• Clinical Research •

# Meibomian gland atrophy in children with allergic conjunctivitis

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Received: 2024-08-19 Accepted: 2024-10-23

## Abstract

● **AIM:** To investigate the factors influencing meibomian gland atrophy (MGA) in children with allergic conjunctivitis (AC).

● **METHODS:** In this cross-sectional study, 60 children with AC aged 6-17y and 20 age-matched children without signs or symptoms of ocular surface dysfunction were included. Information on the duration of AC, untreated time, electronic screen time (EST), outdoor exercise time, body mass index (BMI), and frequency of eye rubbing was collected using a health history form. The Standard Patient Evaluation of Eye Dryness (SPEED) score was used for dry eye assessment. Images of the meibomian glands (MGs) were obtained using Keratograph 5M, and the rate of meibomian gland atrophy (MGAR) was calculated using Image J. All subjects underwent routine eye examinations.

● **RESULTS:** The average age of the AC group was 10.43±2.75y (range 6-17y) and 10.35±3.42y (range 6-14y) in the control group. The MGAR in the AC group was 33.42%±11.91%, significantly higher than that in the control group (18.10%±11.74%, $P$<0.001). Moreover, the MGAR in younger children (aged 12 and below) was significantly higher than in older children ($P$<0.05). Multi-factor linear regression analysis revealed that EST non-projector was a risk factor for MGAR ($\beta$=0.332, 95%CI 0.04-0.22, $P$=0.004), while outdoor exercise time was a protective factor against MGAR ($\beta$=-0.407, 95%CI -0.39 to -0.10, $P$=0.001). The untreated time of AC was identified as a risk factor for MGAR ($\beta$=0.24, 95%CI 0.07-1.98, $P$=0.037), and the frequency of eye rubbing was associated with MG distortion score ($P$=0.00).

● **CONCLUSION:** Children with AC exhibit exacerbate MGA, with the degree of atrophy worsening as the untreated time of AC prolongs. Children under 12 years old show a higher MGAR, and EST non-projector negatively impacts MGA, while increased outdoor exercise time acts as a protective factor against MGA.

● **KEYWORDS:** allergic conjunctivitis; meibomian gland atrophy; children

**DOI:10.18240/ijo.2025.05.07**

**Citation:** He WF, Wu YP, Zheng JW, Huang BG, Zuo JJ, Li JY, Jiang D, Ma HX. Meibomian gland atrophy in children with allergic conjunctivitis. *Int J Ophthalmol* 2025;18(5):832-839

## INTRODUCTION

Allergic conjunctivitis (AC) is one of the most common allergic diseases, affecting more than one billion people worldwide, especially in children and adolescents[1-4]. The incidence rate can be as high as 30%, with symptoms recurring in the long term, severely impacting the quality of life in children and imposing a heavy economic burden on their families and society[2,5-6].

Previous studies have shown a higher prevalence of dry eye in patients with AC[7]. It has been suggested that AC was independently associated with dry eye disease (DED) in children[8]. The morphological change of meibomian gland is an important feature of evaporative dry eye and an important cause of dry eye[9-10]. Arita *et al*[11] observed morphological changes in the meibomian glands of patients with perennial allergic conjunctivitis (PAC) was higher than controls (45% *vs* 8.5%, $P$<0.0001) in adults. They also found that the rate of meibomian gland duct distortion was significantly greater in patients with PAC (45%) compared to controls (8.5%, $P$<0.0001). However, there have been few studies that have examined the morphology of meibomian glands in children with AC. Therefore, we designed research which recruited

sixty children with AC and twenty asymptomatic participants aged 6 to 17y from March 2023 to August 2023 to observe the morphological changes of meibomian gland in AC children and explore its related factors.

Since most studies have shown that meibomian gland atrophy (MGA) is primarily related to aging, the majority of research on factors associated with MGA has focused on adults. Currently, factors believed to contribute to MGA include age[12-14], contact lens wear[15-16], ocular graft-versus-host disease[17], radiotherapy[18], isotretinoin[19], type 2 diabetes mellitus[20], hormonal birth control[21], rosacea[22], and meibomian gland dysfunction (MGD)[23]. Factors that promote meibomian gland distortion and atrophy include cataract surgery[24] and AC[25].

Despite studies have shown that the structure of meibomian glands is intact at birth[12]. In reality, the meibomian glands in children are not entirely healthy. Zhao *et al*[26] observed 266 asymptomatic children, and they found that meibomian gland deficiency, between 20%-30%, was found in 45.5% of children. There was 5% of children had meibomian gland deficiency over 40%. Only 16 children had no meibomian gland deficiency among the 266 subjects. However, they did not analyze the reasons for the absence of meibomian glands in children. Most factors influencing MGA in adults do not apply to children, with the exceptions of AC and contact lens wear. Previous studies have noted morphological changes in the meibomian glands of patients with contact lens-related allergic conjunctivitis (CLAC), suggesting that allergic reactions, rather than contact lens wear, may contribute to meibomian gland distortion[27]. Nevertheless, there is limited literature available on the morphology of meibomian glands in children with AC. Therefore, the objective of this study was to observe the morphological characteristics of meibomian glands in children with AC and investigate the factors associated with MGA in these patients. A comprehensive understanding of the rate of MGA in children with AC could be valuable in predicting and preventing the development of MGD and DED in this population.

## PARTICIPANTS AND METHODS

**Ethical Approval** Approval for this study was obtained from the Research Ethics Committee of the Eye Hospital of Wenzhou Medical University. Eye Hospital of Wenzhou Medical University (2023-070-K-58-01). All procedures followed the principles of the Declaration of Helsinki. Written and verbal informed consent was obtained from all participants and their guardians before their inclusion in the study.

**Participants** The recruitment process was conducted at the Affiliated Eye Hospital of Wenzhou Medical University from March 2023 to August 2023. A total of eighty children, aged between 6 and 17y, participated in this cross-sectional study. Sixty individuals diagnosed with AC were recruited from the corneal clinic, while the remaining twenty asymptomatic participants were chosen from the optometry clinic to form the control group.

The inclusion criteria included the ability to undergo relevant ophthalmic examinations, absence of ocular trauma, surgery, eye infections, contact lens use, systemic diseases (such as rosacea, chemoradiotherapy, or immune system diseases), long-term use of systemic medication, and no recent ocular medication within the past 3mo (except for artificial tears).

The diagnoses were made by a single doctor with clinical expertise, following the diagnostic criteria outlined in the AAO 2019 AC guidelines[28]. In our study, children with AC either had initial onset or recurrence, and had not received any treatment in the previous three months.

**Clinical Measures** Participants and their parents completed The Standard Patient Evaluation of Eye Dryness (SPEED) questionnaire[29] and a health history form. The health history form included information on untreated time (time from onset of symptoms to first medical attention), duration of AC, seasonal nature of onset, frequency of eye rubbing (rarely, sometimes, frequently), outdoor exercise time, and electronic screen time (EST). Since all subjects reported using projectors for instruction in schools, we categorized electronic screen use time into EST-projector and EST-nonprojector (smartphones, computers, tablets, telephone watches, televisions).

The ophthalmic examination followed the principle of non-invasive to invasive. Initially, an ophthalmic examination with slit-lamp biomicroscopy was conducted to rule out other ocular diseases, and the severity of AC involvement was assessed using a 5-5-5 score[30]. The LipiView interferometer (Tear Science Inc., Morrisville, NC, USA) was utilized to measure the lipid layer thickness (LLT). Tear meniscus height (TMH), noninvasive tear break-up time (NIBUT), and meibography of both upper and lower eyelids were performed using the Keratograph 5M (K5M, Wetzlar, Germany). A blinded rater employed the Image J software to calculate the MGA, defined as the proportion of lost gland area relative to the total tarsus area[31]. Given the differences in MGA between upper and lower eyelids, the correlation analysis of MGA utilized the mean atrophy area value of both glands. Meibomian gland loss (MGL) was graded as follows: Grade 0: no MGL; Grade 1: <33% MGL; Grade 2: 33%-66% MGL; Grade 3: >66% MGL; and severe MGL≥33% MGL[32]. The presence of distortion was assessed based on the angle and area of the meibomian gland, with corresponding grading criteria[26]. The total number of visible meibomian glands on each eyelid was quantified. Additionally, fluorescein break-up time (FBUT) examinations were conducted following sodium fluorescein staining (Figure 1).

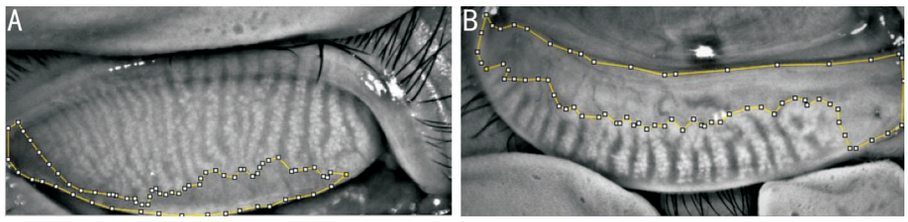


**Figure 1 The rate of meibomian gland atrophy (MGAR) analyzed using Image J** The "polygonselections" function of Image J was used to outline the edges of the atrophy area on the upper eyelid (A) and lower eyelid (B). The total area of the tarsus was measured by the same method. The MGAR was defined as the ratio of the area of MGA to the total area of the tarsus.

**Statistical Analysis** The experiments were carried out utilizing the SPSS statistics software (version 26.0; SPSS Inc., USA). The normality of the data was assessed through the examination of skewness and kurtosis. Continuous variables are reported as mean±standard deviation, while categorical variables are presented as numbers (percentages). Chi-square tests were used to compare differences in sex and eye rubbing between the AC and control groups. Multivariate regression analysis was employed to investigate the potential correlation between meibomian gland atrophy rate (MGAR) and various factors, including age, the disease duration, EST non-projector, outdoor exercise time, and eye rubbing. Age, untreated time, EST-non-projector and outdoor exercise time were included in the multivariate linear regression analysis. Statistical significance was set at $P<0.05$.

## RESULTS

A total of 80 eyes (right eyes) from 80 children were included in the study. The AC group comprised 60 children with an average age of 10.43±2.75y (range 6-17y), including 45 males and 15 females. The control group included 20 individuals with an average age of 10.35±3.42y (age 6 to 14y), comprising 11 males and 9 females. There was no age difference between the two groups. Compared to the control group, the AC group exhibited significantly higher MGAR, average Meiboscore, distortion score, SPEED scores, lower FTBUT, and LLT (Table 1).

In the AC group, no individuals were classified as grade 0, while 31 individuals (51.67%) exhibited severe MGA. In the control group, 3 individuals (15%) were classified as grade 0, and 2 individuals (10%) showed severe MGA. The AC group had 29 individuals (48.33%) classified as grade 1, with 13 individuals (44.83%) having a MGAR of ≤ 25%. In contrast, the control group had 15 individuals (75%) classified as grade 1, with 11 individuals (73.33%) having a MGAR of ≤25%.

**Association of Age, Sex, and Body Mass Index on MGAR** The AC group was categorized into different subgroups based on age, sex, and body mass index (BMI) to investigate the association of these potential risk factors. Younger patients (≤12y) had a higher MGAR (35.22%±12.29%, $P=0.026$) compared to older patients (>12y). Multivariate linear regression analysis revealed that age was a significant risk factor for MGAR in children with AC ($\beta$=-0.36, 95%CI: -2.550 to -0.570, $P=0.002$). There was no correlation between sex ($r$=-0.120, $P=0.289$) and BMI ($r=0.155$, $P=0.17$) with MGAR. Univariate analysis showed that after categorization by sex and BMI, sex ($\beta$= -0.125, 95%CI: -10.530 to 3.690, $P=0.339$) and BMI ($\beta=0.189$, 95%CI: -1.750 to 11.350, $P=0.148$) were not identified as potential influential factors for MGA in children with AC.

**Table 1 Descriptive statistics of clinical and demographic variables in case and control groups**

| Parameters | Groups | | *P* |
|---|---|---|---|
| | AC (*n*=60) | Control (*n*=20) | |
| Age (y) | 10.43±2.75 | 10.35±3.42 | 0.913 |
| BMI | 17.54±2.76 | 17.08±3.13 | 0.537 |
| TMH (mm) | 0.18±0.08 | 0.21±0.08 | 0.091 |
| NIBUT (s) | 10.54±6.59 | 13.02±5.71 | 0.144 |
| FBUT (s) | 7.51±3.32 | 11.45±4.52 | <0.001[b] |
| Upper eyelid MGAR (%) | 23.55±16.11 | 9.78±10.11 | 0.001[b] |
| Upper eyelid MGL | 1.18±0.62 | 0.60±0.50 | <0.001[b] |
| Lower eyelid MGAR (%) | 43.29±14.30 | 26.43±19.09 | 0.001[b] |
| Lower eyelid MGL | 1.80±0.55 | 1.20±0.83 | 0.006[b] |
| MGAR-ave (%) | 33.42±11.91 | 18.10±11.74 | <0.001[b] |
| MGL-ave | 1.49±0.43 | 0.90±0.55 | <0.001[b] |
| SPEED | 3.10±2.10 | 0.11±0.47 | <0.001[b] |
| LLT, μm | 54.45±21.92 | 68.77±20.30 | 0.038[a] |
| Number-ave | 21.46±3.32 | 23.00±2.89 | 0.068 |
| Distortion-ave | 2.12±1.19 | 1.02±0.68 | <0.001[b] |
| EST-projector (min/d) | 46.50±30.47 | 37.75±24.84 | 0.249 |
| EST-nonprojector (h/d) | 5.25±1.21 | 5.25±1.19 | 1.000 |
| Outdoor exercise time (min/d) | 37.92±19.64 | 32.75±20.49 | 0.317 |

[a]$P<0.05$; [b]$P<0.01$. AC: Allergic conjunctivitis; BMI: Body mass index; TMH: Tear meniscus height; NIBUT: Non-invasive tear break-up time; MGL: Meibomian gland loss; FBUT: Fluorescein break-up time; SPEED: Standard patient evaluation of eye dryness; LLT: Lipid layer thickness; EST: Electronic screen time; MGAR-ave: Mean MGAR, which is the sum of the upper and lower MGAR divided by 2; MGAR: Meibomian gland atrophy rate.

**Association of Eye Rubbing on MGAR** The frequency of eye rubbing differed significantly between the AC and control groups ($\chi^2=13.998$, $P<0.05$). In the AC group, it was not

**Table 2 Meibomian gland morphologic evaluation between different subgroups**

| Parameters | MGAR (%) | Meiboscore | TMH (mm) | LLT (μm) | Distortion | Number | 5-5-5 score |
|---|---|---|---|---|---|---|---|
| Age (y) | | | | | | | |
| <12 | 35.22±12.29 | 1.57±0.43 | 0.16±0.06 | 53.29±22.17 | 2.23±1.24 | 21.31±3.60 | 65.09±67.60 |
| ≥12 | 28.47±9.45 | 1.28±0.36 | 0.21±0.10 | 57.07±21.87 | 1.81±1.03 | 21.88±2.43 | 60.94±63.57 |
| Sex | | | | | | | |
| Male | 34.27±10.16 | 1.55±0.37 | 0.17±0.07 | 53.64±21.02 | 2.08±1.19 | 21.63±3.39 | 76.36±70.93 |
| Female | 30.85±16.25 | 1.33±0.56 | 0.19±0.10 | 56.69±25.01 | 2.23±1.24 | 20.93±3.17 | 26.87±24.45 |
| BMI | | | | | | | |
| <18.5 | 31.90±10.57 | 1.45±0.38 | 0.17±0.08 | 54.60±22.88 | 2.16±1.18 | 21.48±3.23 | 52.95±59.69 |
| ≥18.5 | 36.70±14.14 | 1.58±0.51 | 0.19±0.07 | 54.07±20.12 | 2.03±1.24 | 21.42±3.60 | 87.79±74.17 |
| Eye rubbing, *n* (%) | | | | | | | |
| 1 (rare) | 32.41±14.53 | 1.44±0.51 | 0.15±0.04 | 62.88±27.42 | 0.83±0.42 | 21.31±3.49 | 41.67±57.42 |
| 2 (sometimes) | 33.24±11.76 | 1.50±0.42 | 0.19±0.09 | 52.52±19.28 | 2.17±0.69 | 21.64±2.88 | 67.38±68.44 |
| 3 (frequently) | 34.83±9.21 | 1.53±0.34 | 0.18±0.08 | 45.09±11.59 | 3.47±0.81 | 21.34±3.97 | 83.56±67.70 |

MGAR: The rate of meibomian gland atrophy; TMH: Tear meniscus height; LLT: Lipid layer thickness; BMI: Body mass index.

correlated with MGAR ($r$=0.289, $P$=0.54), and the univariate analysis indicated that the frequency of eye rubbing was not a risk factor for MGAR ($P$>0.05). Nonetheless, we observed a significant association between the frequency of eye rubbing and meibomian gland distortion score in the AC group ($P$=0.00), while no such correlation was found in the control group ($P$=0.051).

**Association of EST and Outdoor Exercise Time on MGAR** There was no significant correlation between EST-projector and MGAR in the AC group ($P$=0.383), but MGAR was significantly correlated with EST non-projector ($r$=0.309, $P$=0.005). Further multifactor linear regression analysis indicated that EST non-projector was a risk factor for MGAR [$\beta$=0.332, 95% confidence interval (CI): 0.040 to 0.220; $P$=0.004]. Outdoor exercise time was also associated with MGAR in patients with AC in univariate analysis ($\beta$=-0.318, 95%CI: -0.380 to -0.080, $P$=0.003). Further multifactor linear regression analysis indicated that outdoor exercise time was a protective factor for MGAR ($\beta$=-0.407, 95%CI: -0.390 to -0.100, $P$=0.001; Table 2).

**Association of Duration of AC and Untreated Time on MGAR** The duration of AC was 19.01±19.10mo (0.5-72mo). The duration of AC was not associated with MGAR ($P$=0.708). The untreated duration of AC was 3.30±3.90mo. Univariate linear regression analysis showed that MGAR increased with the untreated duration ($\beta$=0.287, 95%CI: 0.150 to 2.280, $P$=0.026). Multivariate analysis revealed that the untreated duration of AC was a risk factor for MGAR ($\beta$=0.240, 95%CI: 0.070 to 1.980, $P$=0.037; Tables 3-4).

One patient diagnosed with AC presented with prominent upper eyelid papillae and underdeveloped meibomian glands during the initial examination. Following a 3-week treatment regimen consisting of 0.1% flumirone eye drops and olopatadine hydrochloride eye drops administered twice daily, tacrolimus eye drops four times daily, and sodium hyaluronate

**Table 3 Univariate linear regression analysis of systemic factors associated with meibomian gland atrophy**

| Factors | $\beta$ (95%CI) | *P* |
|---|---|---|
| Sex | | |
| Male | Reference | Reference |
| Female | -0.125 (-10.530, 3.690) | 0.339 |
| Age (y) | | |
| ≤12 | Reference | Reference |
| >12 | -0.253 (-13.540, 0.045) | 0.051 |
| BMI | | |
| <18.5 | Reference | Reference |
| ≥18.5 | 0.189 (-1.750, 11.350) | 0.148 |
| Eye rubbing | | |
| Rare | Reference | Reference |
| Sometimes | 0.035 (-6.590, 8.250) | 0.824 |
| Frequently | 0.090 (-5.900, 10.730) | 0.563 |
| EST-non-projector (min/d) | 0.260 (0.000, 0.200) | 0.045[a] |
| EST-projector (h/d) | -0.170 (-4.220, 0.870) | 0.193 |
| Outdoor exercise time (min/d) | -0.381 (-0.380, -0.080) | 0.003[a] |
| Untreated time (mo) | 0.287 (0.150, 2.280) | 0.026[a] |
| 5-5-5 score | 0.214 (-0.01, 0.090) | 0.100 |
| Duration of AC | 0.049 (-0.130, 0.200) | 0.708 |

BMI: Body mass index; EST: Electronic screen time; AC: Allergic conjunctivitis; CI: Confidence interval.

**Table 4 Multivariate analysis of the associations with meibomian gland atrophy**

| Factors | $\beta$ (95%CI) | *P* |
|---|---|---|
| Age | -0.360 (-2.550, -0.570) | 0.002[b] |
| EST-non-projector (min/d) | 0.332 (0.040, 0.220) | 0.004[b] |
| Outdoor exercise time (min/d) | -0.407 (-0.390, -0.100) | 0.001[b] |
| Untreated time (mon) | 0.240 (0.070, 1.980) | 0.037[a] |

EST: Electronic screen time; CI: Confidence interval.

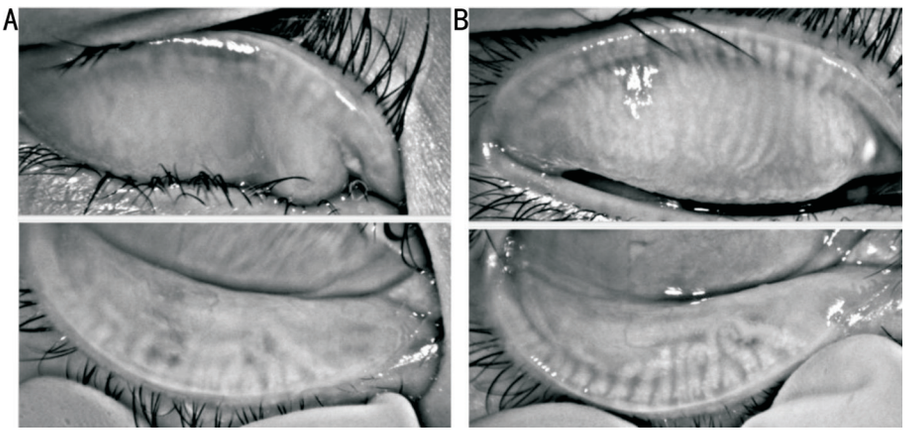


**Figure 2 Degree of meibomian gland development in same patient before (A) and after 3wk of treatment (B) is significantly different.**

eye drops every 2h, marked improvement in the meibomian glands was observed (Figure 2).

## DISCUSSION

Over the past 30y, there has been a trend of increasing incidence of allergic diseases, making it the sixth most common chronic disease globally[33]. AC occurs in up to 30% of the pediatric population[33-34]. However, allergic diseases like allergic rhinitis and asthma often receive more attention than AC, especially in children. The diagnosis and treatment of AC in children are frequently delayed due to atypical symptoms or inaccurate descriptions provided by the children themselves[1,35-36]. Long-term recurrent AC can cause morphological changes and functional disorders of the meibomian glands[37], potentially leading to or worsening dry eye[38-40]. Currently, there is limited research on the morphological changes of meibomian glands in children with AC. Our study aims to investigate the morphological characteristics of meibomian glands in children with AC and the factors that influence these morphological changes.

The percentage of severe MGA in the AC group was significantly higher compared to the healthy control group (51.67% *vs* 10%). Additionally, in Grade 1 MGA, the atrophy area was smaller in the control group than in the AC group. The meibomian gland distortion score was also significantly higher in the AC group than in the control group, indicating a more severe impact of AC on meibomian gland morphology compared to the normal control group, which is consistent with previous research[11,25,27].

In addition, we observed that MGA in the lower eyelids was more severe than in the upper eyelids, regardless of whether it was in the AC group or the control group. Previous studies have also indicated that MGL in the lower eyelid was higher than in the upper eyelid[9,23,41]. This difference may be attributed to the more pronounced blinking movements in the upper eyelids and the influence of gravity, causing meibum stagnation in the ducts and openings of the lower eyelid's meibomian glands, leading to duct dilation, acinar atrophy, and ultimately resulting in MGL[23]. To mitigate research errors arising from physiological disparities between the upper and lower eyelids, the average value of MGA in both upper and lower eyelids was utilized as an evaluation index in this study.

Previous studies have suggested that children with AC have decreased LLT and NIBUT[25]. However, this study only found that LLT and FBUT in the AC group were lower than those in the control group. Dry eye symptoms were significantly higher in the AC group compared to the control group, while NIBUT did not differ between the two groups. This discrepancy may be attributed to poor cooperation from children during NIBUT examination and limitations in the instrument design, potentially leading to errors in evaluating tear film stability. Certainly, the negative results could also be attributed to our small sample size. NIBUT has been widely used in numerous studies, including those involving pediatric populations[42]. Additionally, this study did not find a significant correlation between MGA and symptoms of discomfort and signs of dry eye, including LLT and FBUT, in the AC group. Previous research has also indicated that there is no direct relationship between tear film break-up time and LLT, with some individuals showing a paradoxical phenomenon of shortened NIBUT and increased LLT[43]. This implies that an increase in LLT alone may not necessarily enhance tear film stability, as maintaining a balance between the aqueous layer and lipid layer is crucial for tear film stability[43].

This study revealed that the extent of MGA in children under 12 years old was greater than in those aged 12 and above. This suggests that the severity of MGA is higher in younger children with AC, possibly due to a lower tolerance of meibomian gland acinar tissue to inflammation at a younger age, leading to more significant damage to the meibomian glands. However, further validation is required through a combination of qualitative and quantitative analysis of the microbiota and inflammatory factors in the meibum. Additionally, our study did not find a

significant correlation between gender, BMI, and MGAR in children with AC. Since only one child with AC had a BMI over 24, more targeted research is needed to explore the impact of obesity on MGA in children with AC.

Research on adult AC has shown a positive association between the severity of ocular surface damage and the duration of allergic reactions, as well as a negative correlation with tear film stability[44]. However, our study did not find a significant correlation between the duration of AC and MGAR, but did find a significant correlation between the untreated duration of AC and MGAR. Multiple linear regression analysis results indicated that the untreated duration of AC is a risk factor for MGA in children with AC ($\beta$=0.287, 95%CI: 0.150 to 2.280, $P$=0.026). This suggests that recurrent inflammatory reactions left untreated before diagnosis may negatively impact the meibomian glands. Regardless of disease duration, timely and effective inflammation control may help reduce or prevent meibomian gland damage. Therefore, early detection and treatment of AC in children may be critical in preventing MGA and dry eye.

Our study found that MGAR was only associated with EST non-projectors, but not with EST projectors. Previous studies have shown a significant increase in incomplete blinking percentage when using electronic screens[45], and an increase in EST is positively correlated with MGA[32]. Ma *et al*[46] reported that smartphone or tablet use is associated with dry eye, suggesting that short-distance viewing of smartphones and tablets may have a greater impact on the ocular surface compared to long-distance viewing of computers and televisions. Despite the classification of display screens into projector and non-projector categories in our questionnaire, we did not meticulously differentiate between the specific types of display screens. Owing to the retrospective nature of our cross-sectional study, participants found it difficult to recall with precision the types and durations of display screens they were exposed to daily. As such, our findings concerning the impact of display screens on meibomian glands in children with AC should be considered as an exploratory hypothesis rather than a definitive conclusion. Specifically, it prompts the inquiry into whether the extent of screen time serves as a contributing factor affecting the health of meibomian glands in this demographic.

Tanabe *et al*[47] proposed the concept of frictional force between the eyelid and the ocular surface, defining it as a friction-related disease (FRD). A previous study has reported that diseases within the FRDs can lead to mechanical trauma and are linked to meibomian gland morphology[48]. In this study, participants in the AC group reported more frequent eye rubbing than those in the control group. The results show that frequent eye rubbing was associated with higher meibomian gland distortion scores in the AC group (sometimes: $\beta$=0.525, 95%CI: 0.879 to 1.723, $P$<0.001; frequent: $\beta$=0.752, 95%CI: 1.757 to 2.785, $P$<0.001). However, frequent eye rubbing was not associated with higher MGAR scores ($P$=0.684). This suggests that mechanical friction only alters the position of the meibomian gland ducts, rather than damaging the acinar tissue structure of the meibomian glands. Longer-term longitudinal studies are needed to confirm this finding.

Numerous studies have shown that outdoor activities have positive effects on the physical and mental health of children, including reducing myopia[49], alleviating chronic pain[50], and promoting child development[51]. However, many children with AC tend to limit their outdoor activities due to allergies to dust and pollen. Our study reveals that children with AC who spend more time outdoors have lower MGAR ($\beta$=-0.318, 95%CI: -0.380 to -0.080, $P$=0.003). Previous research has also indicated that outdoor activities can help improve allergic asthma[52]. Therefore, we recommend that children with AC should still engage in outdoor activities, but they should choose outdoor exercise venues based on the types of allergens present.

During our study, we encountered a patient with AC who exhibited significant allergic symptoms, including extensive giant papillae on both upper and lower conjunctiva, and almost complete absence of the meibomian gland duct structure in imaging of the upper eyelid. After three weeks of local medication treatment, the meibomian glands became visible. Due to the unique nature of this case, the patient's data was not included in the study. The severe inflammatory response in this patient led to increased conjunctival papillae and tissue edema, causing unclear infrared imaging that could be mistaken for MGA. However, after treatment, as inflammation and edema decreased, the meibomian glands appeared to "regenerate" due to being previously obscured by the conjunctiva. It is highly improbable for meibomian glands to undergo extensive regeneration within a three-week period. This highlights the importance of cautiously considering the potential regeneration of meibomian glands in children. The one limitation of this study is that we did not detect the allergens of each child with AC, so we could not evaluate whether different allergens had different effects on meibomian gland morphology. This is because allergen detection is an invasive procedure, and only a small number of children and their parents were willing to cooperate with allergen detection. Therefore, we did not include this indicator in the study. Another limitation of our study was that it did not take into account the impact of refractive status on meibomian gland morphology. Recent research by Zhao *et al*[42] has shown that the NIBUT is significantly shorter in myopic children compared to non-myopic children, and that myopic children are also more

susceptible to dry eye syndrome. Therefore, different refractive states may also have a certain impact on the morphology of the meibomian glands. Therefore, it is necessary to include refractive state as a factor affecting the morphology of the meibomian glands of children in future studies.

In conclusion, AC in children can worsen MGA, which deteriorates with prolonged untreated duration before diagnosis. Timely detection and effective treatment can mitigate MGA, especially by monitoring changes in lower meibomian gland morphology, which is crucial for younger children. Moreover, children with AC should limit prolonged use of electronic screens at close range. Increasing outdoor activities appropriately and organizing activities in a rational manner may help reduce MGAR in children with AC.

**ACKNOWLEDGEMENTS**

**Authors' Contributions:** Design of the study: He WF and Ma HX; conduct of the study and data collection: He WF, Wu YP, and Ma HX; analysis and interpretation and manuscript preparation and review: He WF, Wu YP, Zheng JW, Huang BG, Zuo JJ, Li JY, Jiang D, and Ma HX. All authors read and approved the final version of the article.

**Foundation:** Supported by the Natural Science Foundation of the Zhejiang Province (No.LGD22H120002).

**Conflicts of Interest: He WF,** None; **Wu YP,** None; **Zheng JW,** None; **Huang BG,** None; **Zuo JJ,** None; **Li JY,** None; **Jiang D,** None; **Ma HX,** None.

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