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Symptoms of dry eye related to the relative humidity of living places

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A R T I C L E I N F O

Keywords:
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Relative humidity

A B S T R A C T

Purpose: To investigate the impact of relative humidity (RH) and climate variables of the place of residence on symptoms of dry eye disease (DED) in primary eye care practice.
Methods: A cross-sectional analysis of the Ocular Surface Disease Index (OSDI) dry eye classification of 1.033 patients [classified as non-DED (OSDI ≤22) and DED (OSDI >22)] was conducted in a multicentre study in Spain. Participants were classified according to the 5-year RH value (data from the Spanish Climate Agency -www.aemet.es) into two groups: those who lived in low RH (<70%) places and those who lived in high RH (≥70%) places. Additionally, differences in daily climate records (EU Copernicus Climate Change Service) were assessed.
Results: The prevalence of DED symptoms was 15.5% (95% CI 13.2%–17.6%). Participants who lived in places with <70% RH showed a higher prevalence of DED (17.7%; 95% CI 14.5%–21.1%; P < 0.01 adjusted for age and sex) than those who lived in places with ≥70% RH (13.6%; 95% CI 11.1%–16.7%) and a closer, but not statistically significant, risk for DED (OR = 1.34, 95% CI 0.96 to 1.89; P = 0.09) than previously described DED risk factors [age older than 50 years (OR = 1.51, 95% CI 1.06 to 2.16; P = 0.02) and female sex (OR = 1.99, 95% CI 1.36 to 2.90; P < 0.01)]. Some climate data showed statistically significant differences (P < 0.05) between participants with DED and non-DED (mean wind gusts; atmospheric pressure; mean and minimum relative humidity); these variables did not significantly increase DED risk (OR close to 1.0 and P > 0.05).
Conclusion: This study is the first to describe the impact of climate data on dryness symptomatology in Spain, confirming that participants who live in locations with RH <70% have a higher prevalence (corrected for age and sex) of DED. These findings support the use of climate databases in DED research.

1. Introduction

Dry eye disease (DED) is a common, worldwide, inflammatory, multifactorial ocular surface disease with high prevalence (5% to 50% of the population) that deteriorates the quality of daily life.[1,2] DED represents a diagnostic challenge in primary care practice[3] due to the variety of symptoms (highlighting eye irritation, redness, itching, grittiness, foreign body sensation, excessive tearing, and visual blurring or disturbance [4]) and inconsistent disease signs, with the presence or absence of ocular surface damage, mainly corneal and/or ocular surface staining (fluorescein, rose bengal, lissamine green), tear BUT, and Schirmer test.[2,5].

Age (especially older than 50 years) and sex (female) are considered the main risk factors for DED.[2] Additionally, DED is influenced by four main factors:[6] a) systemic conditions (hormonal changes, rheumatic diseases, systemic lupus erythematosus and others), b) use of some medical treatments, c) some eye conditions (blepharitis, meibomian gland dysfunction, allergic conjunctivitis, eye infections, cataract and refractive surgery, eyedrop use or contact lens wear) and d) environmental factors (wind, dust, air-conditioning flow, low humidity, exposure to smoke, use of digital devices, etc.).[7,8].

Patient-reported outcome measures (PROMs) are commonly used in clinical and research practice [9,10], and the Ocular Surface Disease Index (OSDI) is one of the most reliable surveys[11] used to assess the severity of patients' symptomatology.[8,12] The OSDI score is a valid and consistent instrument for distinguishing between patients with or without DED [11,13-15] and is commonly used in DED epidemiological studies.[16,17].

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[1] **EMO** is the Spanish acronyms of Optometry Multicentres Studies (Estudios Multicentricos de Optometría).

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Few reports have assessed the impact of seasonal or weather-related variables on DED [18-21], mainly using environmental exposure chambers [22] or telephone interviews, [18] suggesting an increase in dry eye symptomatology with environmental characteristics (low temperature and humidity, [7,23] wind [18] and pollution [19,24,25]), but DED is also affected by several factors such as lifestyle, urban environments and activity level, etc. However, to the best of the authors' knowledge, no previous studies have been conducted in Spain to describe whether geographical differences related to the climate of patients' place of residence have an impact on dryness symptomatology using real data of climate variables.

The aim of this study was to assess the differences in DED symptomatology measured with the OSDI questionnaire regarding climate data of the geographic location in a large population in Spain, with a special focus on the relative humidity (RH) of the place of residence. This analysis intends to help eye care practitioners in patient management and education.

2. Materials and methods

2.1. Study design

This was a cross-sectional multicentre study enrolling patients to attend primary eye care centres of the EMO (Estudios Multicentricos en Optometria) research group across 12 different Spanish locations (Fig. 1). Each centre was classified according to the 5-year average RH values published by the Spanish meteorological agency [(Agencia Española de Meteorologia (https://www.aemet.es)] into two groups: six locations with low RH (<70%) and six other locations with higher RH (≥70%) according to international references that recommend a comfortable humidity between 30% and 70% RH.[26-28].

Additionally, the daily mean, minimum, and maximum values of the climate data for five different variables [skin temperature (°C), wind gusts (m/s), air temperature (°C), atmospheric pressure (Pa) and RH (%)] corresponding to the visit date were collected from the EU-funded Copernicus Climate Change Service [29] according to the latitude and longitude of each research centre location. This service provides several climate records from 1979 to the present day on regular latitude-longitude grids with a reasonable spatial resolution. Climate data were downloaded through the application programming interface.

The institutional review board of the Human Sciences Ethics Committee of Valladolid Area-Este Clinic Hospital (Castilla y Leon public health system-SACYL) approved the study protocol (PI-201606), and the study was conducted according to the tenets of the Helsinki Declaration. All participants were informed about the nature of the study and its consequences prior to obtaining their written informed consent to participate.

2.2. Study procedures

All participants were evaluated in a single visit and underwent an extensive clinical history to detect risk factors associated with DED (age, sex, systemic disease, allergies, smoking, antidepressant medication, etc.). Additionally, a comprehensive eye examination was performed, including visual acuity measurement (Snellen optotypes), manifest refraction (with phoropter or trial frame following four steps: initial sphere check, cylinder axis refinement, cylinder power refinement and second sphere check), and anterior ocular surface assessment, including fluorescein dye observation under a slit lamp using cobalt blue illumination (ocular surface findings were assessed with Efron grading scales [30], following recommendations of TFOS Dry Eye Workshop (DEWS) [12] and the National Eye Institute).[31] Prior to study start, all researchers were trained in study protocol, to minimize the impact of the inter-practitioner variability in study procedures.

Participants with any disorder affecting tear secretion (such as hyperthyroidism, rheumatism, lupus, any autoimmune disease, previous

Fig. 1. Representation of the EMO (Optometry Multicentre Studies) group centres. Symbols with black circle centres represent locations with RH <70%, and white squares represent locations with RH ≥70%.

diagnosis of DED, cicatricial conjunctivitis, pterygium, eyelid trichiasis or others); history of any eye medication use in the last 3 months to treat any eye condition (glaucoma, etc.); active anterior eye inflammation (such as blepharitis, conjunctivitis, keratitis, scleritis, uveitis, etc.); the use of contact lenses in the last 3 months and any previous ocular trauma or surgery in the last 6 months were excluded.

2.3. Dry eye evaluation

Subjective symptoms of DED were evaluated with the Spanish [32] version of the OSDI questionnaire, as it is reliable, valid and consistent in distinguishing between patients with and without DED. [11,13-15] The OSDI questionnaire was developed by Allergan Inc. (Irvine, US) in 2000, [13] and the current version includes a 12-item self-administered questionnaire that evaluates the frequency of symptoms over the preceding week in approximately 5 min. The OSDI questionnaire is structured into three main domains: ocular symptoms (5 questions), vision-related daily function (4 questions) and environmental triggers (3 questions). Participants answered the twelve questions with a Likert-type scale from 0 to 4 total, where 0 indicates none of the time; 1, some of the time; 2, half of the time; 3, most of the time; and 4, all of the time. To calculate the total OSDI score, the sum of scores multiplied by 100 was divided by the total number of questions answered multiplied by 4. The OSDI score ranges between 0 and 100, where higher scores represent a greater severity of symptoms as follows: no symptoms (score ≤12), mild symptoms (score between 13 and 22), moderate symptoms (score between 23 and 32), or severe symptoms (score between 33 and 100).[33] Additionally, participants were grouped into two categories, non-DED (OSDI ≤22) and DED (OSDI >22), following recommendations to provide comparable results with previous epidemiological DED reports.[2].

2.4. Data analysis

For statistical analysis, SPSS software version 27.0 (SPSS, Inc., Chicago, IL, USA) was used. Normal distribution of the variables was assessed with the Kolmogorov-Smirnov test ($P < 0.05$ indicated that the data were normally distributed). Mean, standard deviation, median, interquartile range (IQR) and percentages were used to describe the data when were appropriated. Continuous variables (climate data) were assessed with the Mann-Whitney *U* test, and categorical variables were assessed with the chi-square test.

DED prevalence was reported as percentages with 95% confidence intervals (95% CIs) calculated using bootstrapping through random repetition of 1,000 samples. Unadjusted and adjusted for age and sex (log linear analysis), differences in DED prevalence with age, sex and RH of place of residence were calculated with cross-tables. After adjusting for other baseline comorbidities, odds ratios (ORs) and 95% CIs were calculated with multivariate logistic regression analysis to assess the relationships of age (older than 50 years), sex (female) and RH (<70%) as independent variables with DED (OSDI >22). All statistical analyses were considered significant at $P < 0.05$.

3. Results

3.1. Demographic information

A total of 1.077 patients were screened, and after exclusion criteria analysis, a cohort of 1.033 adults was included in the statistical analysis. A total of 405 (39.2%) were male, and 638 (60.8%) were female. Participants ranged in age from 18 to 97 years (mean of 52.5±14.8 years old). The mean spherical equivalent (sphere + ½ cylinder) was −0.07 ± 2.23 D (ranging from +7.75 to −15.00 D) and best spectacle-corrected visual acuity of 20/25 or better.

The 475 (46.0%) participants living in <70% RH places and the other 558 (54.0%) in ≥70% RH places did not show statistically significant differences in age (53.2±15.2 and 52.0±14.5 years, respectively; p = 0.08 Mann-Whitney *U* test) with a similar percentage of females in each group (45.7% and 54.3%, respectively, $X_1^2 = 0.05$, p = 0.44 chi-square). Fig. 2 summarizes climate differences between places of residence.

3.2. Dry eye prevalence

According to the OSDI score grading, 742 (71.8%; 95% CI from 69.0% to 74.6%) participants were classified as non-DED (OSDI score <12), 131 (12.7%; 95% CI from 10.7% to 14.7%) as mild DED (OSDI score 13–22); 76 (7.4%; 95% CI from 5.7% to 9.0%) as moderate (OSDI score 23–32) and 84 (8.1%; 95% CI from 6.4% to 9.8%) as severe (OSDI score 33–100) (Fig. 3 left). Therefore, 873 (84.5%; 95% CI from 82.4% to 86.8%) participants had an OSDI score ≤22, and 160 (15.5%; 95% CI from 13.2% to 17.6%) had an OSDI score >22 (Fig. 3 right).

Patients living in <70% RH places showed a higher percentage of dry eye symptoms (17.7%; 95% CI from 14.5% to 21.1%) than those living in ≥70% RH places (13.6%; 95% CI from 11.1% to 16.7%). This difference was statistically significant after adjustment for age and sex ($X_4^2 = 21.29$, $P < 0.01$). Fig. 3 summarizes the DED prevalence for all samples and in each RH group.

4. Dry eye prevalence differences with demographic characteristics

There was a higher proportion of females (73.1%), participants older than 50 years (66.3%) and participants living in locations with RH <70% (52.5%) with dry eye (OSDI score ≥22) (Table 1).

4.1. Dry eye differences with climate variables

Fig. 4 summarizes the differences in climate variables (skin temperature, wind gusts, atmospheric pressure, and RH) between participants with and without DED.

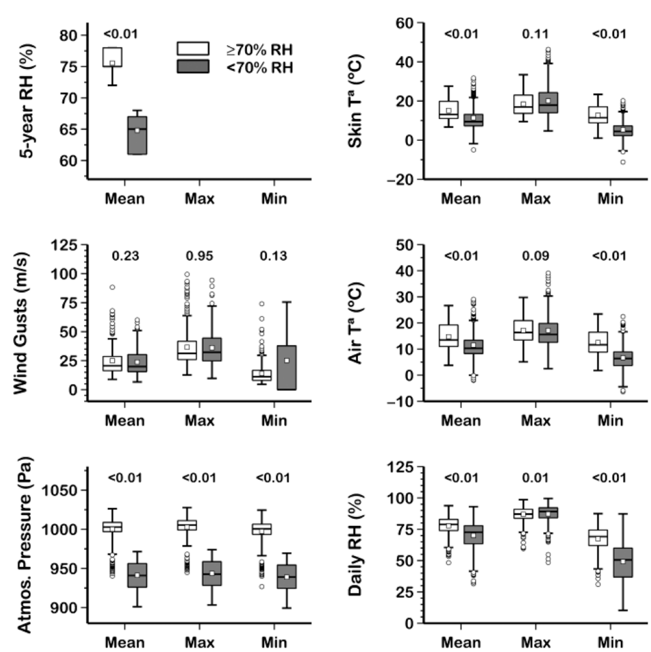

Fig. 2. Summary of differences in climate data between RH groups. For 5-year RH data, only the mean value was available, so no maximum and minimum data are represented (www.aemet.es). Median, IQR and Mann-Whitney *U* test p value is presented for each variable.

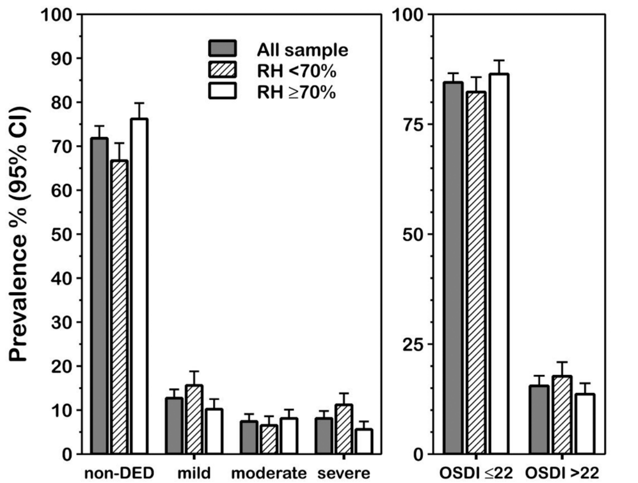

Fig. 3. Summary of OSDI score. Left: Non-DED (OSDI score <12); Mild (OSDI score 13–22); moderate (OSDI score 23–32) and severe (OSDI score 33–100) DED are represented. Right: OSDI score ≤22 and OSDI score >22 are represented. 95% CI bars are represented.

Table 1
- Demographic characteristics according to OSDI score. * Unadjusted chi-square p value.

Characteristic	Non-DED (OSDI ≤ 22) n = 873	DED (OSDI > 22) n = 160	P Value*
Sex			$X_1^2 = 12.08$, <0.01
Female	511 (58.5%)	117 (73.1%)	
Male	362 (41.5%)	43 (26.9%)	
Age (y)			$X_1^2 = 4.61$, 0.02
<49	374 (42.8%)	54 (33.8%)	
≥50	499 (57.2%)	106 (66.3%)	
RH			$X_1^2 = 3.24$, 0.04
<70%	391 (44.8%)	84 (52.5%)	
≥70%	482 (55.2%)	76 (47.5%)	

4.2. Association of dry eye with climate variables

There was no substantial increase in the risk for DED with any assessed climate parameter (OR close to 1.0; P > 0.05; Table 2).

The multivariable logistic regression model showed a trend of increasing DED in females (OR of 1.98; 95% CI 1.36 to 2.88; $X_1^2 = 12{,}77$, p < 0.01), participants older than 50 years (OR of 1.51; 95% CI 1.06 to 2.16; $X_1^2 = 5.08$, p = 0.02) and those who lived in locations with RH <70% (OR of 1.34; 95% CI 0.96 to 1.89; $X_1^2 = 2.87$, p < 0.09), as summarized in Fig. 5.

5. Discussion

The present study assessed the impact of the RH of patients' living places and other climatic variables (using real climate data) on DED prevalence (classified with an OSDI cut-off value higher than 22) in Spain because low RH is considered a triggering factor for dry eye.[18,23] This observation follows physical laws because low humidity increases the evaporation rate at surfaces and is supported by animal [34] and human[35] laboratory research.

Several population-based studies have reported a heterogeneous prevalence of DED (from 5% to 50% of the population using different criteria for DED classification -TEFOS DEWS epidemiology report-).[2] However, differences in DED definition, populations, studied samples and research methodology make it difficult to compare results among studies; for example, different reports found prevalences close to 7.0%,[36,37] 10%,[38-42] 20%[7,43,44], 30%[45-47] and 50%[48] using different DED criteria. However, based on the 95% CI, a DED (OSDI >22) prevalence between 13.2% and 17.6% was found in this study (Fig. 3), which is close to the global prevalence of 11.6% described in a recent *meta*-analysis report.[40].

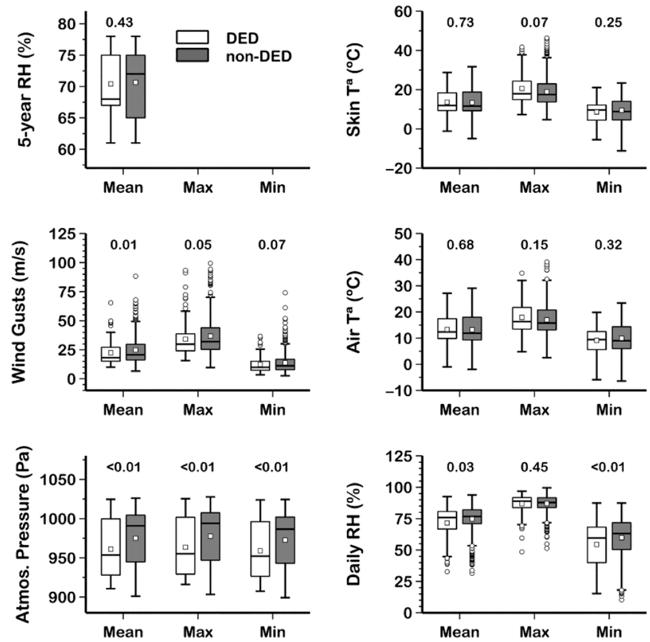

Fig. 4. Summary of differences in climate data between groups classified as non-DED (OSDI ≤22) and DED (OSDI >22). For 5-year RH data, only the mean value is available, so no maximum and minimum data are represented (www.aemet.es). Median, IQR and Mann-Whitney *U* test p value is presented for each variable.

These results are broadly consistent with previous reports that found a higher DED prevalence among participants older than 50 years and women (Table 1).[2,7,19,36,38] Previous studies have highlighted differences in DED prevalence (from 4.1% to 23.7%)[2] or the risk of developing DED in living regions of participants[2,36] with limited analysis of these differences (attributed to geographic, climatic or environmental variations, such as traffic-related pollutants).[2,18-21,24,25].

DED prevalence (OSDI >22) according to the 5-year average RH was assessed, classifying participants into two groups (RH <70% and ≥70%) and assessing the quantitative data of five different daily climate variables available from open-access repositories. Statistically significant higher DED prevalence in participants who lived in locations with <70% RH (Fig. 3) [24,25] corrected for age and sex (p = 0.01) was found, with some differences in climate variables (Fig. 4), including wind gusts, atmospheric pressure[49] and daily RH, which confirmed the impact of climatic variations on dry eye symptomatology.[19] A similar risk—but not statistically significant—for DED (OR = 1.34) among participants who lived in locations with low RH (<70%) to well-known main risk factors for DED[2], such as age older than 50 years (OR = 1.51) and female sex (OR = 1.98) (Fig. 5), was observed.

According to the theoretic model of DED progression,[50] which suggests a continuous or constant process with only minor daily or environmental variations,[18] there are three main DED stages: first DED initiation, second reflex compensation, and finally loss of the compensatory response. This model proposes that without intervention, disease may worsen, and early management could help to avoid DED progression and minimize its impact on subjects' ocular surface and quality of life, reducing the economic burden of dry eye.[2] The results of this study are plausible with this model, suggesting that the impact of

Table 2
Coefficients of the model predicting DED (OSDI > 22) with climate variables. Logistic regression of the climate variables. R^2 = 0.80 (Hosmer y Lemeshow), 0.08 (Cox y Snell) and 0.13 (Nagelkerke). Model X^2_{17} = 82.96P < 0.01. * 95% bootstrap confidence intervals based on 1,000 samples).

Variable	Coefficient (95% CI)*	Odds Ratio (95% CI)	P Value
Constant	27.72 (5.93 to 39.58)	–	<0.01 (X^2_1 = 7.64)
Skin temperature (°C)			
Mean	−0.27 (-0.69 to 0.19)	0.76 (0.48 to 1.20)	0.240 (X^2_1 = 1.38)
Max	0.13 (-0.10 to 0.35)	1.13 (0.90 to 1.43)	0.30 (X^2_1 = 1.08)
Min	0.20 (-0.26 to 0.30)	1.02 (0.77 to 1.35)	0.90 (X^2_1 = 0.02)
Wind gusts (m/s)			
Mean	−0.07 (-0.16 to 0.01)	0.93 (0.86 to 1.02)	0.11 (X^2_1 = 2.58)
Max	0.03 (-0.01 to 0.08)	1.03 (0.99 to 1.08)	0.13 (X^2_1 = 2.33)
Min	0.03 (-0.03 to 0.08)	1.03 (0.97 to 1.09)	0.38 (X^2_1 = 0.76)
Air temperature (°C)			
Mean	0.28 (-0.36 to 0.90)	1.32 (0.73 to 2.39)	0.35 (X^2_1 = 0.87)
Max	−0.09 (-0.41 to 0.25)	0.92 (0.68 to 1.25)	0.59 (X^2_1 = 0.29)
Min	−0.11 (-0–45 to 0.26)	0.90 (0.64 to 1.25)	0.52 (X^2_1 = 0.42)
Atmospheric pressure (Pa)			
Mean	−0.03 (-0.43 to 0.34)	0.98 (0.68 to 1.38)	0.85 (X^2_1 = 0.04)
Max	−0.06 (-0.30 to 0.15)	0.94 (0.76 to 1.16)	0.55 (X^2_1 = 0.36)
Min	0.07 (-0.11 to 0.28)	1.07 (0.90 to 1.27)	0.46 (X^2_1 = 0.56)
Relative Humidity (%)			
Mean	−0.09 (-0.20 to 0.01)	0.91 (0.83 to 1.01)	0.06 (X^2_1 = 3.49)
Max	0.05 (-0.01 to 0.14)	1.06 (0.99 to 1.13)	0.11 (X^2_1 = 2.62)
Min	0.04 (-0.02 to 0.11)	1.04 (0.98 to 1.10)	0.17 (X^2_1 = 1.89)

long-term exposure to low RH could be an additional precursor of DED that provokes a higher prevalence in this population. Therefore, the generalizability of these study findings is enhanced by enrolling a large number of participants classified according to the RH of their place of residence without significant differences in age (p = 0.08) and sex distribution (p = 0.44). In fact, the results of this study could be of paramount relevance, suggesting that maintaining appropriate humidity and temperature in the ambient air, for example, at patients' homes or workplaces, could be recommended for eye health, especially in patients who live in locations with low RH. Additionally, these results will help practitioners to improve DED management in a comprehensive way, taking into account the impact of climate on patients' symptomatology to manage early dry eye symptoms and avoid disease progression, including recommendations to use humidifiers in the treatment plan to reduce exposure to the adverse environment.[51] Further research is necessary to explore the use of climate information in future epidemiologic and clinical research.

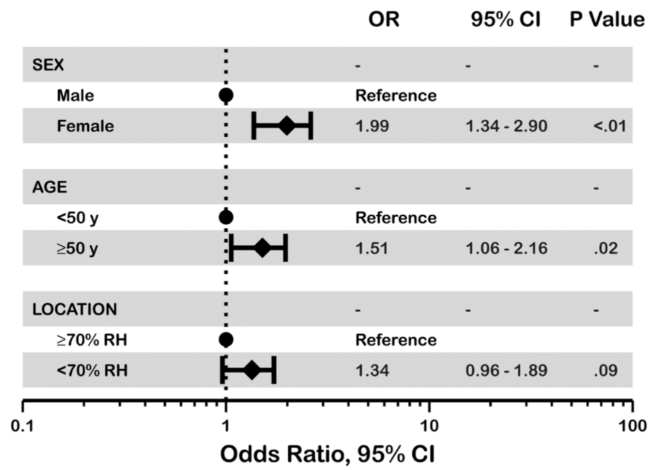

Fig. 5. Association of DED with main risk factors. The results of multivariate logistic regression model for DED (OSDI >22) versus non-DED (OSDI ≤22) for independent variables of age, sex and RH. CI = confidence interval; DED = dry eye disease; OR = odds ratio; RH = relative humidity.

5.1. Study limitations

This study has some limitations. The main limitation is related to the use of the OSDI questionnaire to identify DED patients, which may result in misclassification of DED (which requires assessment of clinical signs and tear osmolality). However, an OSDI cut-off value higher than 22 has been proposed by the TFOS DEWS II Epidemiology Report[2], and this instrument has been validated to distinguish between patients with and without DED.[11,13-15] Second, this study assessed a population sample of participants with and without symptoms of dry eye to define DED prevalence, so the OR calculated could differ in patients diagnosed with DED. However, this population is adequate to explore the prevalence and risk factors for DED onset. Third, due to the multicentre study design, slightly differences between practitioners in clinical performance and sings grading could be expected, but the research team was trained in study protocol prior to research started and same grading scale was use in all centres [12,30,31] to minimize the impact of intra-observer variability in study results. Additionally, climate variables were collected using the latitude and longitude of each research centre location, which could differ from the participants' address or workplace. However, it is not expected that there would be large distances between participants' addresses and their primary eye care centres, where participants were assessed. Finally, it is important to highlight that all participants were from northern Spain, as Fig. 1 describes. Future research could use participants to collect climate data because DED progression models suggest that long-term climate may have a greater impact than daily variations.

6. Conclusions

In conclusion, the results of this study include a large population assessed with the OSDI dry eye questionnaire, showing a prevalence of 15.5% (95% CI from 13.2% to 17.6%). These results are the first to describe the impact of climate data on dryness symptomatology in Spain, confirming that participants who live in locations with RH <70% showed a higher prevalence (corrected for age and sex) of DED. However, although close to previous DED risk factors, such as age (older than 50 years old showed an OR of 1.51; 95% CI 1.06 to 2.16) and sex (women showed an OR of 1.98; 95% CI 1.36 to 2.88), RH <70% was not a statistically significant risk factor (OR 1.34; 95% CI 0.96 to 1.89) for DED. These results may be useful for managing and educating patients with DED to minimize disease progression and its impact on their quality of life.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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