under certain patient demographics. Among all the variables analyzed in

this study, only ambient temperature was negatively correlated with both OSDI and SPEED. This finding convincingly suggests that low ambient temperature correlates with DED symptoms.

Intriguingly, a previous study showed that temperature is positively correlated with DED incidence in Taiwan.[10] However, the effect size is relatively small (odds ratio = 1.005–1.016), and the data were obtained from the cohort database of the National Health Insurance of Taiwan, which identifies DED patients by disease coding from 2004 to 2013. During that time, the diagnosis of DED was mostly made based on the Schirmer test, which is known for variable test result and suboptimal ability to discriminate between normal and DED subjects.[18] The authors also found that every 10% increment of relative humidity was related to approximately 6.7% reduction in DED occurrence, suggesting that moisture in the air might have mitigated the DED symptoms. In contrast, the diagnosis of DED in this study was based on the criteria by the Asia Dry Eye Society, and the severity of symptoms was assessed by OSDI and SPEED questionnaire.[2] Only patients presented with DED symptoms (OSDI average 41.8 ± 19.8) and unstable tear film (TBUT average 2.6 ± 0.7 s) were included. Since short TBUT dry eye is the predominant manifestation of DED,[18] our approach offers better insight into the role of different environmental factors contributing to the symptom severity among DED patients.

In previous studies, air pollution is associated with DED signs, symptoms, and incidence.[6,7,16] In Taiwan, air pollution is often worse during winter monsoon due to long-range transport of air pollutants from East Asia.[19,20] Despite that the relative humidity is relatively stable, wind speed is usually higher in winter season in Taiwan, leading us to hypothesize that higher OSDI and SPEED scores were in fact caused by these environmental or meteorological factors, instead of low ambient temperature. However, among these factors, only temperature remained negatively correlated with DED

Table 3: Pearson's correlation matrix among meteorological parameters

	Temp	RH	Wind	PM10	PM2.5	AQI	SO_2	CO	O_3	NO	NO_2	THC	NMHC	CH_4
Temp	1													
RH	−0.33***	1												
Wind	−0.08	−0.14**	1											
PM10	0.22***	−0.35***	−0.32***	1										
PM2.5	−0.08	−0.12*	−0.32***	0.74***	1									
AQI	−0.02	−0.23***	−0.29***	0.82***	0.89***	1								
SO_2	0.28***	0.11*	−0.21***	0.34***	0.32***	0.33***	1							
CO	−0.3***	0.27***	−0.51***	0.42***	0.63***	0.55***	0.22***	1						
O_3	−0.28***	−0.36***	0.28***	0.13*	0.04	0.26***	−0.15**	−0.25***	1					
NO	0	0.18***	−0.39***	0.2***	0.31***	0.24***	0.18***	0.71***	−0.59***	1				
NO_2	−0.34***	0.25***	−0.55***	0.45***	0.63***	0.58***	0.21***	0.92***	−0.14*	0.61***	1			
THC	−0.15**	0.25***	−0.6***	0.5***	0.62***	0.56***	0.33***	0.94***	−0.27***	0.67***	0.9***	1		
NMHC	0.08	0.22***	−0.65***	0.49***	0.54***	0.49***	0.37***	0.86***	−0.41***	0.75***	0.82***	0.95***	1	
CH_4	−0.45***	0.25***	−0.41***	0.41***	0.63***	0.56***	0.22***	0.88***	−0.03	0.45***	0.85***	0.89***	0.7***	1

*$P<0.05$, **$P<0.01$, ***$P<0.001$. Temp=Ambient temperature, RH=Relative humidity, Wind=Wind speed, AQI=Air quality index, THC=Total hydrocarbon, NMHC=Nonmethane hydrocarbon

Table 4: Multivariate linear regression analysis between OSDI and the variables

	β	95% CI	P
Model 1			
Schirmer	−0.7285	−1.192−−0.2646	0.0022
Temp	−0.918	−1.389−−0.4466	<0.001
CO	0.1006	−0.03822-0.2395	0.1549
Model 2			
Schirmer	−0.738	−1.202−−0.2744	0.0019
Temp	−0.9226	−1.400−−0.4455	<0.001
NO_2	0.2328	−0.1420-0.6076	0.2226
Model 3			
Schirmer	−0.7148	−1.178−−0.2510	0.0026
Temp	−0.9412	−1.387−−0.4956	<0.0001
THC	12.76	−2.039-27.55	0.0908
Model 4			
Schirmer	−0.7271	−1.190−−0.2639	0.0022
Temp	−0.8335	−1.338−−0.3293	0.0013
CH_4	2.593	−0.5664-5.752	0.1074

Temp=Ambient temperature, THC=Total hydrocarbon, CI=Confidence interval

symptom scores after multivariate regression analysis. A previous study showed that low ambient temperature may cause plugging or constriction of the meibomian gland orifice, thereby decreasing lipid layer thickness and compromising the tear film stability.[21] Nevertheless, regression analysis in our study failed to identify the effect of TBUT, LLT, and MGE on OSDI or SPEED scores. These seemingly contradictory observations may result from the cutoff value of TBUT (≦5 s) in our study, thereby selecting the patients with unstable tear film and obscuring the overall effect of tear film stability on DED symptoms.

Another possibility that low ambient temperature contributes to DED symptoms may be through stimulating the corneal nerve and eliciting ocular discomfort. Corneal sensory nerves can be generally classified as polymodal nociceptor, cold thermoceptor, and mechano-nociceptor neurons.[22] Among these, cold thermoceptor neurons, regarded as the regulator of basal tear secretion due to its response to hyperosmolarity, can also be triggered by cooling, which induces unpleasant sensations in humans.[23,24] Intriguingly, the prevalence of DED is around 30% in Taiwan compared with 20%–30% in Japan, South Korea, and Shandong province of China, where the latitude is higher and the temperature in winter is usually colder.[25-28] This discrepancy may be explained by different life styles among countries. For example, air conditioners or heaters are less used in winter in Taiwan compared with high-altitude countries. In Taiwan, motorcycles are the most common means of transportation, thereby exposing the riders to environmental factors more. All these aspects may aggravate DED symptoms in our patients. Further studies may be performed to evaluate the influence of life style in the susceptibility of DED symptoms caused by low ambient temperature.

One confounding factor that could have been encountered is that OSDI questionnaire assesses dry eye symptoms in the past week of the patient's life. However, we correlated this OSDI with the environmental parameters on the day of examination. The effects could thus be nullified and underestimated. In addition, OSDI scores of 13–22, 23–32, >33 represent mild, moderate, and severe DED, respectively.[12] The mean OSDI of our patients was 41.8 ± 19.8, indicating that the symptom severity was relatively high in our patients. Therefore, the symptom scores of some patients may be near plateau, leading to underestimation of the effect of environmental factors on DED symptoms.

There are some limitations in our study. Our case number was only 351, which is relatively small compared with

Table 5: Univariate linear regression analysis between SPEED and the variables

Variables	β	95% CI	P
Age	−0.3879	−0.6630−−0.1128	0.0058
Sex	0.0003	−0.008785-0.009384	0.9483
TBUT	−0.0123	−0.02684-0.002285	0.0982
LLT	0.0355	−0.08723-0.1582	0.5699
MGE	−0.0398	−0.1161-0.03652	0.3058
Schirmer	−0.0699	−0.1591-0.01938	0.1245
Temp	−0.1921	−0.2807−−0.1036	<0.001
RH	0.0426	−0.1366-0.2217	0.6406
Wind	−0.0003	−0.01206-0.01147	0.9608
PM10	0.0149	−0.2785-0.3083	0.9204
PM2.5	0.1839	0.04499-0.3229	0.0096
AQI	0.3236	−0.05929-0.7066	0.0974
SO_2	−0.0163	−0.05010-0.01747	0.343
CO	0.4588	0.1511-0.7665	0.0036
O_3	0.1202	−0.08877-0.3291	0.2588
NO	0.042	−0.02518-0.1091	0.2199
NO_2	0.1388	0.02334-0.2542	0.0186
THC	0.0326	0.0004262-0.06484	0.0471
NMHC	0.0008	−0.001276-0.002829	0.4573
CH_4	0.0251	0.01083-0.03940	<0.001

TBUT=Tear film break-up time, LLT=Lipid layer thickness, MGE=Meibomian glands expressible, Temp=Ambient temperature, RH=Relative humidity, Wind=Wind speed, AQI=Air quality index, THC=Total hydrocarbon, NMHC=Nonmethane hydrocarbon, CI=Confidence interval

Table 6: Multivariate linear regression analysis between SPEED and the variables

	β	95% CI	P
Model 1			
Age	−0.0513	−0.08980−−0.01286	0.0091
Temp	−0.2266	−0.3517−−0.1016	<0.001
PM2.5	0.07596	−0.02278-0.1747	0.1312
CO	0.01222	−0.03435-0.05880	0.606
Model 2			
Age	−0.051	−0.08982−−0.01223	0.0101
Temp	−0.2461	−0.3721−−0.1201	<0.001
PM2.5	0.07858	−0.03485-0.1920	0.1739
NO_2	0.00088	−0.1394-0.1412	0.9902
Model 3			
Age	−0.0517	−0.09026−−0.01311	0.0088
Temp	−0.2374	−0.3569−−0.1179	<0.001
PM2.5	0.053	−0.05555-0.1616	0.3376
THC	1.856	−3.625-7.336	0.5059
Model 4			
Age	−0.0509	−0.08930−−0.01245	0.0096
Temp	−0.227	−0.3659−−0.08824	0.0014
PM2.5	0.08253	−0.02045-0.1855	0.1159
CH_4	0.1593	−0.9544-1.273	0.7786

Temp=Ambient temperature, THC=Total hydrocarbon, CI=Confidence interval

other studies. Furthermore, 73.2% of the patients included in 1-year time span were female, raising the concern that the conclusion may only be applied to female group. However, the sex distribution in our study reflected the fact that female is a dominant risk factor of DED prevalence.[1] Although we found marginally higher OSDI in female patients (42.74 ± 19.80 in female vs. 39.08 ± 19.40 in male), the difference was not statistically significant by univariate regression analysis ($P = 0.12$), indicating that the contribution of sex to symptom severity was less obvious. To exclude confounding by geographical factors, we only enrolled patients living in four adjacent districts in New Taipei City, where the air pollution in winter is generally mild compared with southern part of Taiwan. This may explain that air pollutants have no obvious effect in DED symptom severity in our multivariate regression models. The localized nature of our findings may also hinder the extrapolation to other regions in the world, since the average temperature is variable. Although further studies conducted in areas with different extents of air pollution and average ambient temperature may be warranted, our findings still have merit that local meteorological data are crucial in determining the severity of DED symptoms of nearby patients. Finally, to better understand the causal relationship between DED symptoms and environmental factors, a longitudinal cohort study is more convincing. However, most DED patients come to hospital for treatment to relieve symptoms and signs in the real world. Consequently, patients usually receive treatment soon after diagnosis that may mask symptom severity under different environmental conditions. In this study, we only included the data of DED patients only at the time of their first visit to our dry eye clinic. Compared with longitudinal approach, our results still have merits to depict the symptom severity of first-time DED patients in different seasons in the real world.

Conclusion

Our study demonstrated that low ambient temperature is correlated with OSDI and SPEED scores. This finding may shed light on the environment effect on DED symptoms.

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Conflicts of interest
Dr. Shu-Wen Chang, an editorial board member at *Taiwan Journal of Ophthalmology*, had no role in the peer review process of or decision to publish this article.

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