Prevalence of Asymptomatic and Symptomatic Meibomian Gland Dysfunction in the General Population of Spain

Eloy Viso,[1] *María Teresa Rodríguez-Ares,*[2,3] *Dolores Abelenda,*[1] *Benjamín Oubiña,*[1] *and Francisco Gude*[4]

Purpose. To describe epidemiologic characteristics of asymptomatic and symptomatic meibomian gland dysfunction (MGD) in a general adult population in northwestern Spain.

Methods. A total of 1155 subjects aged 40 years and older were selected by an age-stratified random sample procedure in O Salnés, Spain. A standardized symptoms questionnaire was administered and a comprehensive ophthalmic evaluation, which included ocular surface tests, was carried out. Absent, viscous, or waxy white secretion upon digital expression, lid margin telangiectasia or plugging of the meibomian gland orifices was considered evidence of MGD. The prevalence and associations of asymptomatic and symptomatic MGD, and their effects on the ocular surface, were investigated.

Results. From 937 eligible subjects, 619 (66.1%) participated (mean age [SD], 63.4 [14.5] years; range, 40–96; 37.0% males). The prevalence of asymptomatic MGD was 21.9% (95% confidence interval [CI], 18.8–25.3). This prevalence increased with age ($P = 0.000$) and was higher in males than in females ($P = 0.003$). The prevalence of symptomatic MGD was 8.6% (95% CI, 6.7–10.9). This prevalence also increased with age ($P = 0.000$) but was not associated with sex. Abnormal tear breakup time and fluorescein staining prevalence estimates were higher among asymptomatic subjects. After controlling for age and sex, asymptomatic MGD was associated with diabetes (adjusted odds ratio [OR_a] 2.23) and cardiovascular disease (OR_a 1.80), and symptomatic MGD with rosacea (OR_a 3.50) and rheumatoid arthritis (OR_a 16.50).

Conclusions. Asymptomatic MGD is more common than symptomatic MGD. Symptomatology is not associated with secondary damage to the ocular surface. Some systemic diseases may lower whereas others may raise the risk of developing symptoms. Symptom-based approaches do not seem appropriate for MGD estimation. (*Invest Ophthalmol Vis Sci.* 2012;53:2601–2606) DOI:10.1167/iovs.11-9228

From the [1]Servicio de Oftalmología, Complexo Hospitalario de Pontevedra, Spain; the [2]Servicio de Oftalmología, Hospital Clínico Universitario de Santiago de Compostela, Spain; the [3]Departmento de Oftalmología, Universidad de Santiago de Compostela, Spain; and the [4]Unidad de Epidemiología Clínica, Hospital Clínico Universitario de Santiago de Compostela, Spain.

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Corresponding author: Eloy Viso, Servicio de Oftalmología, Complexo Hospitalario de Pontevedra, 36004 Pontevedra, Spain; evo@mundo-r.com.

In the recent International Workshop on Meibomian Gland Dysfunction (MGD), this disorder was defined as a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction and/or qualitative/quantitative changes in the glandular secretion, which may result in alteration of the tear film, clinical apparent inflammation, ocular surface disease, and symptoms of eye irritation.[1] Consequently, the report of the epidemiology subcommittee of this workshop recommended not only measures derived from clinical evaluation and by purely objective means, but also a symptomatic assessment for the detection of MGD.[2] However, although symptoms, alone or in combination, are used for assessing ocular surface disorders such as dry eye (DE) in many studies,[3–8] their relevance for MGD estimation is not known as the proportion of asymptomatic population-based patients has not yet been investigated.

It is also unknown whether the lack of symptoms in MGD patients represents a mild form or an early stage of the disease and, whether symptoms, which may severely affect quality of life,[9,10] derive from the altered meibomian gland or meibum secretion, or otherwise are the result of secondary damage to the ocular surface. Similarly, although there is some evidence that supports the association of systemic factors such as androgen deficiency[11,12] or dyslipidemia[13] with MGD, there is no clinical confirmation of these associations and their relation with symptoms in the general population.

The Salnés Eye Study was designed to provide population-based epidemiologic information of ocular diseases in the population 40 years and older living in O Salnés, Spain. In previous reports we described the prevalence of DE and its associations.[14,15] In this article, we analyze the prevalence and associated factors of asymptomatic and symptomatic MGD and the impact of these disorders on the ocular surface.

Methods

Study Design and Setting

This cross-sectional study was performed in O Salnés area (42 degrees north of the equator) in northwestern Spain. This maritime area covers an area of 170 km^2 and had a total population of 72,500 of whom 33,649 were 40 years and older in 2005, when the study began. The climate in this location is rainy and temperate with mean annual rainfall of up to 1600 l/m^2.

Participants

An aged-stratified random sample of the population 40 years and older ($n = 1155$) was drawn from the National Health Service Registry, which covers more than 95% of the population. The sample was stratified in age groups as follows: 40 to 49 years, 50 to 59 years, 60 to 69 years, 70 to 79 years, and 80 years and older. A computer program generated a random sample of equal numbers ($n = 225$) of subjects in each age

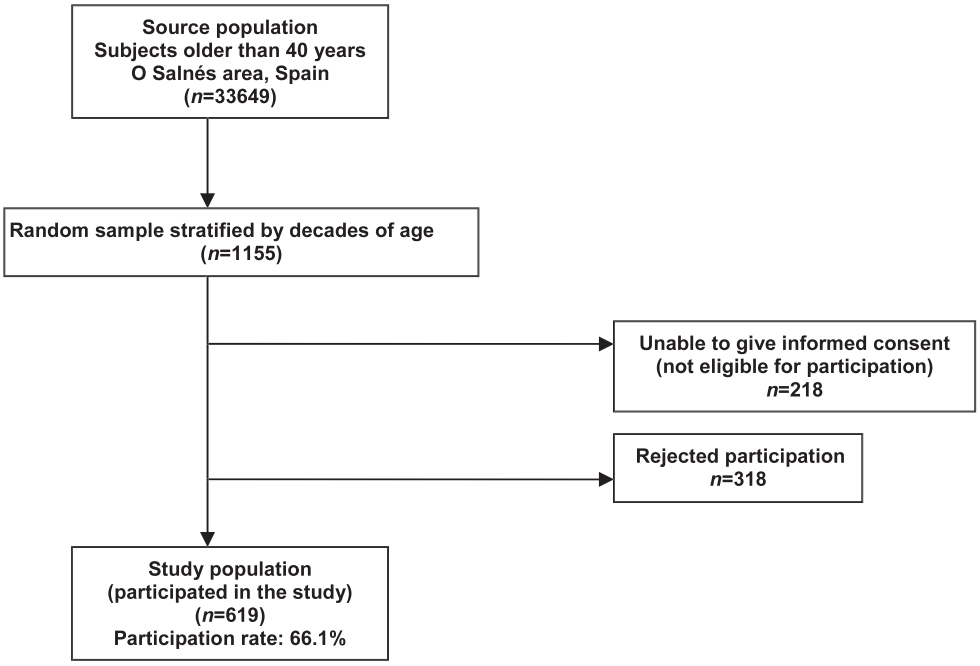

Figure 1. Study profile.

group, except for the last group (≥80 years), which was oversampled because of an expected lower response rate ($n = 255$). These 1155 individuals were invited to participate in the study by a personal letter. Participants were neither paid nor assisted to attend for the evaluation. Those unable to give informed consent were considered ineligible to participate in the study. The study profile is summarized in Figure 1. A detailed description has been published elsewhere.[14]

Data Collection

From May 2005 to March 2006, all subjects were successively convened for evaluation. A structured questionnaire was administered by trained physicians. It included (1) basic demographic data, (2) predominantly indoor or outdoor occupational activity, (3) alcohol consumption and smoking, and (4) a DE questionnaire. Occupational activity was evaluated on the basis of average daytime sun exposure experienced. Occupations such as fisherman or construction worker, which involved spending at least half the day outdoors, were considered outdoor occupational activities, whereas occupations such as factory worker or government officer, which involved spending less than half the day outdoors, were considered indoor occupational activities.

Alcohol intake was registered in each subject by adding up the total number of standard drinking units (one bottle of beer, one glass of wine, or one unit of spirit; all of them approximately equivalent to 10 g ethanol) habitually consumed per week. Subjects were classified according to alcohol intake into three groups as follows: (1) abstainers, (2) light drinkers (consumers of 1–14 units per week), and (3) heavy drinkers (consumers of more than 14 units per week). Subjects were classified according to smoking habit into three groups as follows: (1) nonsmokers, (2) ex-smokers (a person who had smoked regularly in the past and had quit smoking 1 year or more before the date of the interview), and (3) current smokers (a person who smokes any tobacco product either daily or occasionally). A questionnaire, which had previously been used by Schein et al.[3] was used to evaluate symptoms. Subjects were considered symptomatic when at least one of the symptoms of the questionnaire was experienced often or all the time (Table 1).

A comprehensive medical history including medication use was collected with special attention to common systemic disorders such as diabetes, cardiovascular disease, or hypertension; and disorders associated with ocular surface disease such as rosacea and allergy. A subject was considered to have diabetes if he or she had been diagnosed by a physician and was treated with insulin or oral hypoglycemic agents. Study participants were deemed to have cardiovascular disease, hypertension, rosacea, or allergy if they reported being told by a physician that they had those diseases.

A thorough slit lamp examination of the ocular surface was carried out. The eyelid margins, the meibomian gland orifices, and the meibomian gland secretions were carefully examined for signs of MGD, and these were classified according to modified previous criteria.[16] An aggregate score derived from the application of moderate pressure on the upper and lower central lid zones (corresponding to a total of 16 gland orifices) was used to grade meibum quality and expressivity. The criteria for the diagnosis of MGD included one or more of the following: (1) absent, viscous or waxy white secretion upon digital expression, (2) presence of two or more lid margin telangiectases, and (3) plugging of two or more gland orifices. MGD was graded as either present or absent. The ocular surface was also evaluated with the following tests: tear film breakup time (TBUT), fluorescein and rose bengal staining, and the Schirmer test. TBUT and fluorescein staining were performed following the instillation of one drop of sodium fluorescein 1% in the lower conjunctival sac. The tear film was observed by using a slit lamp with a cobalt-blue filter, after asking the patient to blink several times. The time, in seconds, between the last blink and the first desiccation spot was recorded. The mean of three of these recordings, taken after one single instillation of a drop of fluorescein, was registered as the TBUT. Fluorescein staining of the

Table 1. Dry Eye Questionnaire

Do your eyes ever feel dry?
Do you ever feel a gritty or sandy sensation in your eyes?
Do your eyes ever have a burning sensation?
Are your eyes ever red?
Do you notice much crusting on your lashes?
Do your eyelids ever get stuck?

Possible answers were "never," "rarely," "sometimes," "often," or "all the time."

cornea, which was measured after the first reading of TBUT, was graded as follows: 0 (no staining), 1 (mild staining, limited to less than one-third of the corneal surface), 2 (moderate staining, between 1 and 3), and 3 (severe staining, occupying half or more of the corneal surface). TBUT $\leq$ 10 seconds and fluorescein staining score $\geq$1 were considered positive. Rose bengal staining was assessed after touching the inferior fornix with a 1.5-mg rose bengal strip wetted with preservative-free sterile saline solution. The exposed interpalpebral portions of the nasal and temporal conjunctiva and the cornea were graded on a scale from 0 (no staining) to 3 (confluent staining) according to the van Bijsterveld method (score range, 0–9).[17] A score $\geq$3, using this grading method, was considered positive.

The Schirmer test was performed in both eyes. Five minutes following instillation of one drop oxybuprocaine hydrochloride (0.4%), the inferior fornix was gently blotted and a precalibrated standard filter strip was placed in the lower temporal fornix, where it remained for 5 minutes. During this time, the participants were instructed to look slightly upwards and blink normally. After removing the strip, the length of the wetting was measured. The test result was considered positive if this measurement was $\leq$5 mm.

The examinations were performed in two sessions on two different dates. The first session included the interviewer-administered questionnaire and the Schirmer test. The second session included the rest of the clinical tests and the systematic biomicroscopic examination, which were performed without previous knowledge of the results of the questionnaire and the Schirmer test. The analyses were conducted on the basis of a person, not per eye. All the examinations were carried out by an experienced ophthalmologist, at the same place, and with the same instrumentation.

Ethical Considerations

Informed written consent, which indicated clearly that subjects could choose to participate or not and that they would receive all the services they usually received whether they chose to participate or not, was obtained from all participants. The study conformed to the Declaration of the Helsinki and was reviewed and approved by the Regional Research Committee.

Statistical Analysis

In order to account for the stratified sampling, a design-based analysis was performed. The sampling procedures used in the study departed from unequal probability selection. Compensatory weights were developed to obtain estimates (prevalence and odds ratios [OR] with their corresponding 95% confidence intervals [CI]) from the original target population in the study area. To account for weighting and the sampling design, the STATA 11.0 (Stata Corp., College Station, TX) statistical package was employed. To examine which factors were associated with asymptomatic and symptomatic MGD, multinomial logistic regression analyses controlling for age and sex were performed. Age (years) entered the equation as a quantitative variable. The remaining variables were categorical (binary) and entered the equation as "1" (present or yes) or "0" (absent or no). Interactions terms were also assessed. Two-tailed *P* values lower than 0.05 were considered statistically significant.

Results

From 937 eligible subjects, a total of 619 subjects, all of them Spanish Caucasians, agreed to participate (overall participation rate 66.1%). Mean age (SD) of the sample studied was 63.4 (14.5) years (range, 40–96 years). The study comprised 229 males (37.0%) and 390 females (63.0%). No significant differences in age or sex between subjects who agreed to participate in the study and those who did not were found. There were 141 (69.5%) participants with asymptomatic MGD, equivalent to a weighted prevalence of 21.9% (95% CI, 18.8–25.3) in the population aged 40 years and older. This prevalence increased with age ($P = 0.000$) and was significantly higher among males after controlling for age ($P = 0.003$). There were 62 (30.5%) participants with symptomatic MGD, equivalent to a weighted prevalence of 8.6% (95% CI, 6.7–10.9). This prevalence also increased with age ($P = 0.000$) but was not associated with sex ($P = 0.287$) (Table 2).

The prevalence of TBUT $\leq$ 10 and of fluorescein staining were significantly higher among subjects with asymptomatic MGD ($P = 0.003$ and $P = 0.009$, respectively), but there were no significant differences in relation to the Schirmer test or rose bengal staining between subjects with asymptomatic and those with symptomatic MGD (Table 3).

The age- and sex-adjusted odds ratios (OR_a) for the association of asymptomatic and symptomatic MGD with demographic, lifestyle, and systemic factors are presented in Table 4. Moderate alcohol consumption was inversely associated with MGD (OR_a 0.63; 95% CI, 0.42–0.96), whereas past smoking was directly associated (OR_a 1.76; 95% CI, 1.04–3.00). A protective association was found between asymptomatic MGD and higher educational level (OR_a 0.37; 95% CI, 0.14–0.99). Diabetes (OR_a 2.23; 95% CI, 1.30–8.84) and cardiovascular disease (OR_a 1.80; 95% CI, 1.06–3.07) were associated with asymptomatic but not with symptomatic MGD. Conversely, rosacea (OR_a 3.50; 95% CI, 1.01–12.10) and rheumatoid arthritis (OR_a 16.50; 95% CI, 2.03–134.30) were associated with symptomatic but not with asymptomatic MGD. No association was found with systemic diseases such as hypertension or allergy. Interaction terms were not statistically significant.

Discussion

The main finding of this study was that less than half of the subjects with MGD had symptoms, which accounted for a prevalence of 8.6% of symptomatic and a prevalence of 21.9% of asymptomatic MGD in the population aged 40 years and older. Other studies only provide global MGD prevalence estimates, and these cover a substantial range from 3.5% in the Salisbury Eye Evaluation Study[3] to more than 69% in the Beijing Eye Study.[7] This striking variation in prevalence rates is probably explained by the differences in methodology and in the criteria used to define MGD. We included signs of the two categories described in the new MGD classification[1] in the definition used in this study to reduce the number of false negatives and removed indirect indicators to reduce the number of false positives. As regards symptoms, we used the questionnaire developed by Schein et al.[3] because it was the most widely used in population-based studies and because it included symptoms such as eyes stuck shut that have been considered,[18,19] despite a lack of sufficient evidence, characteristic of MGD. Unlike in other disorders associated with DE, the lower proportion of symptomatic subjects detected with these criteria does not favor the assessment of symptoms as a suitable screening tool for MGD. These results also alert to the possibility of unnoticed progression of the disorder and perhaps the necessity of its treatment in the absence of symptoms to prevent the development of complications.

Asymptomatic and symptomatic MGD prevalence increased with age, although a decrease was detected in subjects between 50 and 59 years old. This decrease probably reflects the lower prevalence in this decade of life of the two major categories:[1] hypersecretory, observed more often in younger subjects; and obstructive/hyposecretory, more common in older individuals.[20,21] Siak et al.[22] found no age differences in a population-based study performed in Singapore. It is conceiv-

Table 2. Prevalence of Asymptomatic and Symptomatic Meibomian Gland Dysfunction by Age and Sex

	Asymptomatic MGD			Symptomatic MGD			
	At Risk	No. (%)	Prevalence*	No. (%)	Prevalence*	No.	Total Prevalence*
Female	390	76 (66.1)	19.1 (15.5–23.4)	39 (33.9)	8.4 (6.1–11.3)	115	27.5 (23.3–32.1)
Age groups (years)							
40–49	83	23 (85.2)	27.7 (19.1–38.3)	4 (14.8)	4.8 (1.8–12.2)	27	32.5 (23.3–43.3)
50–59	77	7 (70)	9.1 (4.4–17.9)	3 (30)	3.9 (1.3–11.4)	10	13.0 (7.1–22.5)
60–69	78	11 (68.7)	14.1 (8.0–23.7)	5 (31.3)	6.4 (2.7–14.5)	16	20.5 (13.0–30.9)
70–79	79	15 (60)	19.0 (11.8–29.1)	10 (40)	12.6 (6.9–21.9)	25	31.6 (22.4–42.6)
≥80	73	20 (54)	27.4 (18.5–38.6)	17 (46)	23.3 (15.0–34.2)	37	50.7 (39.4–61.8)
			$P = 0.000$		$P = 0.000$		$P = 0.000$
Male	229	65 (73.9)	26.5 (21.2–32.7)	23 (26.1)	9.0 (5.9–13.3)	88	35.3 (29.4–41.7)
Age groups (years)							
40–49	51	14 (73.7)	27.5 (16.9–41.3)	5 (26.3)	9.8 (4.1–21.6)	19	37.2 (25.1–51.3)
50–59	55	9 (90)	16.4 (8.7–28.6)	1 (10)	1.8 (0.3–11.9)	10	18.2 (10.0–30.7)
60–69	45	10 (76.9)	22.2 (12.3–36.7)	3 (23.1)	6.7 (2.2–18.9)	13	28.9 (17.5–43.7)
70–79	45	16 (69.6)	35.6 (23.0–50.5)	7 (30.4)	15.6 (7.6–29.3)	23	51.1 (36.7–65.3)
≥80	33	16 (69.6)	48.5 (32.2–65.1)	7 (30.4)	21.2 (10.4–38.4)	23	69.7 (52.2–82.9)
			$P = 0.002$		$P = 0.002$		$P = 0.000$
Both sexes	619	141 (69.5)	21.9 (18.8–25.3)	62 (30.5)	8.6 (6.7–10.9)	203	30.5 (26.9–34.1)
Age groups (years)							
40–49	134	37 (80.4)	27.6 (20.7–35.8)	9 (19.6)	6.7 (3.5–12.4)	46	34.3 (26.8–42.7)
50–59	132	16 (80)	12.2 (7.6–18.8)	4 (20)	3.0 (1.1–7.9)	20	15.2 (2.0–22.3)
60–69	123	21 (72.4)	17.1 (11.4–24.7)	8 (27.6)	6.5 (3.3–12.4)	29	23.6 (16.9–31.8)
70–79	124	31 (64.6)	25.0 (18.2–33.3)	17 (35.4)	13.7 (8.7–20.9)	48	38.7 (30.6–47.5)
≥80	106	36 (60)	34.0 (25.7–43.4)	24 (40)	8.6 (6.7–10.9)	60	56.6 (47.1–65.6)
			$P = 0.000$		$P = 0.000$		$P = 0.000$

Figures are the number of subjects in each age group, the number of affected subjects (percentages within parentheses), and prevalence values in percentages, with 95% CI within parentheses.

* Weighted values.

able that a genetic predisposition of Asians to MGD might determine the high prevalence rates across all age groups observed in this study. Other population-based studies also report higher rates among Asian populations,[5–8] but we cannot compare our findings with theirs because age-specific data were not provided.

Our results indicate an association between MGD and the male sex. This association, which has also been reported in other population-based studies,[22] must not be explained by a selection bias in male participation, as the low proportion of males in the sample derives not only from a true difference in sex distribution in the population of reference but also from the nonproportionate sampling method used in this study, with the same number of subjects in each stratum. In agreement with clinic-based studies,[23] which tend to select symptomatic patients, no association was found with respect to symptoms (as if a factor increased the symptoms threshold in males or diminished it in females).

Surprisingly, although no differences were found with respect to the Schirmer test or rose bengal staining, subjects with the asymptomatic form of the disorder showed worse TBUT and fluorescein values than symptomatic ones. These findings suggest that symptoms may not be correlated with signs of damage to the ocular surface. A lack of association between symptoms and signs has also been reported in other ocular surface disorders in several studies.[24–26] However, further research is needed to understand the basis for symptoms in MGD and their relationship with the ocular surface.

Conflicting results have been reported regarding the association between smoking or alcohol consumption and ocular surface–related symptoms. In this study, past, but not current, smoking was significantly associated with symptomatic MGD. The damage to the ocular surface system caused by the chronic exposure to tobacco compounds[27] could predispose MGD patients to symptoms. Contrarily, the anesthetic effect on the ocular surface of the acute exposure to these compounds reported in several studies[28] could explain the lack of association observed between symptomatic MGD and current smoking. The inverse association between moderate alcohol drinking and MGD remained significant after adjusting for confounding variables and did not depend on the presence

Table 3. Prevalence of Clinical Signs of Dry Eye in Relation to Asymptomatic and Symptomatic Meibomian Gland Dysfunction

	No MGD	Asymptomatic MGD	Symptomatic MGD	*P* Value
Schirmer ≤ 5	38.1 (33.6–42.9)	34.8 (27.1–43.4)	34.9 (23.9–47.9)	0.737
TBUT ≤ 10	12.7 (9.7–16.3)	24.9 (18.3–33.0)	15.5 (8.2–27.5)	0.003
F ≥ 1	5.3 (3.5–7.9)	12.7 (8.1–19.2)	6.2 (2.3–15.9)	0.009
RB ≥ 3	8.3 (6.0–11.4)	23.7 (17.1–31.8)	24.2 (15.2–36.2)	0.000

Figures are weighted prevalence values in percentages, with 95% CI within parentheses. F, fluorescein staining; RB, rose bengal staining.

Table 4. Factors Associated with Asymptomatic and Symptomatic Meibomian Gland Dysfunction

	Asymptomatic MGD OR_a	Symptomatic MGD OR_a	Global MGD OR_a
Age groups (years)			
40–49	Ref	Ref	Ref
50–59	0.33 (0.17–0.62)*	0.34 (0.10–1.15)	0.33 (0.18–0.60)*
60–69	0.53 (0.29–0.98)*	0.83 (0.31–2.25)	0.59 (0.34–1.03)
70–79	0.98 (0.55–1.74)	2.20 (0.93–5.23)	1.22 (0.73–2.03)
≥80	1.97 (1.09–3.55)*	5.24 (2.25–12.24)*	2.61 (1.54–4.42)*
Sex			
Female	Ref	Ref	Ref
Male	1.86 (1.24–2.79)*	1.37 (0.77–2.44)	1.61 (1.11–2.34)*
Educational level			
None	Ref	Ref	Ref
Elementary	0.50 (0.30–0.86)*	0.78 (0.40–1.50)	0.58 (0.37–0.92)*
Secondary	0.78 (0.38–1.57)	0.56 (0.18–1.72)	0.81 (0.43–1.52)
University	0.37 (0.14–0.99)*	NA	0.28 (0.11–0.74)*
Alcohol intake			
Abstainers	Ref	Ref	Ref
1–14 units/week	0.68 (0.44–1.05)	0.55 (0.30–1.00)	0.63 (0.42–0.96)*
>14 units/week	1.09 (0.51–2.31)	0.86 (0.27–2.70)	1.09 (0.54–2.18)
Smoking habits			
Nonsmokers	Ref	Ref	Ref
Ex-smokers	1.57 (0.86–2.86)	2.55 (1.15–5.69)*	1.76 (1.04–3.00)*
Smokers	1.16 (0.60–2.26)	1.26 (0.35–4.48)	1.19 (0.63–2.21)
Work environment			
Indoors	Ref	Ref	Ref
Outdoors	1.47 (0.90–2.41)	1.51 (0.76–2.99)	1.46 (0.94–2.27)
Rosacea			
No rosacea	Ref	Ref	Ref
Rosacea	2.12 (0.75–6.00)	3.50 (1.01–12.10)*	2.27 (0.94–5.48)
Allergy			
No allergy	Ref	Ref	Ref
Allergy	1.33 (0.55–3.25)	1.18 (0.25–5.56)	1.33 (0.59–3.03)
Diabetes			
No diabetes	Ref	Ref	Ref
Diabetes	2.23 (1.30–3.84)*	1.54 (0.72–3.30)	2.04 (1.23–3.39)*
Hypertension			
No hypertension	Ref	Ref	Ref
Hypertension	1.31 (0.83–2.07)	1.70 (0.90–3.21)	1.38 (0.92–2.06)
CVD			
No CVD	Ref	Ref	Ref
CVD	1.80 (1.06–3.07)*	1.84 (0.94–3.60)	1.82 (1.11–2.98)*
RA			
No RA	Ref	Ref	Ref
RA	4.84 (0.72–32.60)	16.50 (2.03–134.30)*	6.92 (1.47–32.61)*

Values represent number of subjects with row percentages within parentheses. Interaction terms were not statistically significant. OR_a, age- and sex-adjusted odds ratio with 95% CI within parentheses; Ref, reference group; CVD, cardiovascular disease; RA, rheumatoid arthritis.

* Associations that are statistically significant.

or absence of symptoms. This apparently beneficial effect has not been demonstrated in other ocular surface disorders and may be the result of the influence of alcohol on lipid metabolism. We also report an association with pinguecula in a previous study,[29] but not with ocular surface diseases such as DE or pterygium, which is in agreement with other studies.[30]

Being part of the highly integrated lachrymal functional unit, the meibomian glands are expected to be influenced by multiple systemic factors among which androgen deficiency,[11,12] rosacea,[31,32] and Sjögren syndrome[33,34] are the most consistently reported. Diseases as common as dyslipemia[13] have also been found to have a harmful effect on meibomian gland functioning, and their treatment should probably be part of the treatment strategy of MGD if these associations are corroborated. We detected associations with several diseases and found that they had an effect on the occurrence of symptoms. Diabetes and cardiovascular disease were associated with asymptomatic MGD. Conversely, rosacea and rheumatoid arthritis were associated with the symptomatic form of the disease. Several mechanisms such as sensory neuropathy could explain the absence of symptoms found in some of these disorders, whereas the inflammatory response to changes in lipid secretion[35] could be one of the causes behind the presence of symptoms associated with the other conditions.

The main strength of this study was the population-based approach, which enabled us to obtain a representative sample of the population, but the 33.9% of the eligible subjects that did not participate was a source of potential selection bias. To evaluate the possibility of this bias, sex and age were compared between subjects who participated and those who did not. The similar proportions found in this evaluation confirmed the representative character of the sample (data not shown). The

examination of all the subjects by a single ophthalmologist was also a limitation of the study because, although it minimized interobserver error, it prevented reproducibility assessments. The study was also limited by its cross-sectional design, which can identify associated factors but cannot reveal causal relationships.

In summary, in this population-based study, asymptomatic MGD was found to be more than twice as common as symptomatic MGD. The occurrence of symptoms does not correlate with the severity of the damage to the ocular surface. Alcohol use and tobacco smoking have opposite associations with MGD. Systemic diseases such as rosacea and rheumatoid arthritis may promote symptoms, whereas others such as diabetes or cardiovascular disease may prevent symptoms. Further research is needed to broaden our understanding of the factors associated with MGD and their relationship with symptoms.

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