• Clinical Research •

Standardization of meibomian gland dysfunction in an Egyptian population sample using a non-contact meibography technique

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Abstract

● **AIM:** To develop normative data for meibomian gland dysfunction (MGD) parameters, using non-contact meibography technique of Sirius Costruzione Strumenti Oftalmici (CSO) machine, in an Egyptian population sample.

● **METHODS:** Observational, cross-sectional, analytic study, in which 104 Egyptian volunteers were included. Both upper lids were examined, using "*Sirius* CSO" machine. Each eyelid was given a degree of meibomian gland loss (MGL), which was calculated by the software of the machine.

● **RESULTS:** Mean percentage MGL in right upper lid was of 30.9%±12.6%, and that of left upper lid was 32.6%±11.8%. Thirty-four volunteers (32.7%) had first-degree MGL in their right upper lid, and 67.3% had second-degree loss. One volunteer (1%) had zero-degree MGL in left upper lid, 28 (26.9%) had first-degree loss, and 75 (72.1%) had second-degree loss. Degree of MGL in right upper eyelid was not related to age, but degree of MGL in left upper eyelid increased with age. There was statistically significant difference between both genders for degree of MGL in right eye (P=0.036) and in left eye (P=0.027).

● **CONCLUSION:** Noncontact meibography is a useful non-invasive tool for diagnosing MGL. MGL is diagnosed in 100% of apparently normal individuals; 26.9%-32.7% of which have first-degree MGL, and 67.3%-72.1% have second-degree MGL.

● **KEYWORDS:** Egyptian population; meibomian gland dysfunction; non-contact meibography; standardization; upper lid

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INTRODUCTION

Although the etiology of meibomian gland dysfunction (MGD) may differ from that of aqueous-deficient dry eye disease, the two conditions share many clinical features. MGD is one of the most common causes of abnormality of the tear film lipid layer and evaporative dry eye[1]. In the International Workshop on 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[2].

There are different methods for assessing MGD: primary objective including biochemical analyses of the meibomian glands or secretions (*e.g.*, assays, chromatography, mass spectrometry, and spectroscopy), secondary objective approaches (evaporimetry, lipid layer interferometry augmented with computerized assessment, and osmolarity), subjective clinical approaches (biomicroscopy of lid margins, evaluation of capping or plugging of meibomian gland orifices and expressibility and quality of meibum, and *in vivo* analysis of meibomian glands themselves through meibography), and subjective patient-reported approaches (itching, burning, heavy/puffy eyelids, dryness, and watery/teary eyes)[3-26].

Since there is broad overlap in MGD symptoms and those for aqueous deficient and evaporative dry eye, effort is needed to identify specific symptoms or develop instruments that would separate patients with MGD from those with other ocular surface problems.

The aim of this study was to develop normative data for MGD parameters, using a non-contact meibography technique of the Sirius machine of Costruzione Strumenti Oftalmici (CSO), Italy, in an Egyptian population sample. Being a new technique, this will add value for future studies concerned with MGD and factors causing it.

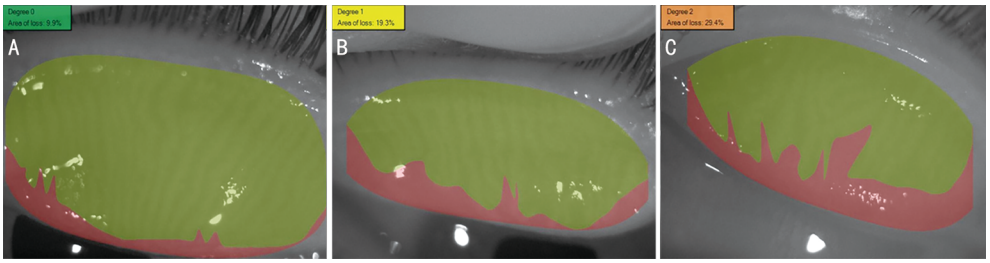

Figure 1 Phoenix software grading system A: Grade 0 MGL; B: Grade 1 MGL; C: Grade 2 MGL. MGL: Meibomian gland loss.

SUBJECTS AND METHODS

Ethical Approval This was conducted in accordance with Declaration of Helsinki, and received approval from the Institutional Review Board (Cairo University IRB number: 2013-02-8). All participants received a thorough explanation of the study design and aims. Study participants and their guardians gave informed consent before initiation of any study-related procedures.

This is an observational, cross-sectional, analytic study that was conducted on 208 upper eyelids of 104 volunteers (55 males and 49 females) in the interval between March 2013 and November 2016. Volunteers were recruited from the staff of the Ophthalmology Diagnostic and Laser Unit (ODLU) of Kasr Al-Ainy Hospital and patients presenting to the unit for checkup or spectacle prescription.

Patient Selection

Inclusion criteria Normal healthy individuals aged from 10 to 70y.

Exclusion criteria Ocular surface disease; trachomatous scarring (TS)-presence of scarring in tarsal conjunctiva (WHO classification); history of ocular or lid trauma or surgery, chronic topical drug use, and systemic disease including diabetes mellitus, hypertension, and autoimmune diseases.

Methodology Each upper lid was everted separately and photographed using the non-contact meibography instrument of the Sirius machine of CSO. Non-contact meibography consists of a slit-lamp equipped with an infrared (IR) charge-coupled device video camera and an IR-transmitting filter, to allow observation of meibomian glands in an everted lid without contact. This is combined with software for analysis of the degree of meibomian gland dropout[27].

Sirius is a high precision instrument for tomography of the anterior ocular segment and the 3D cornea analysis by merging Scheimpflug technology (which allows the measurement of the internal ocular structures) with Placido topography. It also has a built-in IR camera combined with IR light source, used for non-contact meibography.

A trans-illuminating light probe was not necessary. The machine software calculated the degree of meibomian glands loss (MGL), and a grade was given for each eyelid, according to the phoenix software grading system. Grade 0: 0-10% (Figure 1A); Grade 1: 10%-25% (Figure 1B); Grade 2: 25%-75% (Figure 1C); Grade 3: 75%-100% (not seen in our study).

Statistical Analysis Statistical analysis was done using SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 18 for the Microsoft Windows. Qualitative data were expressed as frequencies and percentages. Quantitative data were expressed as mean±standard deviation (SD) for parametric data. For comparing categorical data, Chi-square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5. Differences between groups were assessed through independent *t*-test and one way ANOVA for parametric. Correlation analysis between variables was done applying Pearson's ranked correlation test (for parametric data). All tests were two tailed and considered significant at $P<0.05$.

RESULTS

Patient Data We had 104 patients with a mean age of 35.1±10.4y (16-66y) with 55 males (52.9%). They were divided into 6 age groups: 10-20, 21-30, 31-40, 41-50, 51-60 and 61-70y.

Meibomio-graphic Data

Percentage of meibomian gland loss The mean percentage MGL in the right upper lid was 30.9%±12.6% (11.1%-68.4%), while that of the left upper lid was 32.6%±11.8% (9.9%-65%). The mean average percentage MGL for both upper lids was 31.7%±11.4% (11.6%-60.1%).

Degree of meibomian gland loss Thirty-four volunteers (32.7%) had first-degree MGL in their right upper lid, and 67.3% had second-degree loss. One volunteer had zero-degree MGL in left upper lid, 28 volunteers (26.9%) had first-degree loss, and the remaining 72.1% had second-degree loss.

Correlation of Meibomian Gland Dysfunction with Age

Percentage of meibomian gland loss Correlating the age to percentage of MGL for right upper eyelid, left upper eyelid and the average percent of MGL for both upper eyelids, using Pearson's rank correlation, was statistically insignificant ($P=0.978$, $P=0.891$, and $P=0.931$, respectively).

Degree of meibomian gland loss Relating the age to the degree of MGL was statistically insignificant for both eyes ($P=0.353$ for the right eye and $P=0.170$ for the left eye; Table 1).

When we tested the degree of MGL for each age group, in the right eye it was statistically insignificant (P=0.697), but when we tested the degree of MGL for each age group, in the left eye it was statistically significant (P=0.002; Table 2).

We also tested the percentage of MGL for each age group using One way ANOVA, and it was statistically insignificant in the right eye (P=0.951), in the left eye (P=0.545), and for the average loss of MG in both eyes (P=0.911).

Correlation of Meibomian Gland Dysfunction with Gender

Degree of meibomian gland loss There was a statistically significant difference between both genders for the degree of MGL in both the right upper eyelid (P=0.036) and in the left upper eyelid (P=0.027; Table 3).

Percentage of meibomian gland loss Comparing the percentage of MGL between both genders was statistically insignificant for the right upper eyelid (P=0.789) and also for the left upper eyelid (P=0.628) and for the average percentage of loss of both eyelids (P=0.690).

Comparing Right Upper Eyelid to Left Upper Eyelid Meibomian Gland Loss Comparing the degree of MGL of the right upper eyelid to the left upper eyelid was statistically insignificant (P=0.449; Table 4). Also comparing the percentage of MGL of the right upper eyelid to the left upper eyelid it was statistically insignificant (P=0.330).

Table 1 Relating the age to degree of MGL

MGL degree	Right eye		Left eye	
	n	Mean±SD, %	*n*	Mean±SD, %
0	-	-	1	-
1	34	33.7±9.1	28	34.6±8.5
2	70	35.7±10.9	75	35.5±10.8
P	0.353		0.170	

MGL: Meibomian gland loss. P<0.05 is considered statistically significant.

Table 2 Degree of MGL in each age group for each eye *n* (%)

Age group (y)	Right MGL degree		Left MGL degree		
	1	2	0	1	2
10-20	1 (16.7)	5 (83.3)	1 (16.7)	0	5 (83.3)
21-30	10 (45.5)	12 (54.5)	0	5 (22.7)	17 (77.3)
31-40	15 (32.6)	31 (67.4)	0	20 (43.5)	26 (56.5)
41-50	6 (28.6)	15 (71.4)	0	1 (4.8)	20 (95.2)
51-60	2 (28.6)	5 (71.4)	0	1 (14.3)	6 (85.7)
61-70	0	2 (100)	0	1 (50)	1 (50)
P	0.697		0.002		

MGL: Meibomian gland loss. P<0.05 is considered statistically significant.

Table 3 Relating sex to degree of MGL *n* (%)

Sex	Right MGL degree		Left MGL degree		
	1	2	0	1	2
Male	23 (41.8)	32 (58.2)	0	20 (36.4)	35 (63.6)
Female	11 (22.4)	38 (77.6)	1 (2)	8 (16.3)	40 (81.6)
P	0.036		0.027		

MGL: Meibomian gland loss. P<0.05 is considered statistically significant.

Table 4 Comparing degree of MGL between both eyes *n* (%)

MGL degree	Eye		*P*
	Right	Left	
0	0	1 (100)	0.449
1	34 (54.8)	28 (45.2)	
2	70 (48.3)	75 (51.7)	

MGL: Meibomian gland loss. P<0.05 is considered statistically significant.

DISCUSSION

Upon reviewing previous studies related to non-contact meibography, we found that there were very few studies concerned with normative data, using non-contact meibography machines.

In our study the percentage of MGL in the right upper lid ranged from 11.10% to 68.4% with a mean of 30.9%±12.6%. The percentage of MGL in the left upper lid ranged from 9.9% to 65% with a mean of 32.6%±11.8%. Average percentage MGL for both upper lids ranged from 11.6% to 60.1% with a mean of 31.7%±11.3%.

All of the volunteers had MGL, but with different grades. Thirty-four volunteers (32.7%) had first-degree MGL in their right upper lid, and 67.3% had second-degree loss. One volunteer had zero-degree MGL in left upper lid, 28 (26.9%) had first-degree loss, and the remaining 72.1% all had second-degree loss. So, MGL was bilateral in 99% of the volunteers, and unilateral in only one volunteer.

We found a statistically significant difference between both genders for the degree of MGL in the right upper eyelid (P=0.036) and in the left upper eyelid (P=0.027). In males, the percentage of MGL in the right upper eyelid had an average of 30.6%±14.6% and in the left upper eyelid an average of 32.0%±12.5%. In females, the percentage of MGL in the right upper eyelid had an average of 31.2%±10.1% and in the left upper eyelid an average of 33.2%±11.1%.

We didn't find a statistically significant correlation between the age and the percentage of MGL in both upper eyelids, in our study.

Comparing the degree of MGL of the right upper eyelid to the left upper eyelid was statistically insignificant (P=0.449). Also comparing the percentage of MGL of the right upper eyelid to the left upper eyelid it was statistically insignificant (P=0.330). Arita *et al*[27] examined the morphologic changes in meibomian glands associated with aging and gender using meibography and assessed their relation with slit-lamp findings regarding eyelid and tear film function in a normal population. They showed a significant positive correlation between age and

meiboscore (r=0.428, P<0.0001), as well as in males (r=0.462, P<0.0001) and females (r=0.418, P<0.0001). The meiboscore was significantly positively correlated with the lid margin abnormality score (r=0.359, P<0.0001).

Another study was conducted by Wu *et al*[28] to compare *in vivo* differences in meibomian gland morphology between children and adolescents, using infrared meibography and Image J software analysis (developed by the National Institutes of Health). They showed that MGL was found in both groups, but the meiboscore was not significantly different between the two groups (0.35±0.6 *vs* 0.41±0.8, t=-0.314, P>0.05). The number of meibomian gland ducts (25.85±3.25 *vs* 23.23±3.06, t=-3.437, P<0.05), relative width of the meibomian gland ducts (69.62%±5% *vs* 66.1%±7%, t=-2.454, P<0.05), and percent area of the meibomian gland acini (57.7%±4% *vs* 55.5%±4%, t=2.571, P<0.05) in the upper eyelid were significantly greater in adolescents than in children.

A study done by Suzuki *et al*[29] studied the morphological changes in the meibomian glands of patients with phlyctenular keratitis, using noncontact meibography. The meiboscore in worse eye was used in bilateral phlyctenular keratitis. The mean meiboscore in phlyctenular keratitis patients (upper lid: 2.9±0.3, lower lid: 2.7±0.5) was significantly higher than in controls (upper lid: 0.4±0.6, lower lid: 0.1±0.3). Noncontact meibography enabled visualization of meibomian gland loss in phlyctenular keratitis patients, suggesting a relationship between abnormalities of the meibomian glands in young individuals and the pathogenesis of phlyctenular keratitis.

In an attempt to study inter-examiner reliability in MGD assessment by Powell *et al*[30] meibography grading of meibomian gland atrophy and acini appearance, and slit-lamp grading of lid debris and telangiectasias was conducted on 410 post-menopausal women. They reported that agreement was determined for telangiectasias (40.6%), lid debris (50.9%), gland dropout (42.8%), and acini appearance (54.5%). Inter-examiner reliability for the four clinical outcomes ranged from fair agreement for acini appearance (κ_w=0.23, 95%CI 0.14-0.32) and lid debris (κ_w=0.24, 95%CI 0.16-0.32) to moderate agreement for gland dropout (κ_w=0.50, 95%CI 0.40-0.59) and telangiectasias (κ_w=0.47, 95%CI 0.39-0.55).

Pult and Riede-Pult[31] used non-contact meibography for diagnosis and treatment of non-obvious MGD. This case report described changes of ocular sign, tear film and meibomian gland morphology of a non-obvious MGD patient (lid margin, meibomian gland orifices and ocular signs appeared to be normal) undergoing MGD treatment. Without gland expression and/or meibography this form of MGD would have been overseen. Tear film, ocular signs and symptoms improved significantly after treatment. Expressibility of glands was improved with treatment although the MGD accompanying loss of meibomian glands—evaluated by non-contact meibography—was unchanged.

In conclusion, noncontact meibography is a useful non-invasive tool for diagnosing MGL. Using this technique, MGL was diagnosed in 100% of apparently normal individuals; 26.9%-32.7% of which had first-degree MGL, and 67.3%-72.1% had second-degree MGL. MGL was bilateral in 103 of the 104 volunteers and unilateral in one volunteer.

The mean percentage MGL using this technique was 31.7%±11.4%. MGL was not significantly affected by age difference in our study, while the degree of MGL was significantly affected by gender.

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