International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Severity of Allergic Conjunctivitis (AC) and its Correlation with Severity of Meibomian Gland Loss and Meibomian Gland Duct Distortion on Meibography in Pediatric Population

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Abstract: ***Background & Objectives: To observe morphological changes in the meibomian glands of pediatric patients with allergic conjunctivitis and to assess the relation between degree of morphologic changes (Meibomian Gland Loss and Meibomian Gland Duct Distortion) of the meibomian glands of both eyelids with severity of allergic conjunctivitis. Methods: In this study, 74 eyes of 37 pediatric patients in the age group 5 to 15 years (32 Males and 5 Females) with allergic conjunctivitis was subdivided as proposed by Gokhale et al on slit lamp examination into (29 eyes) Mild, (24 eyes) Moderate and (21 eyes) Severe AC. Meibomian gland loss was assessed subjectively on non-contact meibography with five grade scale (meiboscale) as proposed by Dr. Heiko Pult. The presence of meibomian gland duct distortion was scored 1 when it was present and 0 when it was absent. Results: In our study, there is statistically insignificant correlation between the 3 groups i.e. severity of AC and meibomian gland loss on meibography. There is no statistically significant correlation between the 3 groups i.e. Severity of AC and Meibomian Gland Duct distortion. Meibomian Gland Duct Distortion was found to be in upper eyelid as in previous study conducted by Arita R et al. Conclusions: In our study, there is no statistically significant correlation found between severity of AC and severity of Meibomian gland loss on Meibography as well as with Meibomian Gland Duct Distortion. Small sample size was the limitation of our study so the study should be repeated with a larger sample size.***

Keywords: Meibomian gland, allergic conjunctivitis, meibography

1. Introduction

Allergic conjunctivitis (AC) is a common ocular surface disease in which allergic inflammation induces various reactions and symptoms such as papillary formation, conjunctivalhyperemia, mucus discharge and itchy sensation. Conjunctival tissue lies adjacent to the meibomian glands; therefore, it is possible that AC results in tear film instability through its effects on meibomian glands.

The Meibomian glands (MGs) play an important role in the maintenance of a healthy ocular surface by providing lipids to the superficial tear film. The MGs are found in the upper and lower eyelids between the palpebral conjunctiva and the tarsal plate. Each MG is approximately 3-4 mm in length, ending at the lid margin.

Allergic conjunctivitis cause release of inflammatory mediators in the conjunctival tissue→hyperkeratinization of meibomian gland duct & increase meibum viscosity →obstruction of meibomian orifice → stasis of meibum increased pressure in ductal system → dilatation of ductal system → atrophy of secretory acini → meibomian gland loss (drop out)

Meibography is a well-known technique for the assessment of meibomian gland morphology, meibomian gland changes and the diagnoses of Meibomian gland dysfunction[1, 2]. The premise of meibography was first found in the literature in 1977, when Tapie demonstrated using a transilluminator under an everted eye lid and either white light or a UV Woods light to evaluate the MGs[3]. This technique was then used with infrared (IR) photography to further improve image quality in the early 1980s but it was not until 1991 that the term meibography was used to describe using this technique in vivo to evaluate the MGs[4]. This method of meibography was further termed contact meibography, as it required the transilluminator to touch the patient's lid.

This basic method was used without major change until 2007.

Non-contact meibography was introduced by Arita et al. making meibography much more comfortable for the patient[1, 5]. Non-contact meibography uses IR light (700-1000mm) projected onto the everted eyelid and an IR-sensitive camera to record the image, removing the need for transillumination of the lid[1]. In this technique the everted eye lid is not touched by an instrument. SLM independent systems are the portable non-contact meibograph (PNCM)-which is a small IR Camera including an IR light source-and the EyeTop Topographer, Sirius Scheimpflug Camera and Cobra Fundus Camera (CSO, Costruzione Strumenti Oftalmici, Florence, Italy; bon Optic VertriebsgmbH, Lubeck) and the Oculus Keratograph (Oculus, Wetzlar, Germany) all including meibography options using their internal IR cameras[5].

Normal meibomian glands appear as grapelike clusters with acini that are IR hyper-reflective[2, 5]. Many different grading scales have been published; all of them are four-grade scales[1, 2]. Therefore, a verbal and pictorial five-grade scale (Fig 1) was developed in order to enhance the grading in meibography, making it more sensitive with to smaller increments[5]. The lower and upper lids are each assigned a grade from 0-4, with higher grades indicating higher percentages of lid area with gland loss[6].

The purpose of this study was to examine morphologic changes of the meibomian glands (meibomian gland loss and meibomian gland duct distortion) in pediatric patients with allergic conjunctivitis using non- contact meibography and to assess the relationship between severity of allergic conjunctivitis and morphologic changes of meibomian glands of both eyelids.

2. Literature Survey

This study was conducted in Pediatric Ophthalmology & Squint OPD of Lotus Eye Hospital, Juhu, Mumbai from October 2019 to February 2020.

3. Materials And Methods

We evaluated 74 eyes of 37pediatric patients in the age group 5years to 15 years (32 Males and 5 Females) with allergic conjunctivitis. Severity of AC was clinically diagnosed on slit lamp examination. Exclusion criteria for the subjects included blepharitis, obvious eyelid or ocular surface disorders, contact lens wear, atopic dermatitis, continuous antiglaucoma eye drop use[7, 8], previous eye surgery. Data used in this study were obtained from the both eyes of each subject. Verbal informed consent was obtained from parents of all subjects.

Examinations:
Each eye of all subjects was examined on slit lamp to grade the severity of allergic conjunctivitis. Clinical grading system as proposed by Dr. Nikhil S Gokhale was used[9]. In this clinical grading system, the bulbar and tarsal conjunctiva and the cornea and limbus are evaluated and the severity of involvement is graded clinically. It is usually possible to classify the disease severity into mild, moderate, severe and blinding categories (Fig 2). Patients may have findings that do not fall into the same severity. In these instances the corneal findings are given more importance over conjunctival findings. For example a patient having giant papillae but no corneal or limbal involvement may still be classified for treatment purpose as mild disease because the papillae may be inactive and not causing any corneal erosions[9]. The grading is done in both eyes independently.

Non contact infrared meibography was done on 3nethra classic a Forus Innovation which is a non-mydriatic and non-contact device for imaging the posterior and anterior surfaces of the human eye (Fig 3). Using the noncontact infrared meibography system, the upper and lower eyelids were everted and the meibomian glands were examined. Partial or complete loss of the meibomian glands was scored subjectively using the five grade scale (Meiboscale) for each eyelid as described by Dr. Heiko Pult (Fig 1 A & B). Grade 0 – No meibomian gland loss; Grade 1 - < 25% gland loss; Grade 2 - 25-50% gland loss; Grade 3 - 50-75% gland loss; Grade 4- > 75% gland loss[5]. The meiboscale of upper and lower eyelid of an eye was summed up to get the total meiboscale. So, the total meiboscale for each eye ranged from 0 to 8. The criterium "loss of meibomian glands (MGL) was defined as the proportion of the area of MG loss (Fig 4B) in its relation to the total area of glands if the subject would have had normal meibomian glands (Fig 4A)[1, 10]

Several grading scales have used four grades but a finer scale such as the five- grade meiboscale may improve subjective grading[6] by providing more distinction between levels of gland loss.

The presence of meibomian gland duct distortion was established if the morphology was altered by obviously more than 45 degrees in at least 1 meibomian gland in either the upper or the lower eyelid, as determined by meibography. The distortion was scored 1 when it was present and 0 when it was absent[11].

Statistical Methods

Data was normally distributed. The age was described in mean and standard deviation and qualitative variables like severity of AC, number of patients with each meiboscale has been expressed in percentage and proportions. Comparison proportion between the severity of AC and total meiboscale and severity of AC and meibomian gland duct distortion was checked using ANOVA and Chi-square and Fischer exact test respectively. Analysis was done at 95% Confidence Interval, $p < 0.05$ was considered statistically significant. Entry was done in Excel and analysis was done in EpiInfo 7 software.

4. Results

In the present study of 74 eyes of 37 patients, 32 patients were Male and 5 patients were female (mean age 9.6 $\pm$3.20 years, range 5 – 15 years). Out of 74 eyes, 39.2% (n=29)eyes had mild AC, 32.4% (n=24) eyes had moderate AC and 28.4% (n=21)eyes had severe AC (Table 1)

Median total meiboscale with inter-quartile range in eyes with Mild AC was 1 (1-3), in eyes with Moderate AC was 2 (1.5-3) and in eyes with Severe AC was 2 (2-3) with (F=1.92, P=0.15) which shows there is statistically insignificant correlation between the 3 groups i.e. severity of AC and meibomian gland loss on meibography.

Out of 74 eyes, 71 (95.9%) eyes showed Meibomian Gland Duct Distortion (Table 2) of which it was present in 93.1% of eyes (n=27) with Mild AC, 100% of eyes (n=24) with Moderate AC and 95.2% of eyes (n=20) with Severe AC (Table 3) with (χ^2=1.64, P=0.44) which indicates there is no statistically significant correlation between the 3 groups i. e Severity of AC and Meibomian Gland Duct distortion (Table 4). Meibomian Gland Duct Distortion was found to be in upper eyelid as in previous study.

5. Discussion

Although Meibomian Gland Duct Distortion is found out to be significantly more frequent in patients with AC in previous studies[11], it was not exclusively studied in Paediatric population with AC and neither was it studied with respect to severity of AC.

Arita R et al studied 55 eyes of 55 patients with perennial AC and 47 eyes of 47 healthy volunteers as controls for meibomian gland duct distortion using non-contact meibography and found out that meibomian gland duct distortion was significantly more frequent in patients with AC than in controls irrespective of duration of AC[11].

In the present study, we examined meibomian gland duct distortion using noncontact meibography in paediatric patients with AC of different severity. Our findings indicated that meibomian gland duct distortion was observed in majority of patients with AC (71 of74 eyes) irrespective of the clinical severity of AC. Although the exact mechanisms for the association between AC and meibomian gland duct distortion are unclear, inflammatory changes in the conjunctival tissue might induce pressure on the meibomian glands in the tarsus, which is stiff and has limited room for expansion. Patients with AC frequently rub their eyes, and rubbing is known to induce keratoconus; therefore, the rubbing could induce meibomian gland duct distortion. Previous study have reported that the distortion was confined to the upper eyelid and was not present in the lower eyelid, providing further credence for rubbing being involved in the distortion of the meibomian gland duct of the upper eyelid and not the lower eyelid[11]. In our study also Meibomian Gland Duct Distortion was observed in upper eyelid. The presence of eye rubbing in each subject was not examined; therefore, the association between eye rubbing and the distortion of meibomian gland ducts was not clarified in the present study.

Limitations of this study

Smaller sample size is the drawback of our study. The study should be repeated with a larger sample size.

6. Conclusion

Meibomian gland loss is more frequently found in patients with allergic conjunctivitis but the severity of meibomian gland loss does not increase with increase in severity of AC.

Meibomian gland duct distortion is seen in almost all patients with AC irrespective of the severity of AC.

Acknowledgement

No financial disclosure.

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Figures and Tables

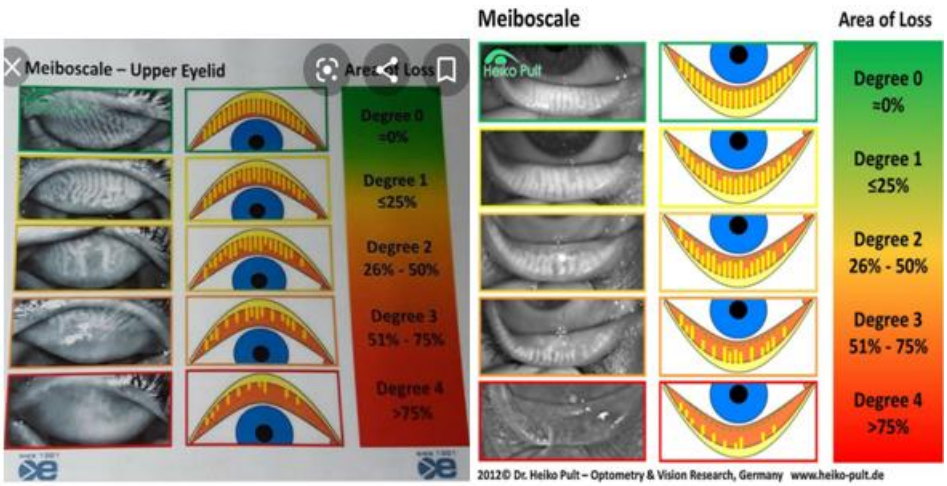

Figure 1

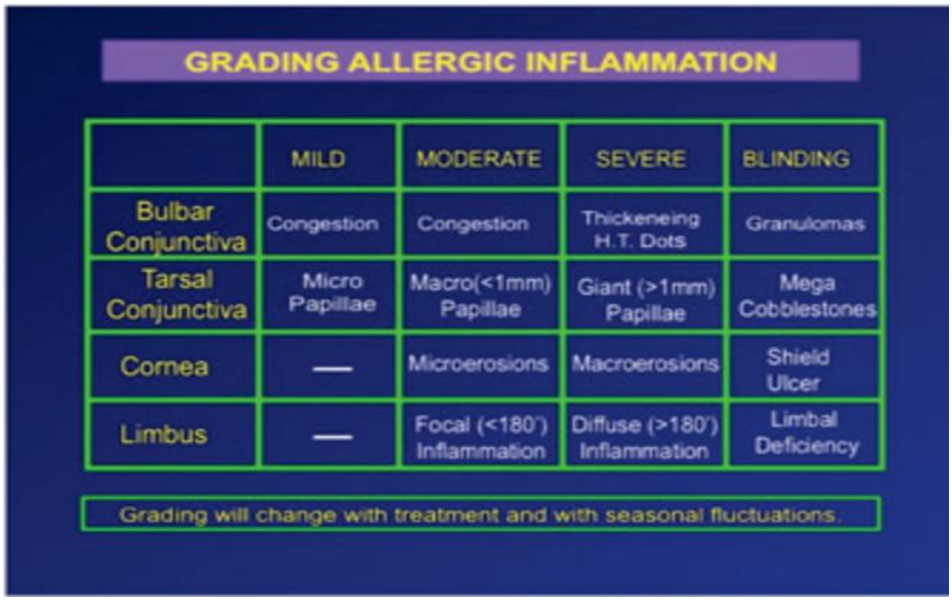

Figure 2

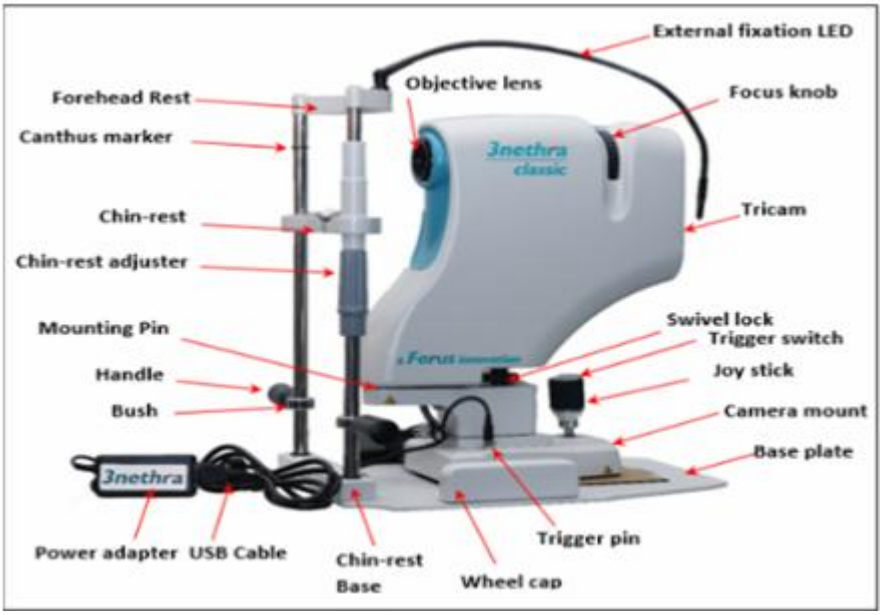

Figure 3

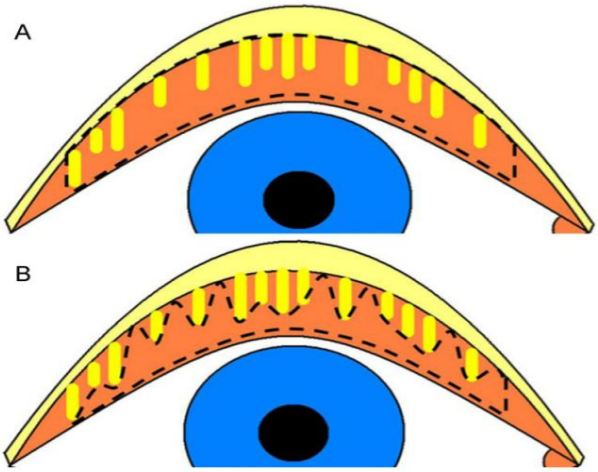

Figure 4

Legends:

Figure 1. Meiboscale for upper eyelid (A) and Meiboscale for lower eyelid (B) as given by Dr. HeikoPult
Figure 2. Clinical Grading of Allergic Conjunctivitis as given by Dr. Nikhil Gokhale
Figure 3: 3nethra – a non-contact meibography system
Figure 4. Definition of total area of meibomian glands (A) and area of loss (B) on which subjective and computerized grading is based on.

Tables:

Table 1:

Severity of AC	Frequency (n)	Percent (%)	Cum. Percent	95% CONF Limit
MILD	29	39.19%	39.19%	28.04% -51.23%
MODERATE	24	32.43%	71.62%	22.00% - 44.32%
SEVERE	21	28.38%	100.00%	18.50% - 40.05%
TOTAL	74	100.00%	100.00%	

Table 2:

Distortion	Frequency	Percent	Cum. Percent	95% CONF Limits
1	71	95.95%	95.95%	88.61% - 99.16%
2	3	4.05%	100.00%	0.84% - 11.39%
TOTAL	74	100.00%	100.00%	

Table 3:

	Meibomian Gland Duct Distortion		
Severity	Yes	No	Total (n)
Mild	27 (93.10%)	2 (6.90%)	29
Moderate	24 (100.00%)	0 (0.00%)	24
Severe	20 (95.24%)	1 (4.76%)	21

Table 4:

	Mild AC	Moderate AC	Severe AC	
Number of Eyes	29	24	21	
Sex (Male/ Female)	28/1	23/1	18/3	
Median Total Meiboscale	1	2	2	P=0.15
Number of eyes with presence of Meibomian gland duct distortion	27	24	20	P=0.44

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