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The eyelids and tear film in contact lens discomfort

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ABSTRACT

Purpose: To investigate characteristics of the eyelid margins, meibomian glands and the tear film of contact lens wearers, and to determine whether these characteristics were related to symptoms of contact lens discomfort.

Methods: A cross sectional study was performed on thirty existing daily wear soft contact lens wearers (6 male; 24 female) with median age of 23 years (range 18–41). Eyelid signs and tear film characteristics were evaluated during a single visit and subjects completed the contact lens and dry eye questionnaire (CLDEQ-8) to evaluate ocular discomfort.

Results: Based on the CLDEQ-8 responses, subjects were classified as symptomatic (n = 17) or asymptomatic (n = 13). Grades of foam at meibomian gland orifices (3 ± 1), expressibility (2 ± 1) and quality of secretions (2 ± 1), tear evaporation rate with (112 ± 54 g/m^2/h) or without (88 ± 45 g/m^2/h) contact lens wear, fluorescein tear breakup time (8 ± 2 seconds) and tear lipid layer thickness (45 ± 17 nm) were significantly associated with symptoms of discomfort in symptomatic lens wearers only ($r^2 > 0.45$; p value < 0.05). Upper lid-wiper epitheliopathy, meibomian gland acini reflectivity and tear meniscus height showed significant correlations with comfort scores in both symptomatic and asymptomatic contact lens wearers ($p < 0.05$). A greater number of Demodex mites was also observed in the upper eyelid of symptomatic lens wearers (2 ± 1) compared to asymptomatic lens wearers (0 ± 0; p value = 0.042).

Conclusions: Morphological irregularities of the meibomian glands and alterations to tear film secretions that affect tear evaporative dynamics were associated with symptoms of discomfort amongst the symptomatic lens wearers.

1. Introduction

Approximately 140–150 million people wear contact lenses globally [1–3]. Of these, 50% experience discomfort during lens wear and at least 25% of wearers are likely to discontinue lens wear permanently [4,5]. Dynamic interactions of eyelids and contact lenses with every blink could potentially be involved in contact lens discomfort [6–8].

Pult et al. [9] observed significantly higher grades of lid wiper epitheliopathy and lid parallel conjunctival folds (LIPCOFs) in contact lens wearers with dry eye symptoms. Increased LIPCOF severity scores and decreased non-invasive tear breakup time were also the most predictive for symptoms in lens wearers [10]. In contrast, some studies have reported that lid wiper epitheliopathy did not correlate with comfort scores in lens wearers [11–13]. Contact lens wearers demonstrate a greater incidence of meibomian gland dysfunction (MGD) [14–17]. Association between MGD and ocular symptoms in lens wearers couldn't be established due to marked variability from individual to individual [15]. Although studies have shown relationship between subjective symptoms and contact lens wear [14,18], few others have found that symptoms did not vary significantly between lens wearers and non-lens wearers [19,20]. Ocular *Demodex* especially, *Demodex folliculorum* in eyelash follicles and *Demodex brevis* in meibomian glands, have been associated with morbidities such as anterior blepharitis, posterior blepharitis involving meibomian gland dysfunction [21,22]. Increase in the numbers of *Demodex* caused an increase in subjective ocular surface symptoms [21]. Furthermore, *Demodex* mites also occur in up to 90% of contact lens wearers; however no association with comfort was established in that study [23].

Young et al. [24] reported that there was no significant difference in symptoms between groups that had different grades of meibomian gland expressibility, while a study by Villani et al. [25] and Pucker et al. [20] demonstrated that contact lens wearers reporting discomfort had compromised meibomian gland expressibility patterns and meibomian gland morphological changes. No difference has been observed in symptoms experienced by lens wearers and age-matched non-contact lens wearers [19,20], but significant associations between higher

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meibum quality score, frequent bulbar and palpebral conjunctival hyperemia, presence of lid margin telangiectasia, rounding, notching and hyperemia of the posterior lid margin, higher grades of orifice plugging and retroplacement of Marx's line have been observed during contact lens use [17–20,26,27]. Studies have also shown that symptoms in contact lens wearers are ameliorated by improvement in eyelid hygiene, indicating the importance of eyelid health and its impact on ocular symptomatology in lens wear [28,29].

Non-invasive tear breakup time and tear meniscus height differ significantly among current contact lens wearers, non-lens wearers and previous contact lens wearers [27,30,31]. Glasson et al. [32] found that the strongest associations with intolerance to contact lens wear were with non-invasive breakup time and lack of tear film volume. Clinical variables such as lid-wiper epitheliopathy, lid parallel conjunctival folds, expressibility of meibomian gland secretions, tear break up time and the meniscus height/area, have been shown to predict contact lens discomfort [33,34]. Nevertheless, the underlying pathophysiology of contact lens discomfort still not fully elucidated and discrepancies with the association of eyelids, meibomian glands and tear film variables with symptoms in contact lens wear still persist. The purpose of the current study was to compare structural differences in the eyelid margins, meibomian glands and the tear film of symptomatic and asymptomatic contact lens wearers, and to determine whether any of these variables were related to symptoms of contact lens discomfort.

2. Materials and methods

All procedures were conducted in accordance with the Declaration of Helsinki (1983), and the study was approved by the Human Research Ethics Committee, University of New South Wales, Sydney, Australia. All subjects provided signed informed consent before being enrolled in the study.

Thirty healthy contact lens wearers (6 male; 24 female) with a median age of 23 years (range 18–41), who had worn contact lens for at least 6 months, used lenses for at least 3 weeks before the evaluation visit and wore lenses for at least four times a week, were enrolled in the study. All contact lenses were worn on a daily wear modality. Exclusion criteria included (i) subjects with corneal fluorescein staining (type, depth and extent) of grade 1 or more based on CCLRU grading scales [35], (ii) subjects who had corneal opacities and/or vascularization of grade 1 or more based on CCLRU grading scales [35], (iii) subjects with any history of any ocular or systemic diseases that might influence the tear film, (iv) the use of any ocular and/or systemic medication, (v) subjects with epilepsy as there would be exposure to flashing lights during the Lipi-view examination (Tear Science®, Morrisville, NC) and (vi) evidence of conjunctival abnormalities such as pterygium or pinguecula. All participants were assessed to ensure that their habitual lenses were of acceptable fitting and all subjects in this study wore optimally fitting lenses. Eyelid signs and tear film characteristics were evaluated during a single visit and subjects were asked to complete the contact lens and dry eye questionnaire (CLDEQ-8). All measurements were conducted on the right eye only, except tear osmolarity measurements, for which measurements were recorded for both eyes and the average was considered for analysis. Measurements of all the study variables were performed without contact lenses except for tear evaporation rate, which was assessed both with and without contact lenses. The order of investigations conducted ranged from least invasive to the most invasive procedure.

2.1. Eyelids

Lid-wiper epitheliopathy was observed by slit lamp biomicroscopy after staining the marginal conjunctiva with a combination of 2% (w/v) sodium fluorescein (Fluor-I-strip A.T. ophthalmic strips 1 mg, Wyeth-Ayerst Laboratories, Rouses Point, NY) and 1% (w/v) lissamine green (OpGreen 1.5 mg, Ophtechnics Unlimited, India). Staining of the lid-wiper region was graded based on the classification devised by Korb et al. [36].

Grading of the lid parallel conjunctival folds (LIPCOFs) [9,10,37,38] and other eyelid margin signs such as ridging of Marx's line, anterior blepharitis, hyperkeratinisation, telangiectasia, lash loss, eyelid vascularity, irregularity or notching of eyelids, rounding of posterior margin (posterior borders of tarso conjunctival layers are normally sharp), redness and thickness of lid margin and lash contamination was based on previously published standardized grading scales [39].

Eyelid sensitivity was assessed using a Cochet-Bonnet aesthesiometer (Luneau Ophthalmologie, Chartres, France). The length of this filament can be varied so that touch pressure applied to the ocular surface is altered. The length where the subject could first perceive the touch of the filament was recorded and then converted to pressure (g/mm^2) [40]. An ascending method of limits was employed to determine the threshold to stimulation. Thresholds were then converted to sensitivity for analysis by taking the inverse of threshold values [40].

Laser scanning confocal microscopy was performed with the Heidelberg Retinal Tomographer II (HRT II) using a Rostock Corneal Module attachment (Heidelberg Engineering GmbH, Heidelberg, Germany) to observe and record *Demodex* colonization of the eyelids. Digital images of the underlying follicles of three central, three nasal and three temporal eyelashes were captured along with the corresponding meibomian glands (Fig. 1). The sum of the *Demodex* counts was recorded for each participant [23].

Meibomian gland morphology was assessed using the Oculus Keratograph 5 M Meibo-Scan (Oculus Optikgerate GmBH, Wetzlar, Germany), a slit lamp unit equipped with an infrared charge-coupled device video camera and an infrared transmitting filter. Meibomian gland signs were then graded based on the previously published meiboscore grading scales [39,41]. Images of meibomian gland acini were captured using confocal microscopy with the Heidelberg Retinal Tomographer II (HRT II) using the Rostock Corneal Module attachment and used to grade the reflectivity in the gland acini for secretion quality [25]. The palpebral conjunctiva of the upper and lower eyelids (after inversion) were assessed using slit lamp bio-microscopy, to record roughness, redness (hyperemia) and staining based on the CCLRU grading scales [35].

2.2. Tear film

Tear volume was measured using a phenol red thread (Zone Quick, Showa Yakuhin Kako Co., Ltd, Japan) of 75 mm length. The wet length of the thread 15 s after insertion into the lower tear meniscus was recorded. Tear meniscus height was measured from images captured using the Oculus Keratograph 5 M (Oculus Optikgerate GmBH, Wetzlar, Germany) as the distance between the darker edge of the lower eyelid and the top of the reflex from the tear strip [42].

The thickness of tear lipid layer was assessed using a Lipi-View Interferometer (Tear Science®, Morrisville, NC) and recorded in nanometres. Invasive tear breakup time was measured once by recording the time taken (in seconds) for any dry spot to form over the tear film following the last blink after staining the ocular surface with 1% fluorescein.

The evaporation rate of the tears on the ocular surface was measured as described previously using a modifed Vapometer (Delfin Technologies, Kuopio, Finland) [43]. To minimize the bias of skin evaporation around the eyelids and skin below the lower eyelids, petroleum jelly (Vaseline® Unilever, Australia) was applied over the upper and lower eyelids, and skin around the eyelids. The Vapometer was then placed on the right eye of the participant and evaporation rate measured. Care was taken to restrict participants from blinking during the measurement. Measurements were also taken with eyes closed to account for any contribution of evaporation from the skin. Three consecutive measurements were taken with the eyes open and eyes closed, and the average of these values was calculated. Measurements were

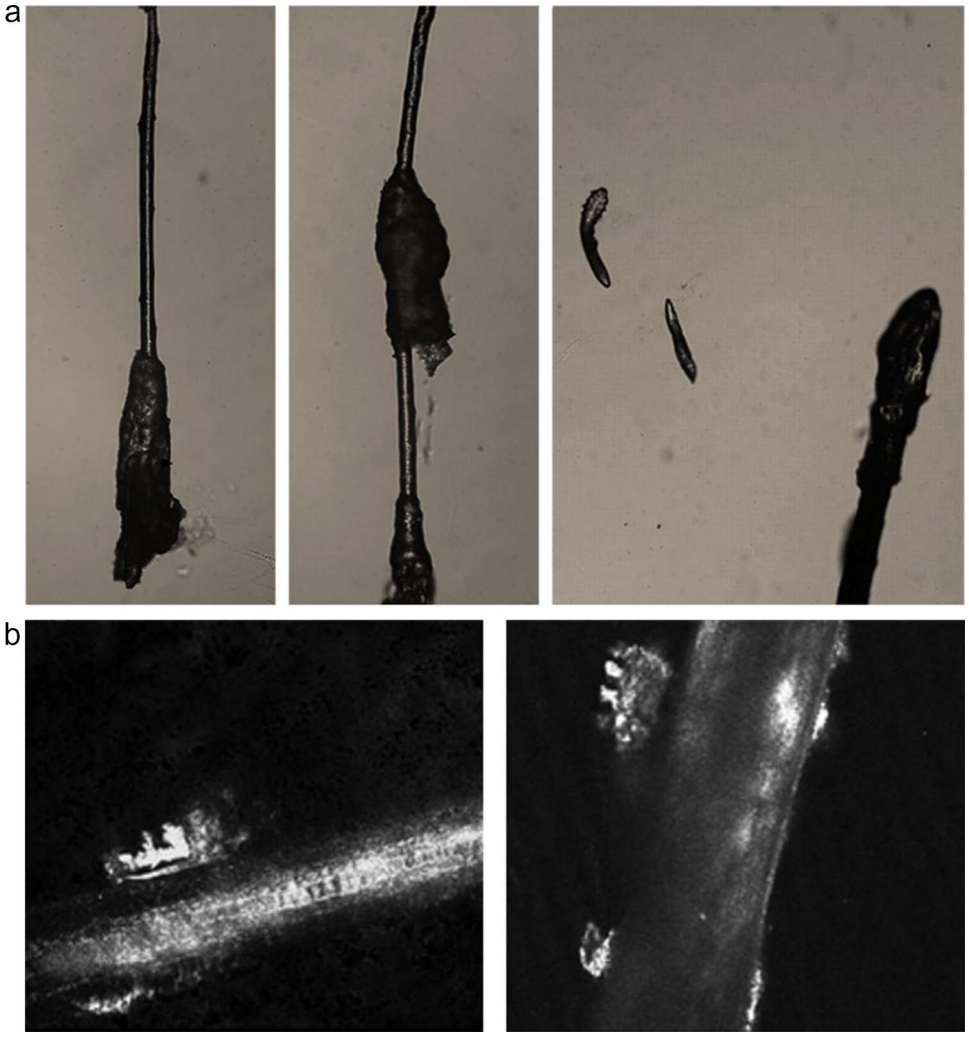

Fig. 1. Colonization of Demodex mites on eyelid margin. (a) View of *Demodex* mites from the epilated lash using light microscope. (b) View of Demodex mites on eyelash follicles using in vivo confocal microscope.

also obtained with the participant's habitual contact lenses in situ after a minimum 30 mins of lens wear. Absolute tear evaporation was calculated based on the closed and open eye tear evaporation rates after accounting for the area and volume of the goggle and the area of the ocular surface [43]. These calculations were repeated for measurements with and without contact lenses. Tear osmolarity was measured using a TearLab™ Osmolarity System (TearLab™ Corp., San Diego, CA), which was calibrated daily prior to use.

2.3. Statistical analysis

Sample size calculations based on the variables non-invasive tear breakup time (mean ± standard deviation in tolerant wearers = 20.2 ± 5.6 s; mean ± standard deviation in intolerant wearers = 13.2 ± 3.2 s) and tear meniscus height (0.43 ± 0.11; 0.31, 0.09) [32] showed that a sample of at least 9 in each group (symptomatic versus asymptomatic lens wearers) was required, whereas calculations based on tear evaporation to determine a significant difference of 36 g/m2/h between repeated measurements [44] at 5% level of significance and 80% of power indicated that a sample of 15 in each group was required. To ensure sufficient sample size for other variables, 30 contact lens wearers were enrolled in this study.

Data analysis was performed using SPSS 22.0 (SPSS Inc., Chicago, IL). Clinical markers were broadly classified as parametric or non-parametric after testing for normality using the Kolmogorov Smirnov test. All variables were not normally distributed except for tear osmolarity, eyelid and palpebral conjunctival sensitivities and comfort scores. The distribution of study variables among the categories of contact lens discomfort were analysed using Kruskal Wallis and Mann-Whitney *U* test for continuous variables and Fisher's exact test for categorical variables. Association of eyelid and tear characteristics with contact lens discomfort were measured using Spearman ρ correlation and linear regression analysis, results were then categorized as moderate (0.4–0.6), good (0.61–0.8) or excellent (0.8–1.0) [45].

3. Results

Participant demographics are shown in Tables 1 and 2. The prevalence of contact lens discomfort in this study sample was 57%. Based on the CLDEQ-8 questionnaire responses, participants were initially categorized into symptomatic (CLDEQ-8 score of ≥13) or asymptomatic (CLDEQ-8 score of < 13) contact lens wearers [46,47]. Later, when Chalmers et al. [46] reported that soft lens wearers with CLDEQ-8 scores of ≥12 points could benefit from management of contact lens related symptoms, re-analysis was performed. However, this change in the cut-off score did not change the proportions of the symptomatic and asymptomatic lens wearers in the participant pool. Therefore no significant changes in the analysis between the two cut offs were observed. The median age of the contact lenses worn by symptomatics to the study visit were older than asymptomatics (10 vs. 5 days, $p = 0.039$), but the inter-quartile ranges indicated a similar distribution among the groups. No other significant demographic differences ($p > 0.05$) were observed between symptomatic and asymptomatic lens wearers (Table 2).

Table 1
Median ± Interquartile Range of Subject Demographics (Mann Whitney *U* Test).

Demographics (Median ± InterquartileRange)	Asymptomatic Lens Wearers	Symptomatics Lens Wearers	p Values
Age (in Years)	23 ± 16	23 ± 13	0.095
No. of Months of Contact Lens Wear	36 ± 24	36 ± 24	0.098
Average Wear Time (Hour/day)	12 ± 4	10 ± 2	0.067
Age of Present Lens (Days)	5 ± 11	10 ± 12	0.039
Lens Parameters: Spherical Power	−2.00 ± 1.38	−3.00 ± 2.13	0.058
Lens Parameters: Cylindrical Power	0.00 ± 0.25	0.00 ± 0.00	0.064
Age of Contact Lens Case (Days)	45 ± 75	60 ± 60	0.055

3.1. Symptomatic vs. asymptomatic lens wearers

The grade of lid-wiper epitheliopathy (upper eyelid only; median ± IQR: symptomatic lens wearers: 2 ± 2 versus asymptomatic lens wearers: 1 ± 1) (Fig. 2), lid parallel conjunctival folds (2 ± 2 vs. 1 ± 0) (Fig. 3), meibomian gland morphology and secretion related factors (Fig. 4) such as gland pouting (2 ± 1 vs. 0 ± 1), capping (2 ± 1 vs. 0 ± 1), foam at the gland orifice (2 ± 1 vs. 0 ± 1), meibomian secretion's volume (2 ± 1 vs. 0 ± 1), quality (2 ± 1 vs. 0 ± 1), expressibility (2 ± 1 vs. 0 ± 1) and meibomian acini reflectivity (3 ± 1 vs. 1 ± 0) were significantly greater in symptomatic lens wearers ($p < 0.05$; Table 4). There were no significant differences in marginal, bulbar or palpebral conjunctival sensitivities between symptomatic and asymptomatic lens wearers (Table 3).

Demodex infestation (number of mites) of the upper eyelid only (2 ± 1 mite vs. 0 ± 0) and tear evaporation rates both with (112 ± 54 g/m^2/h vs. 96 ± 28 g/m^2/h) and without contact lenses (88 ± 45 vs. 76 ± 48) were found to be significantly higher in symptomatic compared to asymptomatic lens wearers ($p < 0.05$; Table 3). Tear volume (10 ± 0 mm vs. 12 ± 3 mm), tear meniscus height (0.11 ± 0 mm vs. 0.16 ± 0 mm), tear film breakup time (8 ± 2 s vs. 10 ± 0 s) were found to be significantly lower in symptomatic compared to asymptomatic lens wearers ($p < 0.05$; Table 3). There were no differences for tear osmolarity, tear lipid layer thickness or *Demodex* infestation between symptomatic and asymptomatic lens wearers.

3.2. Pooled correlations vs. group correlations

When examining for correlations of the collected variables with comfort scores, pooled data of symptomatic and asymptomatic participants showed significant correlations between central, temporal upper lid margin sensitivity and central lower lid margin sensitivity. Sensitivity of zone 4 of only the palpebral conjunctiva significantly correlated with CLDEQ-8 symptoms scores ($r^2 = 0.425$; $p = 0.042$) (Table 5). Lid-wiper epitheliopathy ($r^2 = 0.293$; $p = 0.051$), meibomian gland acini reflectivity ($r^2 = 0.659$; $p = 0.038$) and palpebral roughness ($r^2 = 0.608$; $p = 0.026$) significantly correlated with comfort scores from the CLDEQ-8 questionnaire (Table 5).

When data for the symptomatic and asymptomatic groups were analysed individually, the upper (central: $r^2 = 0.575$, $p = 0.024$; temporal: $r^2 = 0.499$, $p = 0.041$) and lower (central: $r^2 = 0.567$, $p = 0.018$; temporal: $r^2 = 0.530$, $p = 0.029$) eyelid margin sensitivities of symptomatic lens wearers were significantly correlated with CLDEQ-8 comfort scores (i.e. with increase in the sensitivity, comfort scores increased, that is discomfort increased). In addition, the sensitivity of the nasal region of the lower eyelid ($r^2 = 0.568$, $p = 0.018$) and zones 3 ($r^2 = 0.498$, $p = 0.042$), 4 ($r^2 = 0.519$, $p = 0.033$) and 5 ($r^2 = 0.506$, $p = 0.038$) of the upper palpebral conjunctiva also showed moderate correlations with comfort scores for the symptomatic wearers (Table 5). Significant positive correlations were also observed between upper lid-wiper epitheliopathy ($r^2 = 0.406$, $p = 0.038$), lid parallel conjunctival folds ($r^2 = 0.504$, $p = 0.039$), foam at meibomian orifice ($r^2 = 0.592$, $p = 0.046$), meibomian secretion's quality ($r^2 = 0.561$, $p = 0049$), expressibility ($r^2 = 0.574$, $p = 0.049$), gland acini reflectivity ($r^2 = 0.679$, $p = 0.038$), palpebral roughness ($r^2 = 0.621$, $p = 0.02$) and comfort scores in symptomatic lens wearers only (Table 5). Asymptomatic lens wearers also showed significant correlations between upper lid-wiper epitheliopathy ($r^2 = 0.051$, $p = 0.327$), tear meniscus height ($r^2 = -0.745$, $p = 0.003$) acini reflectivity ($r^2 = 0.628$, $p = 0.039$) and roughness ($r^2 = 0.557$, $p = 0.03$) with change in symptom scores (Table 5). The CLDEQ-8 comfort scores were positively correlated with the tear evaporation rate with ($r^2 = 0.42$) and without contact lenses ($r^2 = 0.52$; Fig. 5a) and negatively correlated to the lipid layer thickness ($r^2 = 0.57$; Fig. 5b). There was a negative correlation between the tear evaporation rates with ($r^2 = 0.34$) and without contact lens ($r^2 = 0.60$) and lipid layer

Table 2
Distribution of Contact Lens Demographics.

Demographics		Symptomatic Lens Wearers	Asymptomatic Lens Wearers
Gender	Male	40%	20%
	Female	60%	80%
Frequent Replacement Plan	Monthly Disposables	30%	20%
	Bi Weekly Disposables	50%	40%
	Daily Disposables	20%	40%
Lens Material	**Hydrogel**		
	Etafilcon A (WC = 58% ; Dk = 28; Ionic)	10%	8%
	Silicon Hydrogel		
	Comfilcon A (WC = 48% ; Dk = 128; Non-Ionic)	30%	40%
	Balafilcon A (WC = 36% ; Dk = 112; Ionic)	40%	42%
	Lotrafilcon A (WC = 24% ; Dk = 140; Non-Ionic)	10%	5%
	Lotrafilcon B (WC = 33% ; Dk = 110; Non-Ionic)	10%	5%
Contact Lens Care System	**Biocide of Multipurpose Solutions**		
	Polyquaternium-1 and edetate disodium	42%	40%
	Poly-hexamethylene biguanide /Polyquaternium-1	18%	20%
	Poly-hexamethylene biguanide	30%	30%
	Hydrogen Peroxide Disinfection System	10%	10%

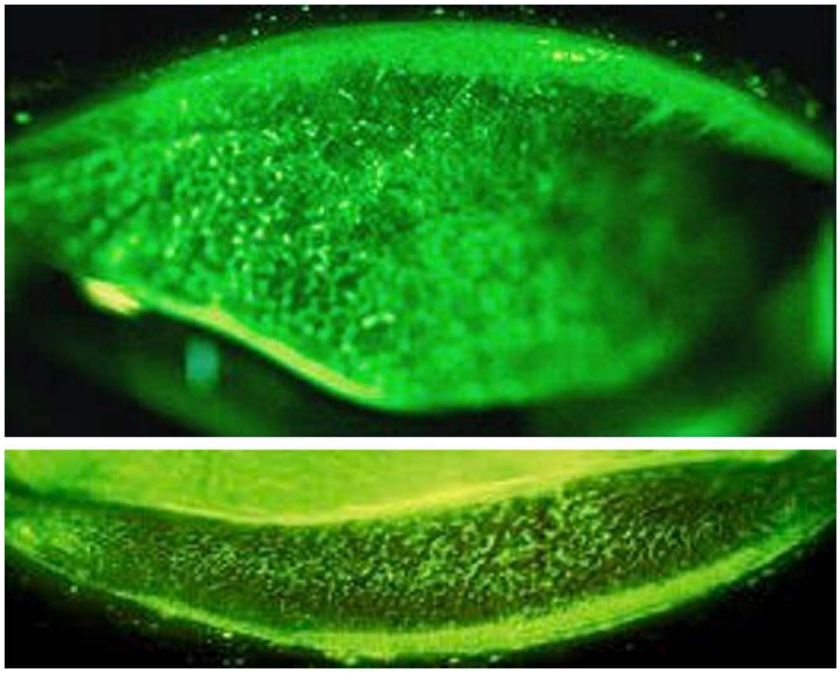

Fig. 2. Lid wiper epitheliopathy.

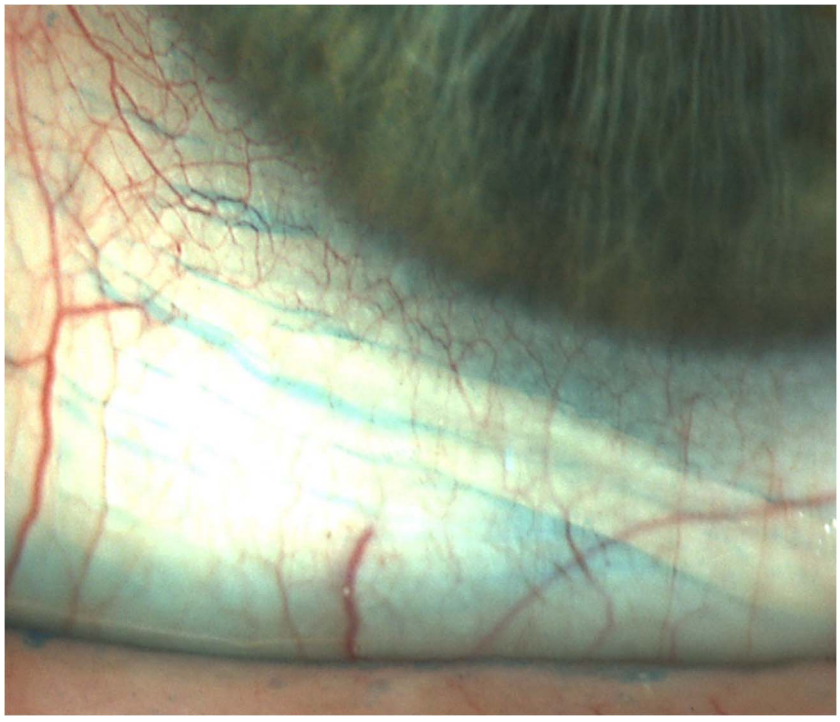

Fig. 3. Lid parallel conjunctival folds.

thickness in pooled data (Fig. 5c).

Higher tear evaporation rates, with (r^2 = 0.447, p = 0.049) and without (r^2 = 0.617, p = 0.033) contact lens were found to significantly associate with comfort scores in only symptomatic lens wearers (Table 5). Symptomatic lens wearers in this study also showed significantly reduced tear meniscus height (0.11 ± 0), and faster tear breakup time (8 ± 2), reduced tear volume (10 ± 0), reduced lipid layer thickness (45 ± 17) and more rapid tear evaporation both with (112 ± 54) and without (88 ± 45) contact lenses compared to asymptomatic lens wearers (Table 3).

4. Discussion

This study evaluated characteristics of the eyelid margin, meibomian glands and tears in contact lens wearers, to understand the relationship between these ocular characteristics and comfort during lens wear. The relationship between meibomian gland morphology and the expressibility of secretions with ocular symptoms in lens wear indicate the substantial role of meibomian gland function in contact lens discomfort. This was also confirmed by the assocciation oberved between higher grades of meibomian acini secretion reflectivity with comfort scores (Table 5). Significant correlations were also found between meibomian gland secretions quality, expressibility and foam at orifices

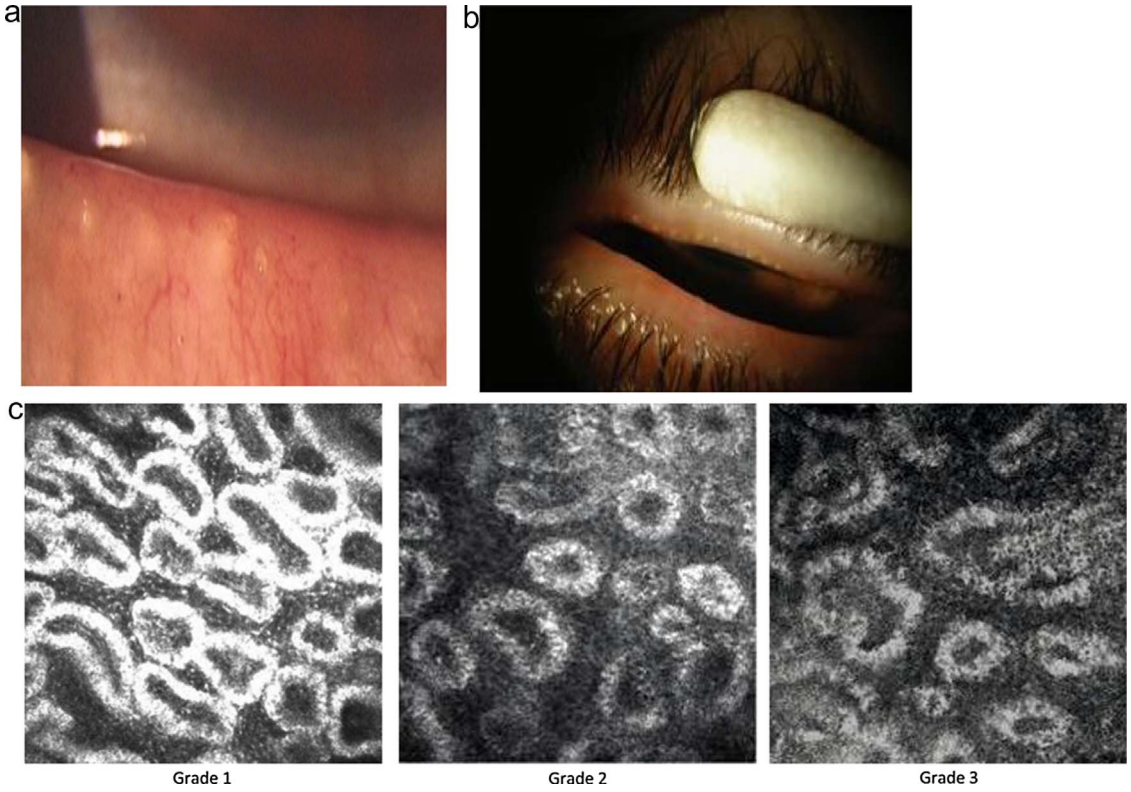

Fig. 4. Meibomian gland health assessment. (a) Capping of the meibomian orifices. (b) Expressibility of the meibomian orifices. (c) Meibomian gland acini reflectivity using in vivo confocal microscopy.

with comfort scores. Contact lens wear may compromise these glands causing increase in acini relectivity, main duct enlargement and lid marign redness and thickness. This was seen numerically in the current study but did not reach significance may be due to insufficient sample size of the study. Similar results have been reported in other studies [14,19,26]. However longitudinal studies are needed to conclude the causal relationship.

Lid parallel conjunctival folds were found to correlate with symptoms only in the symptomatic group while no association was observed in the pooled group or in asymptomatic wearers in this study. Although no significant difference was observed in the grades of lid parallel conjunctival folds between symptomatic and asymptomatic lens wearers, grades in symptomatic lens wearers in this study were greater than asymptomatics supporting earlier findings [9,38,49,50]. This may be due to lack of wide spread of data in asymptomatic lens wearers observed in this study. Other studies have hypothesised that lid parallel conjunctival folds may be associated with comfort [37,38,51,52]. As lid parallel conjunctival folds are located in the area of tear meniscus, they have also been reported to influence the distribution of tear fluid in the tear reservoir along the lower eyelid [53]. This effect could either be an immediate mechanical effect of contact lens wear similar to that of lid-wiper epitheliopathy, explaining the correlations between lid parallel conjunctival folds and lid-wiper epitheliopathy, or a long term effect causing tear film instabilities [9]. It has also been theorized that lid parallel conjunctival folds leads to stagnation of tears obstructing tear flow at the lower meniscus level exposing the lid margin to inflammatory contents of tears leading to higher grades of staining in the lower lid compared to the upper lid [54,55]. However, in the present study lower lid staining was not significantly different between symptomatics and asymptomatics.

Lid-wiper epitheliopathy in the upper eyelid was significantly different between symptomatic and asymptomatic subjects, while no differences were observed for the lower lid wiper. This is consistent with the suggestion that the upper eyelid experiences greater frictional interaction with the ocular and lens surface compared to the lower eyelid [6,9,37,56]. There was no correlation between lower lid-wiper staining and comfort, which is in agreement with a study by Navascues-Cornago et al. [7] However, in contrast to their study, there was a significant correlation between upper eye lid-wiper staining and discomfort in both symptomatic and asymptomatic groups in current study. Although not statistically significant, Navascues-Cornago et al. reported numerically greater lid margin staining in symptomatic contact lens wearers compared to asymptomatic wearers [7]. The variation in results could be due to difference in methodology, such as use of lissamine green strips alone.

The finding that the marginal conjunctiva had greater sensitivity compared to the bulbar or palpebral conjunctiva was consistent with other studies [57–59]. However, no significant differences were observed between the upper and lower eyelid in this study, which is contrary to some other studies that showed greater conjunctival sensitivity of the lower eyelid compared to upper eyelid [58,60]. Sensitivity of upper and lower eyelid margin showed significant correlation with comfort in symptomatic lens wearers only, which could be due to the lack of wide spread of the data of asymptomatic lens wearers in this study population.

A greater number of *Demodex* mites were found in the upper eyelid of symptomatic subjects, but no correlation was found with comfort. Sixty percent (n = 18/30) of the present study subjects were found to harbour *Demodex* in their eyelids, among which 90% (n = 16/18) were symptomatic lens wearers. Although greater number of *Demodex* mites was observed in the upper eyelids of symptomatics compared to asymptomatic lens wearers in this study, no association was found with comfort. This could probably be attributed to the relatively low level of infestation in current study sample population. Up to 90% of contact lens wearers have been found to harbour these mites [23] and approximately 93% of subjects with intolerance to contact lenses were positive for the presence of *Demodex*, while only 6% of patients with *Demodex* reported no symptoms of discomfort [21,61,62]. A proportion

Table 3
Median ± Interquartile Ranges of study variables (continuous) in symptomatic and asymptomatic lens wearers.

Clinical Markers		Test p values	Symptomatic Lens Wearers					Asymptomatic Lens Wearers				
Sensitivity (mm^2/gm)	Bulbar Conjunctival Sensitivities	Kruskal Wallis 0.075	Central 0.70 ± 0.14	Temporal 0.57 ± 0.16	Nasal 0.57 ± 0.11	Superior 0.70 ± 0.12	Inferior 0.86 ± 0.13	Central 0.70 ± 0.18	Temporal 0.57 ± 0.16	Nasal 0.57 ± 0.20	Superior 0.57 ± 0.13	Inferior 0.70 ± 0.15
	Palpebral Conjunctival Sensitivities	Kruskal Wallis 0.072	Zone 1 0.57 ± 0.07	Zone 2 0.70 ± 0.07	Zone 3 0.57 ± 0.17	Zone 4 0.57 ± 0.16	Zone 5 0.57 ± 0.14	Zone 1 0.57 ± 0.04	Zone 2 0.57 ± 0.07	Zone 3 0.57 ± 0.09	Zone 4 0.57 ± 0.08	Zone 5 0.57 ± 0.08
	Marginal Conjunctival Sensitivities (Upper Eyelid)	Kruskal Wallis 0.062	Central 2.23 ± 0.11	Temporal 1.74 ± 0.12	Nasal 1.74 ± 0.19			Central 1.74 ± 0.18	Temporal 1.74 ± 0.14	Nasal 1.74 ± 0.12		
	Marginal Conjunctival Sensitivities (Lower Eyelid)	Kruskal Wallis 0.058	Central 2.23 ± 0.17	Temporal 1.74 ± 0.19	Nasal 1.74 ± 0.16			Central 1.74 ± 0.05	Temporal 1.74 ± 0.05	Nasal 1.74 ± 0.09		
Demodex Infestation (Count)	Upper Eyelid	Mann Whitney 0.042*	2 ± 1					0 ± 0				
	Lower Eyelid	Mann Whitney 0.086	0 ± 1					0 ± 0				
Tear Volume (mm)		Mann Whitney 0.057	10 ± 0					12 ± 3				
Tear Meniscus Height (mm)		Mann Whitney 0.032*	0.11 ± 0					0.16 ± 0				
Tear Break Up Time (Seconds)		Mann Whitney 0.049*	8 ± 2					10 ± 0				
Tear Osmolarity (mOmol/L)		Mann Whitney 0.075	296 ± 21					321 ± 12				
Tear lipid layer thickness (Interference Colour Units)		Mann Whitney 0.052	45 ± 17					67 ± 28				
Tear Evaporation (with lenses) $g\,m^{-2}\,h$		Mann Whitney 0.038*	112 ± 54					96 ± 28				
Tear Evaporation (without lenses) $g\,m^{-2}\,h$		Mann Whitney 0.033*	88 ± 45					76 ± 48				

* − statistically significant, $p < 0.05$.

Table 4
Median ± Interquartile Ranges of study variables (Categorical Variables) in Symptomatic and Asymptomatic Lens Wearers (statistically significant variables with p values < 0.05; Fisher's Exact Test).

Clinical Markers	Symptomatic Lens Wearers	Asymptomatic Lens Wearers
Lash Contamination	1 ± 4	1 ± 0
Lid Margin Redness and Thickness	1 ± 1	1 ± 1
Rounding of Posterior Margin	1 ± 1	0 ± 1
Irregularity/Notching of Eyelids	0 ± 0	0 ± 2
Eyelid Vascularity	0 ± 1	0 ± 0
Lash Loss	0 ± 0	0 ± 0
Telangiectasia	0 ± 0	0 ± 0
Hyperkeratinisation	0 ± 1	0 ± 0
Anterior Blepharitis	0 ± 1	0 ± 0
Marx Line Ridging	0 ± 2	0 ± 0
Antero-Retroplacement of Orifices	0 ± 2	0 ± 0
Lid Wiper Epitheliopathy	Upper Eyelid: 2 ± 4; Lower Eyelid: 1 ± 1	Upper Eyelid: 1 ± 1; Lower Eyelid: 1 ± 0
Lid Parallel Conjunctival Folds	2 ± 4	1 ± 0
Meibomian Gland Orifices Capping	2 ± 3	0 ± 1
Pouting	2 ± 1	0 ± 1
Narrowing and Opaque Scarred	1 ± 1	0 ± 0
Orifices Vascular Invasion	1 ± 1	0 ± 0
Main Duct Enlargement	1 ± 1	0 ± 0
Acini Concretions	0 ± 0	0 ± 0
IVCM Acini Secretion Reflectivity	3 ± 1	1 ± 1
Foam	3 ± 1	0 ± 1
Expressed Secretions Volume	2 ± 1	0 ± 1
Expressed Secretions Quality	2 ± 1	0 ± 1
Expressed Secretions Expressibility	2 ± 1	0 ± 1
MG Blockage	1 ± 1	0 ± 0
MG Dropout	1 ± 1	0 ± 0
MG Redness	1 ± 1	0 ± 0
Palpebral Conjunctiva Roughness	3 ± 1	0 ± 0
Palpebral Conjunctiva Staining	2 ± 1	0 ± 0
Palpebral Conjunctiva Hyperemia	3 ± 1	1 ± 1

Table 5
Associations between eyelid and tear film with contact lens discomfort scores assessed using CLDEQ-8 (Linear regression analysis).

Categories	Study Variables	Pooled Data		Asymptomatics Group (n = 17)		Symptomatics Group (n = 13)	
		r^2 value	p Value	r^2 value	p value	r^2 value	p value
Sensitivity	Upper Eyelid Margin - Central	**0.493**	**0.048**	No Correlation	> 0.05	**0.575**	**0.024**
	Upper Eyelid Margin - Temporal	**0.524**	**0.042**	No Correlation	> 0.05	**0.499**	**0.041**
	Lower Eyelid Margin - Central	**0.514**	**0.042**	No Correlation	> 0.05	**0.567**	**0.018**
	Lower Eyelid Margin - Temporal	No Correlation	> 0.05	No Correlation	> 0.05	**0.53**	**0.029**
	Lower Eyelid Margin - Nasal	No Correlation	> 0.05	No Correlation	> 0.05	**0.568**	**0.018**
	Palpebral Conjunctiva - Zone 3	No Correlation	> 0.05	No Correlation	> 0.05	**0.498**	**0.042**
	Palpebral Conjunctiva - Zone 4	**0.425**	**0.042**	No Correlation	> 0.05	**0.519**	**0.033**
	Palpebral Conjunctiva - Zone 5	No Correlation	> 0.05	No Correlation	> 0.05	**0.506**	**0.038**
Tear Film	Meniscus Height	**−0.649**	**0.016**	**−0.745**	**0.003**	**−0.538**	**0.026**
	Break Up Time	No Correlation	> 0.05	No Correlation	> 0.05	**−0.656**	**0.004**
	Evaporation without CL	No Correlation	> 0.05	No Correlation	> 0.05	**0.617**	**0.033**
	Evaporation with CL	No Correlation	> 0.05	No Correlation	> 0.05	**0.447**	**0.049**
	Lipid Layer Thickness	No Correlation	> 0.05	No Correlation	> 0.05	**0.57**	**0.032**
Eyelid	Lid Wiper Epitheliopathy (Upper)	**0.293**	**0.051**	**0.327**	**0.046**	**0.406**	**0.038**
	LIPCOFs	No Correlation	> 0.05	No Correlation	> 0.05	**0.504**	**0.039**
Meibomian Gland	MG Foam	No Correlation	> 0.05	No Correlation	> 0.05	**0.592**	**0.046**
	MG Secretions Quality	No Correlation	> 0.05	No Correlation	> 0.05	**0.561**	**0.049**
	MG Expressibility	No Correlation	> 0.05	No Correlation	> 0.05	**0.574**	**0.049**
	IVCM Acini Reflectivity	**0.659**	**0.038**	**0.628**	**0.039**	**0.679**	**0.038**
Palpebral Conjunctiva	Roughness	**0.608**	**0.026**	**0.557**	**0.03**	**0.621**	**0.02**

Bold numbers indicate statistically significant values.

of asymptomatic lens wearers in present study had *Demodex* mites indicating that it might not be the sole reason for discomfort, but presence of these mites may exacerbate the symptoms of discomfort to an extent irrespective of subjects being symptomatic or not. A significant relationship between the number of *Demodex* and ocular discomfort measured with ocular surface disease index has been reported [63]. In contrast, another study reported no association between the number of *Demodex* and contact lens discomfort either in non-contact lens wearers or in contact lens wearing group [23]. This difference could be attributed to overall variation in infestation rates (4.0 ± 2.5) in blepharitis [63] and (7.6 ± 5.8) in contact lens wearers and (5.0 ± 3.1) in non-lens wearers [23] compared to present study infestation at the roots of eyelashes (2 ± 1) in symptomatic lens wearers.

The current study found no relationship between tear osmolarity and discomfort, consistent with a previous study [64]. There was a significant association between tear lipid layer thickness and evaporation of tears during lens wear. Previous research has suggested that contact lens wear may disrupt the tear lipid layer leading to increased

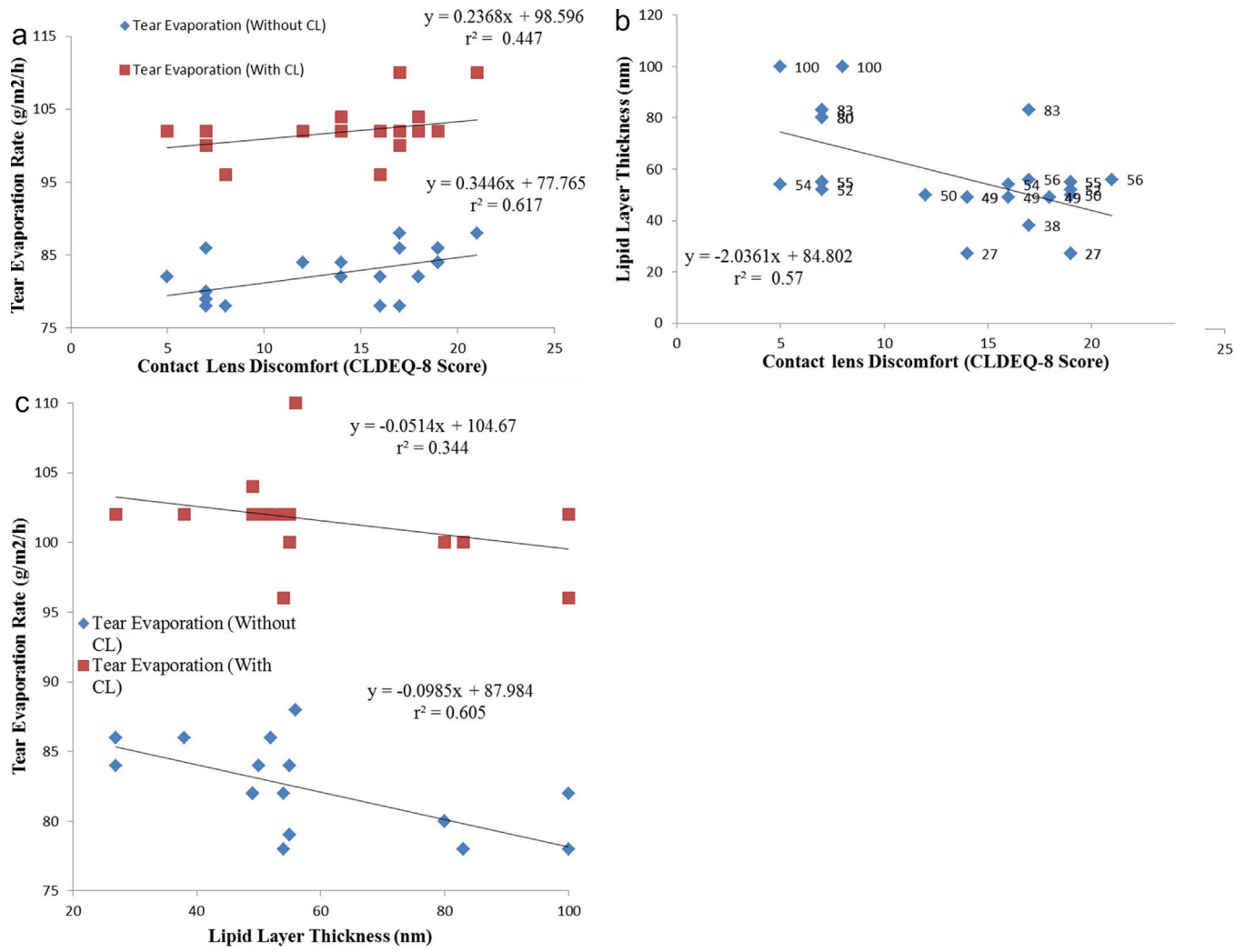

Fig. 5. Association between tear evaporative dynamics in contact lens discomfort. (a) Association between tear evaporation with and without contact lenses (g m^{-2} h) and contact lens discomfort. (b) Association between lipid layer thickness (nm) and contact lens discomfort. (c) Association between lipid layer thickness (nm) and tear evaporation with and without contact lenses (g m^{-2} h).

evaporation [65,66]. Increased tear evaporation may result in reduced tear meniscus volume and increased tear osmolarity value, which destabilized the tear films causing dry eye or foreign body sensation, or both, in the Etafilcon A lens wear group [65]. Indeed, tear film hyperosmolarity during contact lens wear has been shown to be a function of evaporation, contact lens osmolality, or both [67], and elevated contact lens osmolality could contribute to tear film osmolality by producing an osmotic gradient and could be a cause of ocular discomfort [65]. However, The effects of contact lens wear in subjects with dry eye is different, with much larger increases in tear osmolarity [66], because ocular surfaces with dry eye disease may be unable to maintain tear homeostasis in response to environmental or contact lens stress. These differences between ocular surfaces of dry eyes compared to that of contact lens wearers experiencing discomfort without dry eye could be a reason for lack of association between tear osmolarity and comfort scores in this study. This may also indicate differences in tear homeostasis in contact lens discomfort in comparison to dry eye.

In summary, symptomatic contact lens wearers in this study exhibit characteristic eyelid margin irregularities, disruption in meibomian gland morphology and tear film instabilities. Longitudinal studies are required to establish a causal relationship between meibomian gland changes and its influence on comfort in neophytes. In conclusion, morphological irregularities of the meibomian glands, and alterations to tear film secretions that affect tear evaporative dynamics were associated with symptoms of discomfort amongst the symptomatic lens wearers and may play a crucial role in pathogenesis of contact lens discomfort.

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