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A Study of Association of Dry Eye Disease in Allergic Conjunctivitis.

KEYWORDS: Allergic conjunctivitis, dry eye, itching, atopic conjunctivitis, vernal conjunctivitis, dry eye grading severity scheme.

Dr. Anuradha Nath	Dr. Seema Channabasappa	Dr. Mirdehghan M S
Resident of ophthalmology, Vydehi institute of medical science and research centre, Bangalore,India	Professor of ophthalmology, Vydehi institute of medical science and research centre, Bangalore,India	Resident of ophthalmology, Vydehi institute of medical science and research centre, Bangalore,India

ABSTRACT *Allergic conjunctivitis and dry eye are major ocular surface disorder affecting millions of people interfere with the quality of life. A typical clinical symptom of allergic conjunctivitis is "itching", whereas the symptoms of dry eye are "burning sensation". Aim was to study the association of dry eye disease in clinically diagnosed cases of allergic conjunctival disease. Objectives was to observe an association of dry eye disease in allergic conjunctivitis patients and to correlate severity of allergic conjunctival disease with dry eye. Materials and Methods: One hundred patients who satisfied inclusion and exclusion criteria and gave informed consent were studied. Based on novel scoring system (NSS), the severity of allergic conjunctival disease was graded. Dry eye grading was done based on the dry eye grading severity scheme (DEGSS). Occupation was grouped as indoors or outdoors. Other parameters taken were the ocular surface disease index questionnaire (OSDI). The Statistical analysis was done using Chi square test and Fischer exact test. Results: It was observed that allergic conjunctival disease was significantly associated with dry eye (P=0.004) and severity of allergic conjunctival disease had a significant correlation with dry eye disease (P=0.001). Conclusion: In this study it was observed that dry eye disease was associated with atopic and vernal forms of allergic conjunctivitis. Keywords: Allergic conjunctivitis, dry eye, itching, atopic conjunctivitis, vernal conjunctivitis, dry eye grading severity scheme.*

INTRODUCTION:

Allergic conjunctival disease and dry eye are major ocular surface disorders affecting millions of people. The chronic discomfort interferes with the quality of life of the patient for a long period of time [1]. A typical clinical symptom of allergic conjunctivitis is 'itching', whereas the symptoms of dry eye are 'burning sensation', 'irritation', and 'ocular fatigue'.[2]

The most common symptoms present are red eye, itching and burning of eyes. This group of symptoms is nonspecific for any class of ocular surface disease or diagnosis. Dry eye and ocular allergy can occur simultaneously or independently of each other. Due to the overlap of signs and symptoms, it can be confusing to diagnose and treat patients without inducing further complication.[3]

Patients who suffer from ocular allergy are significantly more likely to experience signs and symptoms of dry eye disease. Studies of the tear film in allergic conjunctival disease demonstrate a shared pathology between dry eye and ocular allergy namely inflammation of the cornea and the conjunctival surface.[4]

Toda et al has reported that 12 out of 80 patients with dry eye complained of an itchy feeling. Patients with decrease tear break up time had increase papillary formation of the upper tarsal conjunctiva and an increase serum antigen specific IgE. This report suggested an overlap syndrome in allergic conjunctivitis and dry eye disease.[5]

Atopic keratoconjunctivitis and vernal keratoconjunctivitis are severe manifestation of ocular allergy. Research shows that an allergy related alteration in quality and quantity of aqueous tear production can translate into altered lipid and mucin components of tear film as well. The resulting imbalanced tear film produces inadequate barrier protection resulting in ocular surface inflammation.[6]

Many times the physician treat ocular allergy without treating the underlying dry eye condition of the eye. Patients complain of persistent symptoms and very often consider that their original disease has not been treated properly. This leads to an increase or prolonged use of topical treatment that becomes inappropriate or even toxic. This study attempts to highlight the probable associations of ocular surface inflammation, in this case, allergic conjunctival disease with dry eye.

MATERIALS AND METHODS: This was an observational, descriptive study of 100 patients reporting to the ophthalmology outpatient department, Vydehi Institute of Medical Sciences and Research Centre, Whitefield Bangalore, diagnosed with allergic conjunctivitis. Age group of 20-40 years men and women with history of allergic conjunctivitis, seasonal or frequently relapsing and with history of systemic allergies were included in this study. Patients with contact lens wearers, post refractive surgeries, conjunctival infective/degenerative disorders, patients on medications, topical and systemic causing dry eye disease and other secondary causes of dry eye, patients with clinically suspected autoimmune diseases, post radiation therapy/chemical injuries to the eye, early menopausal and pregnant women were excluded from this study.

The subjects who satisfied inclusion and exclusion criteria were invited to take part in this study. Informed consent was taken from each participant. For analysis of the data, detailed examination was done by slit lamp, the subjects with allergic conjunctival disease were divided into allergic conjunctivitis, atopic conjunctivitis and vernal conjunctivitis. Based on novel scoring system, severity of allergic conjunctival disease was graded as mild, moderate and severe. Dry eye grading was done on each individual based

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on the dry eye grading severity scheme into no dry eye (0), mild (1), moderate (2), severe (3) and very severe (4). Occupation for each individual was grouped as indoors or outdoors.

Tear meniscus height was measured by slit-lamp microscope at the centre of the lower lid margin. The normal average value of 1mm was taken as normal.

Tear break-up time has been defined as the interval between a complete blink and the appearance of the first randomly distributed dry spot on the cornea. It is noted after instilling a drop of fluorescein and examining in the cobalt-blue light of a slit-lamp. A BUT of =>10 seconds was considered as normal.

Schirmer test is the test for tear quantity. It was performed by placing whattman No.41 filter paper in the inferior cul de sac. Aqueous tear production was measured by the length in millimeters that the strip soaking over a period of 5 minutes. Schirmers test with topical anaesthesia, also referred as a basic secretion test was considered. Here basic secretion is measured and results of 5mm or less was considered abnormal.

Other parameters taken into consideration were the ocular surface disease index questionnaire (OSDI). This questionnaire consists of 12 questions, The OSDI is assessed on a scale of 0 to 100, with higher scores representing greater disability. The index demonstrates sensitivity and specificity in distinguishing between normal subjects and patients with dry eye disease. Values to determine dry eye severity calculated using the OSDI formula:

OSDI = (sum of scores) x 25/(# of questions answered).

The overall OSDI score defined the ocular surface as normal (0-12 points) or as having mild (13-22 points), moderate (23-32 points), or severe (33-100 points) disease.

The results were expressed as mean ± standard deviation. Statistical analysis was done using the Chi square test and the Fischer exact test.

STATISTICAL STUDY: Descriptive and inferential statistical analysis has been carried out in the present study.

RESULTS: Duration based, observational study of 100 clinically diagnosed cases of allergic conjunctivitis with informed consent which satisfied the inclusion and exclusion criteria.

Statistical software used:
The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 1

2.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs and tables.[7,8,9,10]

Table 1: Occupation distribution

Occupation	Number of Patients	Percentage (%)
Indoors	58	58
Outdoors	42	42
Total	100	100

Figure 1: Distribution of allergic conjunctival disease in the study group

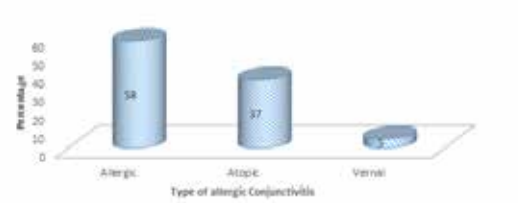

Figure 2: Distribution based on the novel scoring system (severity grading for allergic conjunctival disease)

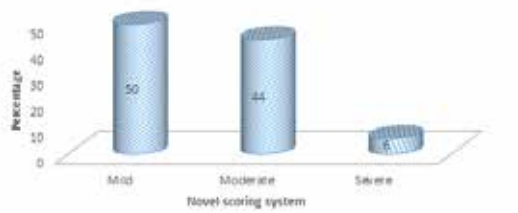

Table 2: Gender correlation of allergic conjunctival disease and dry eye grading severity scheme (DEGSS).

Variables	Gender		P value
	Male (n=64)	Female(n=36)	
Type of allergic Conjunctival disease			
Allergic	38(59.4%)	20(55.6%)	0.183
Atopic	21(32.8%)	16(44.4%)	
Vernal	5(7.8%)	0(0%)	
Severity of dry eye			
0.No dry eye	22(34.4%)	12(33.3%)	0.959
1.Mild dry eye	23(35.9%)	15(41.7%)	
2.Moderate dry eye	16(25%)	8(22.2%)	
3.Severe dry eye	3(4.7%)	1(2.8%)	
4.Very severe dry eye	0(0%)	0(0%)	

Figure 3: Prevalence of dry eye in patients studied

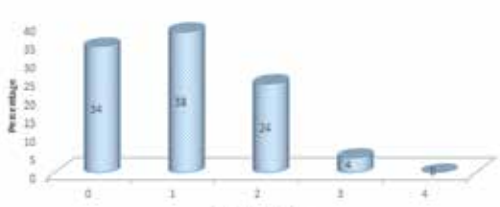

Table 3: Association of dry eye with types of allergic conjunctival disease

Type of allergic Conjunctivitis	Severity of Dry Eye					Total	P Value
	No Dry Eye(0)	Mild(1)	Moderate(2)	Severe(3)	Very Severe(4)		

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Allergic	27(79.4%)	21(55.3%)	10(41.7%)	0(0%)	0	58(58%)	P=0.004
Atopic	7(20.6%)	16(42.1%)	12(50%)	2(50%)	0	37(37%)	
Vernal	0(0%)	1(2.6%)	2(8.3%)	2(50%)	0	5(5%)	
Total	34(100%)	38(100%)	24(100%)	4(100%)	0	100(100%)	

DISCUSSIONS: Allergic conjunctivitis and dry eye diseases are highly variable ocular surface disorders. The unpredictability of each disorder lies in its pathogenesis, as the clinical manifestations can be dramatically modified by external stimuli. Ocular allergies are over diagnosed, whereas dry eye disease is underdiagnosed.[11] Among the various diseases affecting the ocular surface, dry eye is the most common condition.[12] In standard outpatient clinics, it has been reported that 15–30% of new patients are affected by dry eye.[13] Although a decrease in tear production is a common condition in many types of dry eye, the severity of ocular surface lesions varies greatly from disease to disease.[14]Reduction in the modifiable risk factors of dry eye is essential to reduce its prevalence.[15]Few studies have highlighted the overlap between these two ocular surface disorders. In studies conducted by hom MM et al out of 194 patients with itchiness 57.7% (112/194) had clinically significant dry eye, thereby highlighting that there are a segment of patients who concomitantly suffer from allergic conjunctivitis and dry eye.[4] In our study we have tried to observe if there is significant association of dry eye in patients presenting with allergic conjunctivitis in the study group.

THE FINDINGS OF THIS STUDY ARE AS FOLLOWS:
A total number of 100 patients, 64 male and 36 female patients, age group from 20-40 years were included after being diagnosed with allergic conjunctival disease.

Patients with indoor occupation were 58 and outdoor occupation 42

The total number of patients diagnosed to have allergic conjunctivitis were 58, atopic conjunctivitis were 37 and vernal conjunctivitis were 5.

The total number of patients based on severity of allergy according to novel scoring, having mild disease were 50, moderate were 44 and severe were 6. In patients with allergic conjunctivitis, 40 (80%) were with mild disease, moderate 18 (40.9%) and none in severe degree. Patients with atopic conjunctivitis 10 (20%) had mild degree, moderate were 26 (59.1%) and none had severe atopic conjunctivitis. No patients with vernal conjunctivitis had mild grade, 1 (16.7%) patient had moderate grade and 5 (83.3%) had severe grade.

On the basis of DEGSS 34 patients did not show any signs or symptoms of dry eye, 38 patients had mild dry eye, 24 patients had moderate dry eye and 4 patients had severe dry eye. None of the patients in this study had very severe dry eye (grade 4).

The total number of males included with no signs or symptoms of dry eye was 22 (34.4%), mild dry eye were 23 (35.9%), moderate dry eye were 16 (25%) and with severe dry eye were 3 (4.7%). The number of females with no signs and symptoms of dry eye were 12 (33.3%), mild dry eye were 15 (41.1%), moderate dry eye were 8 (22.2%) and with severe dry eye was 1 (2.8%).

The number of patients with indoor occupation having no signs or symptoms of dry eye were 55.9%, mild dry eye were 57.9%, moderate were 62.5%, severe were 50% and none had very severe symptoms of dry eye. Patients with outdoor occupation with no signs or symptoms of dry eye were 44.1%, mild were 42.1%, moderate were 37.5% and severe dry eye were 50%. There was no significant association between type of occupation and dry eye.

An ocular surface disease index questionnaire was also applied for each individual to determine dry eye disease clinically, showed only 1% patient had no clinical symptoms of dry eye, 8% mild symptoms , 27% moderate symptoms and 64% severe clinical symptoms of dry eye.

Patients with allergic conjunctivitis having no signs and symptoms of dry eye were 27 (79.4%), with mild dry eye were 21(55.3%), and moderate were 10 (41.7%) and none had severe or very severe dry eye. Patients with atopic conjunctivitis having no signs or symptoms of dry eye were 7(20.6%), mild were 16(42.1%), moderate were 12(50%) and 2(50%) had severe dry eye. All patients with vernal conjunctivitis had dry eye with 1(2.6%) having mild dry eye, 2 (8.3%) had moderate and 2(50%) had severe dry eye. None of the patients had very severe signs and symptoms of dry eye. There was a strong significance of association of dry eye with types of allergic conjunctival disease. It was concluded that most patients with allergic conjunctivitis had no dry eye, patients with atopic conjunctivitis mostly had mild dry eye and patients with vernal conjunctivitis had moderate to severe dry eye.

Patients with mild type of allergic conjunctival disease having no signs and symptoms of dry eye were 29 (85.3%), mild were 14 (36.8%), moderate were 6 (25%) and with severe dry eye was 1 (25%). Patients with moderate allergic conjunctivitis with no signs and symptoms were 5 (14.7%), mild were 22 (57.9%), moderate were 16 (66.7%) and 1 (25%) patient had severe dry eye. In patients with severe allergic conjunctival disease, all had some form of dry eye. 2 (5.3%) had mild dry eye, 2 (8.3%) had moderate and 2 (50%) had severe dry eye. None of the patients had very severe dry eye. The degree of severity of allergic conjunctival disease was found to be significantly associated with the prevalence of dry eye. In this study mild allergic conjunctival disease was associated with no signs or symptoms of dry eye, moderate grade was associated with mild dry eye and severe grade of allergic conjunctival disease was associated with mild, moderate and severe dry eye.

The number of patients with allergic conjunctivitis with a normal absolute eosinophil count of 50 – 350/mm3 were 34 (58.6%) and with an AEC of > 350/mm3 were 24 (41.4%). Patients with atopic conjunctivitis with a normal range of AEC were 17 (45.9%) and > 350/mm3 were 20 (54.1%). All 5 (100%) patients with vernal conjunctivitis had a raised AEC. None of the patients with allergic conjunctival disease had an AEC of < 50/mm3. Raised AEC was frequently observed and was found to be significantly associated with allergic conjunctival disease.

Patients with allergic conjunctivitis having an OSDI score 0 – 12 (normal) was 1 (1.7%), score of 13 – 22 (mild) were 8 (13.8%), score of 23 – 32 (moderate) were 12 (20.7%) and 33 – 100 (severe) were 37 (63.8%). None of the patients with atopic conjunctivitis had a normal or a mild score. 23 – 32 (moderate) were 15 (40.5%) and 33 – 100 (severe)

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were 22 (59.5%). All patients with vernal conjunctivitis had severe dry eye according to the OSDI questionnaire which were 5(100%). This correlation of allergic conjunctival disease with dry eye based on OSDI scoring was found to be statistically significant (P = 0.031).

Patients with allergic conjunctivitis with a TBUT of < 10 sec were 27 (46.6%) and 29 (50%) for the right and left eye respectively. TBUT of ≥ 10 sec were 30 (53.4%) and 30 (51.7%). Patients with atopic conjunctivitis with a TBUT of < 10 sec were 15 (40.5%) for both eyes and with a TBUT ≥ 10 sec was 22 (59.5%) for both eyes. All patients with vernal conjunctivitis had a TBUT of ≥ 10 sec which were (100%) for both eyes. There was no correlation between abnormal TBUT with type of allergic conjunctival disease.

In patients with allergic conjunctivitis, 32 (55.2%) had an indoor occupation and 26 (44.8%) had an outdoor occupation. Patients with atopic conjunctivitis, 23 (62.2%) had an indoor occupation and 14 (37.8%) had an outdoor occupation. Patients with vernal conjunctivitis 3 (60%) had an indoor occupation and 2 (40%) had an outdoor occupation. There was no statistical correlation found between allergic conjunctival disease and type of occupation.

CONCLUSION: Allergic conjunctivitis and dry eye disease are major ocular surface disorders affecting millions of people. The chronic discomfort interferes with the quality of life of the patients for a long period of time.[1]The most common diagnosis challenging ophthalmologists are ocular allergies and dry eye and most often patients have both.[3]

In our study 100 patients with allergic conjunctival disease were analysed. Each individual was classified into allergic, atopic and vernal conjunctivitis based on clinical signs and symptoms. The severity of allergic conjunctival disease was based on the novel scoring system. All patients were then evaluated for dry eye disease based on the dry eye grading severity scheme and laboratory paramaeters like schirmer's test, tear break up time and tear meniscus height. An ocular surface disease index questionnaire was also used to assess severity of dry eye in all the patients.

In our study it was observed that allergic conjunctival disease was significantly associated with dry eye. It was also seen that the severity of allergic conjunctival disease had a significant correlation with dry eye disease. The dry eye grading severity scheme (DEGSS) being a comprehensive evaluation of dry eye showed a significant correlation between the two clinical conditions. It was also observed in our study that the objective clinical parameters like schirmer's test, TMH and TBUT assessment were not found to be correlating in allergic conjunctival disease patients for evidence of dry eye. In 66 patients with dry eye, 36 patients had a normal TMH, 53 patients had a schirmer's score ≥ 6mm under topical anaesthesia and 14 patients had TBUT ≥ 10 sec. Therefore there is a need for more reliable clinical parameters to be studied upon to be incorporated in assessing dry eye in allergic conjunctival disease. This study emphasises the need for similar studies in the future for better diagnosis and management of these two similar ocular surface conditions encountered frequently.

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