Comparative Analysis of Meibomian Gland Dysfunction in Eyes with and without Eyelid Margin Tattoos

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ABSTRACT

Objective: To compare the presence and severity of meibomian gland (MG) dysfunction among eyes of female subjects with and without eyelid margin tattoos using infrared meibography and colored photographs.

Methods: This is a cross-sectional, descriptive study that involved 38 Filipino females with and without eyelid margin tattoos. Infrared meibography was performed on the upper and lower eyelids of each eye to assess total or partial MG dropout. Colored photographs were taken to evaluate vascularity, irregularity, thickening of the lid margins, and plugging of MG orifices. Severity of MG dysfunction (MGD) was assessed using Arita's MGD proposed grading scale. Independent t-test was used to compare MG dropout and other lid margin parameters between the two groups. Prevalence ratio and prevalence odds ratio were calculated to measure the likelihood of MGD among eyes with eyelid tattoos.

Results: Seventy-four (74) eyes were included in the study (36 in the tattoo group and 38 in the control group). Scores for abnormal vascularity, irregularity, and thickening of the lid margins were significantly higher in the tattoo group compared to the control group ($p<0.0000001$). However, plugging of gland orifices scores between the two groups were found to be similar (upper eyelid: $p=0.65$; lower eyelid: $p=0.91$). Total MG dropout was significantly greater in the tattoo group (upper eyelid: -1.11 ± 0.82; lower eyelid: 1.37 ± 0.75) compared to the control group (upper eyelid: 0.53 ± 0.83; lower eyelid: 0.45 ± 0.76) (upper eyelid: $p=0.003$; lower eyelid: $p=0.000001$) for the upper and lower eyelid, respectively). Analysis of total MG dropout between the two groups showed a prevalence ratio of 2.13.

Conclusion: Eyelid margin tattoos are associated with several eyelid margin abnormalities and increase the risk of meibomian gland droupout.

Keywords: meibomian gland dysfunction, eyelid margin tattoos, infrared meibography

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The prevalence of meibomian gland dysfunction (MGD) in Asians ranges from 40-69% based on population-based studies.[1,2] MGD pertains to abnormalities in the quantity and quality of meibomian gland (MG) secretion. This develops when there is terminal duct obstruction, epithelial hyperkeratinization, meibum stasis, and eventual gland drop out. When sufficiently severe, MGD may lead to evaporative dry eye disease.[2,3]

Development of MGD is multifactorial. Risk factors identified include advanced age, hormonal imbalance or therapy, skin diseases, environmental factors, intake of allergy medications, and contact lens wear.[2,3] Additionally, eyelid margin tattoos have been implicated to contribute to MGD development.[4,5]

Eyelid margin tattoos are permanent cosmetic changes that replace traditional make-up application. During eyelid tattoo application, the upper layers of the eyelid margin skin are infiltrated with pigmented granules with the use of a sterile needle.[6,7] Eyelid margin tattoos have been popular since the 1980s but their adverse effects are poorly studied.[7,8] The demonstrated effects include decreased tear breakup time (TBUT), increased corneal fluorescein staining, and MG dropout.[5] Eyelid margin tattoos may cause MGD from a variety of reasons: needle injury, chronic inflammation, allergenic potential of the pigment, duct obstruction, and blepharitis.[5,8,10]

Meibography is a diagnostic technique used to assess partial or complete MG dropout. It uses infrared light to visualize the entirety of the MG from orifice to fornix.[1] When done in combination with colored photographs of the eyelid margins such as described by Arita et al. in a previous publication, severity of MGD can be assessed.[9]

An extensive review of online literature using PubMed, Google Scholar, and archives of the Philippine Journal of Ophthalmology yielded only a few case reports and one descriptive study that evaluated the association of eyelid margin tattooing with MGD.[4,5,8,10,11,12,13,14] In the present study, we investigated the prevalence ratio of MGD in subjects with and without eyelid margin tattoos with the use of imaging by colored photographs and meibography.

METHODS

This study was approved by the St. Cabrini Medical Center - Asian Eye Institute (SCMC-AEI) Ethics Review Committee and by the University of the East Ramon Magsaysay Memorial Medical Center, Inc. (UERMMMCI) Research Institute for Health Sciences Ethics Review Committee. Patients were recruited between August 2017 and September 2018 from the outpatient clinics of the Asian Eye Institute and the UERMMMCI. Taking into consideration a 15% dropout rate, the calculated sample size was 15 subjects per group. Written informed consent was obtained from all subjects before examination.

Subjects with and without eyelid margin tattoos were recruited to participate in this study. In the tattoo group, the approximate date of tattoo application and retouches were recorded. Patients who have chronic skin diseases and allergies, history of chemical burns, and are taking post-menopausal hormone therapy were ineligible to join. Contact lens wearers and those on concomitant eye drop use (except for artificial tears) were also excluded. Subjects without eyelid margin tattoos in the control group had no ocular comorbidities and no previous ocular surgeries.

Each subject underwent a comprehensive examination. Colored photographs of the lid margins were taken using a Topcon SL D701 Digital slit lamp with DC-4 digital camera (Topcon and Top Ophthalmic Products and Services Corp., Japan) (Figure 1).

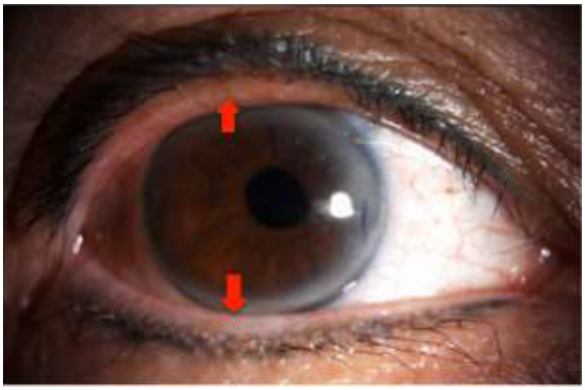

Figure 1. Representative colored photo of an eye with lid margin tattoo. Red arrows represent areas of examination of the eyelid margins.

Afterwards, meibography images were taken with the following settings: infrared selector lever tilted to the right, zero light intensity, and 6x magnification. An experienced examiner everted the upper and lower eyelids, then infrared images of the meibomian glands were obtained (Figure 2). The pictures captured were saved digitally in the Topcon DC-4 imaging software.

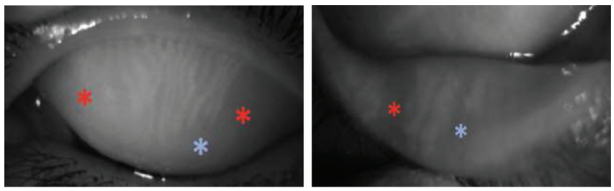

Figure 2. Representative meibography images of the upper and lower eyelid of a study subject. (Red asterisk - areas of complete gland dropout; Blue asterisk - areas of partial gland dropout)

Grading of the colored photographs was done by a single investigator (JG) and validated by a trained external eye disease consultant (TTT). Blinding was precluded because of the nature of the study. Eyelid margin abnormalities were graded according to the proposed grading scale for MGD described in a previous publication by Arita et al.[9] Using this scale, photos were graded based on (1) vascularity of the lid margin - described as hyperemia of the lid margin and the amount of telangiectasia distributed over the full length of the lid margin (Figure 3); (2) plugging of gland orifices - based on the number of abnormal findings such as capping, pouting, and ridging over the full length of the lid margin (Figure 4); (3) lid margin irregularity - based on the number of lid margin irregularities and notching (Figure 5); and (4) thickening - based on the presence of rounding of the lid margin (Figure 6).[9]

Figure 3. Representative images for lid margin vascularity. **(A)** Grade 0 described as no or slight redness. **(B)** Grade 1 described as redness in lid margin but no telangiectasia crossing meibomian gland orifices. **(C)** Grade 2 described as redness in lid margin conjunctiva and telangiectasia crossing meibomian gland orifices in less than half of the full length of the lid. **(D)** Grade 3 described as redness in lid margin conjunctiva and telangiectasia crossing meibomian gland orifices in half or more of the full length of the lid. (Adapted from Arita et al.'s proposed grading scales for meibomian gland dysfunction.)

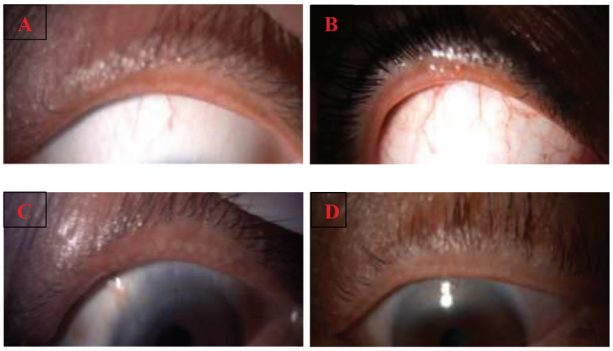

Figure 4. Representative images for plugging of gland orifices. **(A)** Grade 0 described as no plugging. **(B)** Grade 1 described as fewer than 3 plugged gland orifices. **(C)** Grade 2 described as three or more plugged gland orifices in less than half of the full length of the lid. **(D)** Grade 3 described as three or more plugged gland orifices in half or more of the full length of the lid. (Adapted from Arita et al.'s proposed grading scales for meibomian gland dysfunction.)

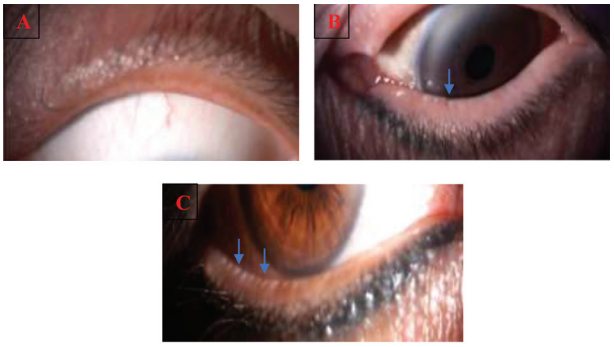

Figure 5. Representative images for lid margin irregularity. **(A)** Grade 0 described as no lid margin irregularity. **(B)** Grade 1 described as fewer than three lid margin irregularities with shallow notching (seen in arrows). **(C)** Grade 2 described as three or more lid margin irregularities with deep notching (seen in arrows). (Adapted from Arita et al.'s proposed grading scales for meibomian gland dysfunction.)

Figure 6. Representative images for lid margin thickening. **(A)** Grade 0 described as no lid margin thickening. **(B)** Grade 1 described as lid margin thickening with localized rounding. **(C)** Grade 2 described as lid margin thickening with diffuse rounding. (Adapted from Arita et al.'s proposed grading scales for meibomian gland dysfunction.)

Partial and complete gland dropouts were measured by reviewing the infrared photographs. Partial gland loss was defined as MG showing incomplete loss from the orifice to fornix, based on their number and length, while complete gland dropout was assessed based on the number of MG with complete loss from orifice to fornix (Figures 7 and 8).[9]

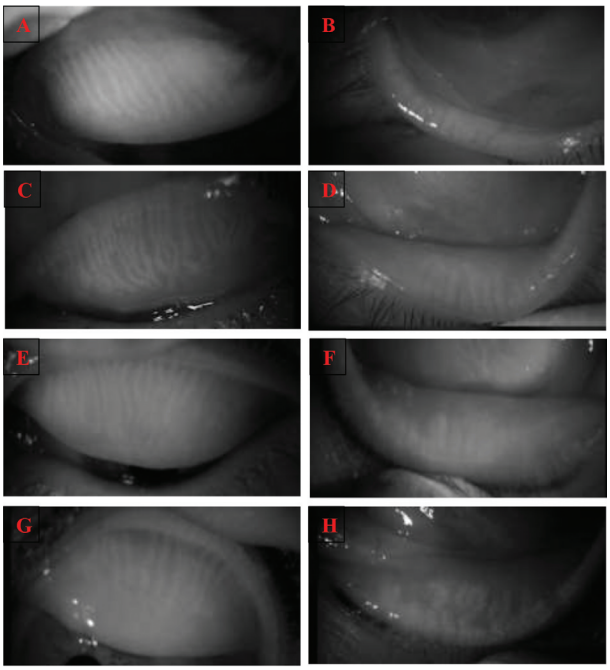

Figure 7. Representative images of partial gland dropout for both upper and lower eyelids. **(A and B)** Grade 0, **(C and D)** Grade 1, **(E and F)** Grade 2 and **(G and H)** Grade 3, based on the quantity and area of partial meibomian gland dropout. (Adapted from Arita et al.'s proposed grading scales for meibomian gland dysfunction.)

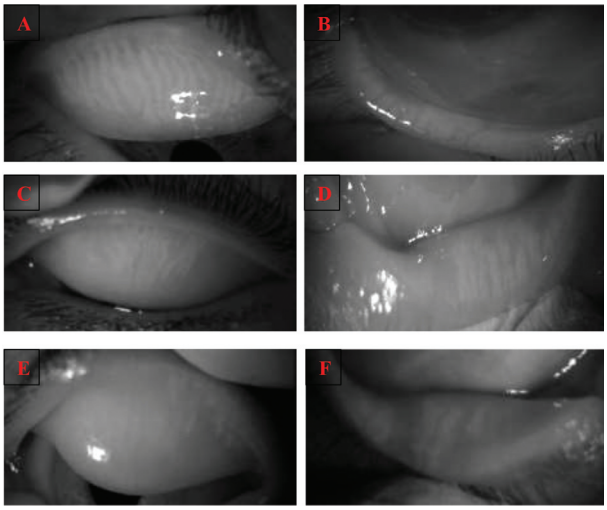

Figure 8. Representative images for complete gland dropout for upper and lower eyelids. **(A and B)** Grade 0 - no gland dropout, **(C and D)** Grade 1 - fewer than 3 gland dropouts, and **(E and F)** Grade 2 – more than 3 gland dropouts from orifice to fornix.

The upper and lower eyelids were graded separately and compared with corresponding reference photos. A grade of zero is given for normal findings, while a higher number in the grading scale denotes an increase in severity of abnormal findings.[9]

Statistical Analysis

Two-sample independent t-test was used to compare the variables between the two groups. A $p<0.05$ was considered statistically significant. Prevalence ratio and prevalence odds ratio were calculated to determine the strength of association of having an eyelid margin tattoo and MG dropout.

RESULTS

Thirty-eight Filipino female subjects were included in the study. There were 19 subjects per group, with a mean age of 64.37 years (range: 39-74) in the tattoo group, and 60 years (range: 50-67) in the control group. The difference between the mean ages of the 2 groups was not statistically significant ($p=0.07$) (Table 1). For those who were able to recall the date of the tattoo application (n=6), the range of tattoo exposure was from 10 to 45 years.

Table 1: Demographic profile of subjects

	Tattoo group (n=19)	Control group (n=19)	p-value
Female gender, n (%)	19 (100%)	19 (100%)	
Mean age (SD)	64.37 (8.87)	60.00 (5.31)	0.07

SD=standard deviation

Only thirty-six eyes in the tattoo group were included in the analysis as one subject in the tattoo group had difficulty with upper eyelid eversion. All eyes (n=38) in the control group were included in the analysis.

Analysis of Meibomian Gland Dysfunction Characteristics

Compared to the control group, mean scores on abnormal lid margin vascularity ($p=0.000197$), lid margin irregularities ($p<0.0000001$) and lid margin thickening ($p<0.0000001$) were significantly greater in the upper eyelids of subjects with tattoos (Table 2).

Evaluation of the lower eyelid disclosed signifi-

cantly higher mean scores for lid margin vascularity ($p<0.0000001$), lid margin irregularities ($p<0.0000001$) and lid margin thickening ($p<0.0000001$) in subjects with eyelid tattoos compared to the control group (Table 2).

Table 2. Grading of meibomian gland dysfunction

Mean scores (SD)	Tattoo group (n=36 eyes)	Control group (n=38 eyes)	p-value	Tattoo group (n=36 eyes)	Control group (n=38 eyes)	p-value
	Upper lid			Lower lid		
Abnormal lid margin findings of vascularity	0.86 (± 0.90)	0.21 (± 0.47)	<0.000197	0.750 (± 0.77)		<0.0000001
Plugging of gland orifices	0.83 (± 0.88)	0.95 (± 1.29)	0.65	0.17 (± 0.447)	0.16 (± 0.49)	0.91
Lid margin irregularity	1.47 (± 0.61)	0	<0.0000001	1.56 (± 0.65)	0.11 (± 0.31)	<0.0000001
Lid margin thickening	0.86 (± 0.72)	0.05 (± 0.23)	<0.0000001	0.92 (± 0.77)	0	<0.0000001

SD: Standard deviation

Meanwhile, differences in the mean scores on plugged gland orifices was not statistically significant between the two groups in both upper and lower eyelids ($p=0.65$ and $p=0.91$, respectively).

The means of scores on partial gland dropout in the upper lids of the control and tattoo group were not statistically different ($p=0.07$). However, in the lower eyelids, there was a significant difference in both groups ($p=0.0000002$) with the tattoo group showing poorer scores (Table 3).

Table 3. Meibomian gland dropout

	Tattoo group (n=36)	Control group (n=38)	p-value
Mean of partial gland dropout score (SD)			
Upper lid	2.44 (± 0.88)	1.76 (± 1.21)	0.07
Lower lid	1.92 (± 1.15)	0.50 (± 1.01)	0.0000002
Mean of complete gland dropout score (SD)			
Upper lid	1.11 (± 0.82)	0.53 (± 0.83)	0.003
Lower lid	1.37 (± 0.75)	0.45 (± 0.76)	0.000001

Table 4. Prevalence ratio of gland dropout in patients with and without eyelid margin tattoos

	Gland dropout	No Gland dropout	TOTAL
Tattoo group	18 (100%)	0 (0%)	18
Control group	9 (47%)	10 (53%)	19
TOTAL	27	10	

Prevalence ratio: 2.13

In both upper and lower eyelids, complete MG dropout mean scores were significantly greater in the tattoo group versus the control group ($p=0.003$ and $p=0.000001$) (Table 3). All subjects with eyelid tattoos had a significant MG dropout both in the upper and lower eyelids, compared to those without eyelid tattoos (9 out of 19 subjects or 47%) (Table 4). Prevalence odds ratio was calculated at 2.13.

DISCUSSION

Eyelid margin tattoos have gained popularity due to their convenience and permanency. However, there are case reports of early and late adverse reactions to permanent eyelid margin tattoos including pruritus, progressive erythema, eye irritation, eyelid margin swelling and scaling. Recent studies show that eyelid tattoos can cause MGD by mechanical destruction from the sharp needle and from the inflammatory reactions to the toxic pigments.[5,12]

Eyelid tissues with tattoos examined under light and electron microscopes showed pigment granules dispersed extracellularly between epidermis and dermis. The pigments used in eyelid margin tattoos contain chemical substances which can incite a granulomatous reaction.[8]

Upon tattoo application, these pigment granules are captured and phagocytosed by macrophages. With time, these pigment-laden macrophages undergo apoptosis and release the pigment particle. Since they are large extracellular particles, they are continuously phagocytosed by neighboring macropages, accounting for their permanency.[8,15] It is also possible for the ink pigments to infiltrate the different layers of the eyelid and contiguous structures. Some pigments within the macrophages remain in the dermis, while others migrate to the local lymph nodes.[10,12]

There have been reports of delayed hypersensitivity reaction postulated to be secondary to localized immune sensitization to certain pigments containing magnesium silicate hydroxide or talc. Histopathologic examination of these cases revealed granulomatous reactions to tattoo pigments characterized by epithelioid granulomas with well-formed epithelioid tubercles, histiocytes, and multinucleated giant cells.[8,12]

In this study, we compared the severity of MGD in patients with and without eyelid margin tattoos. Although most of the study participants were in the elderly age group, the mean age and the number of eyes studied were similar between the two groups.

We initially sought to determine the association between the duration of tattoo exposure and severity of MGD. Unfortunately, majority of the subjects with eyelid margin tattoo (13 out of 19) failed to recall the date of tattoo application. Hence, the relationship between duration of tattoo exposure and MGD cannot be ascertained.

Eyelid margin abnormalities such as vascularity, irregularity and thickening in both upper and lower eyelids were noted to be greater in the tattoo group. In addition, complete gland dropout was significantly higher in the same group. Prevalence odds ratio was calculated at 2.13. It is likely that having an eyelid margin tattoo leads to increased MG dropout and may aggravate pre-existing MGD. This can be due to the possible effects of the tattoo pigments, causing chronic eyelid irritation and inflammation.[8,12,13] Full thickness penetration of the needle during tattoo application can also damage the muscle of Riolan at the gray line leading to irregularities of eyelid margin as well.[10,12] Eventually, direct needle penetration and chronic inflammation from the pigments can obliterate the MGs, resulting to MG dropout and tear film lipid layer abnormalities.[5,13] Furthermore, other reported more serious adverse effects of eyelid margin tattoos include preseptal cellulitis, delayed hypersensitivity granulomatous reactions and extensive pigment spread in the different layers including muscle fibers.[8,11]

This study has several limitations. First, due to the cross-sectional design of the study, the presence of MGD prior to tattoo application was not documented and the possibility of MGD exacerbation after eyelid margin tattoo application cannot be ascertained. The documentation of presence of MGD prior to tattoo application is needed to determine the strength of association between eyelid margin tattoos and MG dropout. Second, data regarding tattoo application (i.e. type of tattoo ink used, technique, and depth of application) and presence of any early adverse reactions were not collected. Third, the absence of masking of the grading examiner may have resulted to observer bias. Lastly, we did not assess dry eye disease using other methods like vital dye staining, TBUT, and self-administered questionnaires.

In conclusion, eyelid margin tattoos are associated with several eyelid margin abnormalities and increase the risk of total MG dropout. Our study suggests that female subjects with eyelid margin tattoos are twice more likely to have MG dropout compared to subjects without eyelid margin tattoos. This finding is important in counseling patients who have been diagnosed to have MGD and who are contemplating to have eyelid margin tattoos.

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