Prevalence of Meibomian Gland Dysfunction and Its Determinants in a Deprived Rural Population of Iran: A Population-Based Cross-Sectional Study

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Abstract- To investigate the prevalence of Meibomian gland dysfunction (MGD) and its relationship with some determinants in underserved villages of Iran. This population-based cross-sectional study was conducted on 3850 subjects that were randomly selected from the villages of two underserved districts in the north and southwest of Iran using multistage cluster sampling. All participants underwent complete ophthalmic examinations, including visual acuity and refraction measurement. Then, slit-lamp biomicroscopy was done by an ophthalmologist to investigate MGD. Of 3850 subjects that were invited, 3314 participated in the study (participation rate=86.07%), of whom 1834 (55.34%) were women. The mean age of the participants was 37.7±21.4 years (range=2-93 years). The prevalence (95% CI) of MGD in at least one eye was 29.20% (27.35 to 31.06). According to the results of multiple regression analysis, MGD had a positive association with the male sex (OR: 1.75; CI 95%: 1.44 to 2.13), age 61-70 years (OR: 7.15; CI 95%: 3.65 to 14.01), and living in southern villages (OR: 1.82; CI 95%: 1.48 to 2.22) and an inverse association with education level (OR: 0.89; CI 95%: 0.80 to 0.98). The results of this study showed a lower prevalence of MGD even in Iranian rural regions compared to other Asian countries. This study found that older age, male sex, and low education level served as MGD risk factors. It seems that improved health conditions are an important factor in preventing MGD.

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Keywords: Meibomian gland dysfunction; Prevalence; Cross-sectional study; Determinants

Introduction

Eyelid disorders are a group of common ocular disorders affecting many patients and an important cause of seeking eye care services in the elderly population. These disorders are of public health significance because they increase the risk of ocular infection. They can also result in visual disturbance and fluctuation, ocular discomfort, and eye strain, affecting daily activities, including reading, working on a computer, and driving (1).

Meibomian gland dysfunction (MGD) is one of the most common eyelid disorders. Although its mechanism is not yet clear, it seems that alterations in the quality and quantity of Meibomian gland secretions (Meibum) result in tear film composition changes (2-4). Changes in the tear film lipid layer affect the tear film homeostasis, resulting in symptoms like dry eye. On the other hand, lacrimal disorders cause ocular surface inflammation, producing symptoms like grittiness, itching, and epiphora. The importance of MGD lies in its inflammatory outcomes as well as its association with

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other ocular diseases since MGD, through its effect on the ocular surface, may result in ocular rosacea (4) and dry eye, especially the evaporative type (5-7), which is associated with red, itchy, and burning eyes (8).

Previous studies found that MGD and aqueous deficiency accounted for 60% and only 20% of dry eye cases, respectively (1,9,10). Prolonged inflammation or obstruction of Meibomian glands may result in the atrophy or loss of function of the glands (7).

Few studies investigated the prevalence of eyelid disorders, especially MGD, and its risk factors in the general population and reported a prevalence of 2.5-70% for MGD (3,7,11-15). Some studies evaluated its risk factors, but they mainly focused on dry eye (8,9,11,12,14-17), while there is a scarcity of data to determine the epidemiologic profile of eyelid disorders, especially MGD (10,18). The lack of information required to improve the health status of people living in underserved areas and the presence of controversial epidemiologic data encouraged us to conduct a population-based study to determine the prevalence of MGD and its association with some determinants in a rural population.

Materials and Methods

The methodology of this study has been described elsewhere (19,20). In summary, this cross-sectional study was conducted in 2015 using multistage cluster sampling. Considering a prevalence of 6.4% for visual impairment (as the main objective of the research project), a Type I error of 0.05, a precision of 1%, a design effect of 1.5, and a loss-to-follow up of 10%, 3850 subjects were required for this study. Then, among all districts of Iran, two districts were randomly selected in the southwest (Shahyun District, Dezful County, Khuzestan Province) and north (Kojur District, Nowshahr County, Mazandaran Province) of Iran (Map 1). Next, the list of all villages in these districts was prepared, and 15 villages from Shahyun and 5 villages from Kojur were selected randomly. In the next stage, after coordination with authorities, all individuals above 1 year of age living in these villages were invited to participate in the study. The objective and examination protocol were explained to the participants, and informed consent was obtained from them (or their legal caregivers if below 18 years of age).

The examinations were done in a room with standard illumination in each village. Demographic data, including age and sex, were collected in pre-designed forms. Complete ophthalmic examinations, including visual acuity and refraction measurement and slit-lamp biomicroscopy, were done for all subjects above 5 years by two optometrists and one ophthalmologist. First, visual acuity was measured with and without refractive correction using a LogMAR chart at 6m. Refraction was done for all subjects using a Topcon auto refractometer, and the best-corrected visual acuity was recorded according to the results of refraction. Slit-lamp biometry was done after optometric examination, and the eyelid edge status was carefully examined to evaluate the presence of MGD. Any change in the Meibomian gland orifices, including bulging, capping, and notching in association with hyperemia, redness, and telangiectasia of the posterior lid margin, was considered MGD. In addition, the presence of a collection of foam or bubbles in the eyelid margin or tear meniscus was considered a sign of MGD.

Statistical analysis

The prevalence and 95% confidence interval (CI) of MGD were calculated in the total population and subgroups using the binomial distribution. Multiple regression analysis was used to evaluate the relationship between MGD and determinants. The design effect resulting from the effect of cluster sampling was considered for standard error correction in all analyses. The level of significance was set at 0.05.

Ethical issues

The Ethics Committee of Shahid Beheshti University of Medical Sciences approved the study protocol, which was conducted in accordance with the tenets of the Helsinki Declaration. All participants signed written informed consent.

Results

Of 3850 subjects that were invited, 3314 participated in the study (participation rate=86.07%), of whom 1834 (55.34%) were women. The mean age of the participants was 37.7±21.4 years (range=2-93 years). The majority of the subjects (22.84%) were in the age range of 6-20 years, and 32.77% of the participants (n=1086) were illiterate.

Table 1 shows the prevalence (95%CI) of MGD in the total population and different subgroups. The prevalence of MGD in at least one eye was 29.20% (27.35 to 31.06) in the total population, 35.24% (32.30 to 38.19) in men, and 24.52% (22.19 to 26.85) in women. According to age, the highest prevalence of MGD (47.83% (40.10 to 55.55)) was seen in the age

group 61-70 years. The prevalence of MGD increased with age, which was independent of sex (Figure 1). According to education level, the highest prevalence of MGD was seen in illiterate subjects (37.47% (34.06 to 40.88)).

Table 1. Prevalence of Meibomian gland dysfunction (MGD) in the rural population in Iran, 2015

Variables		Number	Prevalence (95% CI)
Gender	**Female**	1834	24.52 (22.19 to 26.85)
	Male	1421	35.24 (32.30 to 38.19)
Age	**<=5 yrs. Old**	129	14.13 (7.01 to 21.25)
	6-20 yrs. Old	757	18.33 (15.07 to 21.60)
	21-30 yrs. Old	439	24.28 (19.53 to 29.03)
	31-40 yrs. Old	486	25.07 (20.51 to 29.64)
	41-50 yrs. Old	513	32.79 (27.97 to 37.60)
	51-60 yrs. Old	450	38.01 (32.69 to 43.32)
	61-70 yrs. Old	226	47.83 (40.10 to 55.55)
	>70 yrs. Old	255	46.41 (39.14 to 53.68)
Education	**Illiterate**	1086	37.47 (34.06 to 40.88)
	Primary school	964	27.62 (24.27 to 30.96)
	Guidance School	347	21.77 (16.63 to 26.91)
	High school	614	24.66 (20.62 to 28.70)
	College	244	20.69 (14.67 to 26.71)
Region	**North**	1419	23.89 (21.26 to 26.52)
	Southwest	1835	33.31 (30.75 to 35.86)
Total		3314	29.20 (27.35 to 31.06)

*CI: Confidence Interval

Figure 1. Location of selected rural in our study

Table 2 shows the results of multiple regression analysis between MGD with study variables. The results showed a significant positive association between the male sex and MGD (P<0.001), such that the odds of

MGD were 1.75 times higher in men compared to women. Moreover, compared to the age group below 5 years, the odds ratio (OR) of MGD increased with age, and the highest OR [5.74 (CI: 2.94 to 11.21)] was seen in the age group 61-70 years. Moreover, the odds of MGD have a significant positive association with living in southern villages (OR: 1.82; *P*<0.001) and a significant negative association with years of education (OR: 0.892; *P*=0.014).

Table 2. Result of multiple logistic regression between Meibomian gland dysfunction (MGD) with study variables

Variables	Odds Ratio (95% CI)	*P*
Sex (Female=0)	1.75 (1.44 to 2.13)	<0.001
***Age group**	---	---
6-20 yrs. Old	1.57 (0.82 to 3.03)	0.174
21-30 yrs. Old	2.52 (1.24 to 5.11)	0.010
31-40 yrs. Old	2.69 (1.37 to 5.29)	0.004
41-50 yrs. Old	3.56 (1.86 to 6.79)	<0.001
51-60 yrs. Old	4.51 (2.37 to 8.57)	<0.001
61-70 yrs. Old	7.15 (3.65 to 14.01)	<0.001
>70 yrs. Old	5.74 (2.94 to 11.21)	<0.001
Region (North=0)	1.82 (1.48 to 2.22)	<0.001
Years of education	0.89 (0.80 to 0.98)	0.014

*: lower than 5 yrs. old is the baseline group
CI: Confidence Interval

Table 3. Population-Based and Hospital-Based Studies Providing Estimates of the Prevalence of Meibomian gland dysfunction

Design	Author	Place	Year	Age group	SS	Prevalence (95% CI)
PBCSS	**Siak *et al*., (3)**	---	2012	40 to 79 years	3271	56.3 (53.3–59.4)
	Schein *et al*., (11)	USA	1997	65 year and older	2520	3.5 (02.8– 4.3)
	Lin *et al*., (13)	Chinese	2003	≥65 years	1361	60.8 (59.5–62.1)
	Jie *et al*., (15)	Chinese	2009	≥40 years	1957	69.3 (64.5–73.8)
	Uchino *et al*., (14)	Japanese	2006	67.5±5.7 years	113	61.9 (52.1–70.9)
	McCarty *et al*., (12)	Australia	1998	40-97 years	926	19.9 (17.4–22.7)
	Hashemi *et al*., (7)	Iran	2017	55.9±6.2	4700	26.3 (24.5–28.1)
	Current study	Iran	2015	2-93 years	3314	29.2 (27.3–31.1)
Hospital-based	**Hom *et al*., (21)**	California	1990	-	398	38.9 (40.9–59.9)
	Lekhanont *et al*., (16)	Thailand	2006	≥40 years	550	46.2 (42.0–51.0)
	Horwath-Winter *et al*., (26)	Austria	2003	29-88 years	97	32.9 (23.8–43.5)
	Zhang *et al*., (27)	China	2003	-	115	34.8 (26.2–44.4)
	Shimazaki *et al*., (25)	Japan	1999	54.16±15.6	27	18.5 (06.3–38.8)
	Shimazaki *et al*., (23)	Japan	1995	54.4±14.2	54	61.0 (46.6–73.9)
	Ong *et al*., (24)	Malaysia	1996	-	231	43.0 (36.7–50.0)
	Ong *et al*., (22)	USA	1990	-	-	20*

*: in Non-contact-lens wearers; PBCSS: Population-based cross-sectional study

Discussion

Limited numbers of population-based studies have investigated the prevalence of MGD, and the majority of the available studies focused on dry eye. Moreover, there is little evidence for the relationship between MGD and some risk factors. This study was conducted to evaluate the prevalence of MGD and its relationship with some risk factors, and the results showed that it was associated with age, sex, education level, and living place.

The prevalence of MGD was 29.20% in the study population, which was higher than the prevalence reported in Shahroud Eye Cohort Study (7). The prevalence of MGD varies in different populations (3,7,11-16,21-27) (Table 3).

It is interesting that the prevalence of MGD is higher in Asian countries compared to other countries; for example, its prevalence was 46.2% in the Bangkok study (16), 60.8% in the Shihpai Eye study (13), 61.9% in a Japanese study (14), and 69.3% in the Beijing Eye Study (15). However, MGD has a low prevalence in

Caucasians; for example, its prevalence was 3.5% in the Salisbury Eye Evaluation (11) and 19.9% in the Melbourne Visual Impairment Project (12). Although the reason for this difference is not clear, and caution should be practiced when comparing different studies, several explanations can be presented. One of the reasons may be differences in the age distribution of the subjects, methods used for clinical diagnosis, and genetic background of the participants. It seems that genetic predisposition is one of the possible reasons for the higher prevalence of MGD in the Asian population (7). Different definitions of MGD may be another explanation for the difference in prevalence (6); for example, the Beijing Eye Study (15) used telangiectasia of the lid margin as a diagnostic criterion for MGD, while telangiectasia or plugging of Meibomian glands was used in the Shihpai Eye Study (13) and tear film breakup time was used in the Melbourne Visual Impairment Project (12). Using different criteria for MGD diagnosis makes it difficult to compare and predict its prevalence in different studies (6,7).

Previous studies reported controversial results about the relationship between MGD and sex. Some studies reported a higher prevalence in women (9,15), while some other studies found no difference between men and women (7,13,28). The results of the present study showed a positive association between the male sex and MGD, as the odds of this disease were 1.75 times higher in men. The higher prevalence of MGD in men was seen in all age groups, which is consistent with previous studies (3). This inter-gender difference has been attributed to sex hormones since the Meibomian gland contains androgen receptor mRNA, androgen receptor protein, and type 1 and 2 5α- reductase mRNAs; therefore, sex hormone changes affect its function (29). As a result, any androgen deficiency may result in MGD, lipid profile alterations, tear film instability, and evaporative dry eye (29). Several studies showed that due to the higher prevalence of autoimmune diseases like Sjögren's syndrome in women, they are at increased risk of MGD and dry eye (6,9). Some drugs, like anti-androgen agents, may cause MGD and change the tear film composition in men, which is associated with functional dry eye (29). More studies are required to address these controversies (3).

The results of the present study showed a significant positive association between age and MGD prevalence; the odds of MGD increased with an increase in age to 61-70 years that was independent of sex (the prevalence of MGD increased with age in both sexes) (Figure 2).

Previous studies also confirmed the role of age in MGD (14,16,21,28,30). Den *et al*., (28) studied 354 eyes and found marked abnormalities in the eyelid margin or Meibomian glands after 50 years of age. Hykin and Bron (30) studied 80 subjects aged 5-87 years and found significant opacity in Meibomian gland secretions with an increase in age. Sullivan *et al*., (31) found that aging was associated with marked changes in the lipid profile of human Meibomian gland secretions. A comparison of the results of previous studies shows a higher prevalence of MGD in studies conducted in older populations (Table 3); for example, the prevalence of MGD was higher in a study by Uchino *et al*., (14) who recruited subjects above 60 years than a study by Lekhanont *et al*., (16) that was conducted in the age group above 40 years.

An interesting finding of the present study was a slight decrease in the prevalence of MGD after 61-70 years old; this decrease was observed in both sexes and seems to be due to eyelid atrophy with age, making MGD difficult to diagnose.

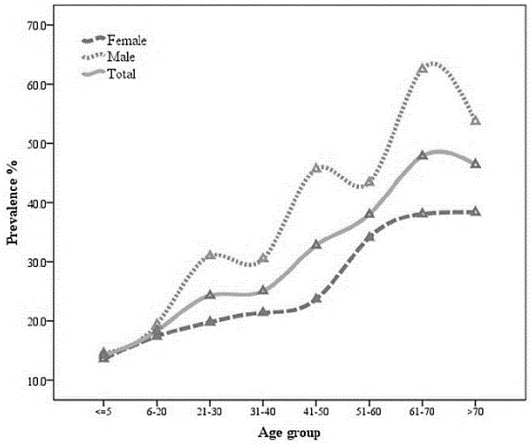

Figure 2. Prevalence of Meibomian gland dysfunction based on age group separated by gender

Another finding of the present study was an inverse association between education level and odds of MGD, which was consistent with previous studies (7). It has been reported that the prevalence of posterior blepharitis, which usually occurs after Meibomian gland inflammation and dysfunction, is higher in populations with low socioeconomic status (32). Moreover, the role of microbial agents in MGD is well documented (33). It seems that the odds of MGD are lower in people with higher education due to maintaining personal hygiene and considering health recommendations, which could explain the observed association between education level and MGD in previous studies (32,33).

Another finding of the present study was an

association between living place and the prevalence of MGD, as the prevalence of MGD was 10% higher in southern versus northern villages. Previous studies also reported the effect of living places on the occurrence of MGD (6,7,15). It is clear that a dry arid climate is associated with evaporative dry eye (6), which may increase the odds of MGD. Therefore, the dry arid climate in the southern villages of Iran may explain the higher prevalence in these regions. Several studies found a much higher prevalence of eyelid disorders in sunlight exposure (6,18,28).

This was the first study in a rural population with a wide age range (2-93 years), and its results may be useful for health policymakers and planners. A large sample size, high-precision data collection, and using a well-trained team were other strengths of this study. However, the observed relationships do not indicate causality due to the study design. Moreover, although we were willing to study the effects of other determinants, including smoking, on MGD, it was not possible to collect the relevant data due to the lack of proper infrastructure.

Overall, this study found that the prevalence of MGD was slightly higher in rural versus urban areas in Iran, although it was lower than in other Asian populations. Moreover, a marked increase was observed in the prevalence of MGD with age that was not affected by gender and was probably due to disorders in the structure and/or function of the Meibomian glands with age. Considering the difference in the prevalence of MGD according to determinants, it is suggested that treatment interventions should focus on older, less literate people to improve their effectiveness.

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