• Clinical Research •

Ocular surface characteristics and dry eye symptoms in primary biliary cholangitis patients complicated with seasonal allergic conjunctivitis

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Abstract

● **AIM:** To evaluate ocular surface characteristics and dry eye symptoms in primary biliary cholangitis (PBC) patients with seasonal allergic conjunctivitis (SAC).

● **METHODS:** This retrospective case-control study included 73 PBC patients: 38 with SAC (PBC+SAC group, 38 eyes) and 35 controls (35 eyes). All the participants underwent comprehensive ocular surface assessment and ocular surface disease index (OSDI) scoring. The severity of ocular allergy in PBC+SAC group was indicated by total ocular symptom score (TOSS), and correlation analysis was carried out between TOSS and ocular parameters.

● **RESULTS:** Age (59.60±10.69y *vs* 58.72±11.13y, *P*=0.629) and gender distribution (34 *vs* 32 females, *P*=0.713) did not differ significantly between groups. Compared to controls, the PBC+SAC group had higher dry eye prevalence (65.79% *vs* 28.57%, *P*=0.002), higher OSDI score [median: 34.3 (interquartile range, IQR: 26.05, 43.6) *vs* 21.2 (IQR: 15.15, 31.2), *P*<0.001], shorter non-invasive tear film breakup time [NIBUT, median: 4.16s (IQR: 2.52, 6.48) *vs* 6.88s (IQR: 4.81, 9.28), *P*<0.001], more severe upper meibomian gland loss (*P*<0.001), higher corneal fluorescein staining score [median: 1 (IQR: 0, 1) *vs* 0 (IQR: 0, 0.25), *P*<0.001], and higher rates of meibomian gland duct thinning (60.53% *vs* 31.43%, *P*=0.004) and distortion (73.68% *vs* 25.71%, *P*=0.001). TOSS was positively correlated with OSDI score (*r*=0.484, *P*<0.001) in PBC+SAC group but not with other ocular parameters (all *P*>0.05).

● **CONCLUSION:** PBC patients with SAC have higher dry eye prevalence and more severe dry eye symptoms, mainly evaporative dry eye with obvious upper meibomian gland morphological abnormalities. Allergic symptom severity is positively correlated with dry eye discomfort, suggesting allergic inflammation may exacerbate ocular surface burden in PBC patients.

● **KEYWORDS:** allergic conjunctivitis; dry eye; primary biliary cholangitis; ocular surface; meibomian gland
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INTRODUCTION

Primary biliary cholangitis (PBC), a prototypical autoimmune liver disease characterized by cholangocyte destruction and cholestasis, predominantly affects middle-aged women with a female-to-male ratio of 9:1[1]. Epidemiologically, the pooled global prevalence of PBC was 18.1 cases per 100 000 people, with a steady upward trend in incidence over the past decade[2]. Clinically, PBC is not merely a localized hepatic disorder: if left untreated with first-line agents such as ursodeoxycholic acid, it progresses to hepatic fibrosis, cirrhosis, and end-stage liver failure, imposing significant morbidity and mortality burdens on affected individuals[3]. Beyond its hepatic manifestations, PBC involves a range of extrahepatic involvement, with the sicca complex-commonly presenting as dry eye and/or dry mouth-being notably prevalent[4]. Study identified aqueous-deficient dry eye as the predominant type in PBC[5], whose pathogenesis may involve autoimmune-mediated lymphocyte infiltration that disrupts lacrimal gland function. This subclinical injury underscores the intimate cross-talk between hepatic autoimmunity and ocular surface integrity, positioning PBC as a disease with inherently high ocular comorbidity risk.

Seasonal allergic conjunctivitis (SAC) represent the most prevalent ocular allergic disorders, affecting 15%-40% of the global population[6]. Mediated by IgE-triggered type I hypersensitivity reactions, these conditions induce conjunctival inflammation, pruritus, and tear film instability. Despite being classified as distinct diseases, more and more studies in the past 20y have found that allergic conjunctivitis and dry eye share similar pathogenetic pathways, predispose to each other, and coexist with significant overlap[7-8]. Ocular allergy can aggravate the vicious cycle of dry eye through multiple key mechanisms, including tear film instability, ocular surface inflammation and damage, altered corneal sensitivity and systemic antihistamines[9].

A critical yet understudied observation is that autoimmune disease patients exhibit heightened susceptibility to allergic comorbidities due to underlying immune dysregulation, specifically impaired Treg function and excessive Th2 polarization[10]. This immune imbalance not only drives PBC's hepatic and systemic manifestations (including pruritus) but also primes the ocular surface for allergic sensitization, creating a pathophysiological link between hepatic disease and ocular allergy. Given that dry eye is frequently linked to multiple systemic diseases[11-12], alterations in the ocular surface can transcend their local significance, providing clinicians with valuable diagnostic and monitoring clues for systemic conditions[13]. While prior studies have elucidated the ocular surface changes in PBC patients and the interplay between allergic conjunctivitis and dry eye in the general population, research addressing their intersection–particularly the overlap of systemic and ocular pruritus in PBC–remains scarce. To address this deficit, the present study aimed to characterize ocular surface features and dry eye symptomology in systemically stable PBC patients with and without SAC and quantify the correlation between allergic symptom severity (assessed *via* Total Ocular Symptom Score, TOSS) and objective ocular surface parameters by aligning assessments with TFOS DEWS III recommendations[14].

PARTICIPANTS AND METHODS

Ethical Approval The research protocol adhered to the tenets of the Declaration of Helsinki, and was approved by the institutional ethics committee of Beijing YouAn Hospital, Capital Medical University (No.2025139). All patient data were de-identified and patient's informed consent was waived by the ethics committee.

Study Participants A case-control retrospective analysis was conducted in this study, between January 2024 and June 2025. Eligible patients were recruited from the Department of Hepatology and Immunology and Department of Hepatology and Gastroenterology, Beijing YouAn Hospital and met the following criteria: aged 18-70y; confirmed diagnosis of PBC based on the 2017 European Association for the Study of the Liver (EASL) criteria[1]; stable systemic conditions (no signs of hepatic decompensation such as ascites or hepatic encephalopathy, and no adjustment of PBC-specific medications like ursodeoxycholic acid within 3mo prior to ocular evaluation). Formal ophthalmic consultation was evaluated at the Department of Ophthalmology in the same hospital. Patients were either diagnosed as PBC+SAC if they met the 2019 AAO Preferred Practice Pattern criteria for SAC[15], with documented recurrent seasonal ocular symptoms (*e.g.*, itching, redness, tearing) in at least the previous year, and were not on medication for the current episode at the time of evaluation or PBC controls (no allergic conjunctivitis: no history of allergic eye disease, no self-reported ocular pruritus, and normal conjunctival appearance on slit-lamp examination). Furthermore, exclusion criteria included history of ocular surgery, contact lens wear, topical drug use known to affect ocular structure.

Ophthalmic Examinations All the participants underwent comprehensive ocular surface assessment performed sequentially from the least to the most invasive to minimize the impact on tear film physiology. Measurements of ocular indicators were performed by the same ophthalmologist (Peng WT), including tear meniscus height (TMH), noninvasive breakup time (NIBUT), infrared meibography measured by Keratograph 5M (K5M, Oculus, Optikgerate, Germany) and tear film lipid layer thickness (LLT) gauged by DED-3H (Kanghua, Chongqing, China). The temperature and humidity of the clinic were controlled between 22℃-24℃ with 50%-55% relative humidity. SAC patients diagnosed and underwent TOSS assessment by the same ophthalmologist (Xie LY) and also had serum-specific IgE tested.

Dry Eye and Allergic Conjunctivitis Symptom Evaluation Dry eye symptomology measured using Ocular Surface Disease Index (OSDI) questionnaire[16] containing a total of 12 questions and ranging from 0 to 100 points, of which questions 1-5 were symptoms of eye discomfort, questions 6-9 were limitations of daily activities, and questions 10-12 were environmental triggers. Allergic conjunctivitis symptomology was measured by TOSS questionnaire[17] which was the sum of itchy, red, and watery eye. For grading, a 4-point scale was used for the three symptoms ranging from 0 to 9 points: 0=no symptom; 1=mild symptom; 2=awareness of symptom but tolerable; 3=symptom unbearable.

Tear Evaluation TMH was measured by K5M using high magnification pre-calibrated digital imaging, and after blinking normally, the center average TMH value was obtained by repeating the measurement 3 times[18-20]. NIBUT was assessed by K5M which contactlessly and automatically recorded the first time and location of the subject's tear film break-

up. After blinking twice, the subject was asked to keep their eyes open and look straight ahead, and three measurements of NIBUT were averaged[18-20]. Tear firm LLT grade was semi-quantitatively evaluated by DED-3H, which reflected the thickness and stability of the lipid layer: grade 1, <15 nm; grade 2, 15 nm; grade 3, 30 nm; grade 4, 30-80 nm; grade 5, 80 nm; grade 6, 80-120 nm. Schirmer I test was performed using a 5 mm×35 mm filter paper (Jingming, Tianjin, China) placed inside the lower eyelid without anesthetic. The filtered paper was taken out after five minutes, and the outcome was recorded.

Ocular Surface Damage Evaluation Using the sodium fluorescein, corneal fluorescein staining (CFS) scoring was gained to represent the degree of corneal epitheliopathy. The score referred to the National Eye Institute/Industry grading scale[21] which divided the cornea into five sections, assigned a value from 0 (absent) to 3 (severe) to each section, and graded based on dye distribution on the background of cobalt blue light, for a range of 0 to 15 points.

Meibomian Gland Evaluation Assessment of the alterations in meibomian glands was performed by the same ophthalmologist (Ruan F). Meibomian gland loss (MGL) of the upper and lower eyelid was graded by infrared meibography using K5M in the Meibo-Scan enhanced contrast according to the criteria of Arita *et al*[22]: grade 0, no MGL; grade 1, MGL was less than 1/3 of the total area; grade 2, MGL accounted for 1/3 to 2/3 of the total area; grade 3, MGL was more than 2/3 of the total area. Additionally, the presence of morphological changes in meibomian glands ducts of upper eyelids such as thinning, dilatation and distortion were also documented at same time. Thinning or dilatation represented the diameter of the duct become thinner or thicker compared to the normal subjects, and distortion referred to any duct bended more than 45°[23].

Dry Eye Diagnosis The diagnostic criteria for dry eye referred to the TFOS DEWS II Diagnostic Methodology report[20], *i.e.*, if the OSDI score ≥13 and the NIBUT<10 seconds or CFS>5 corneal spots, the diagnosis can be made.

Determination of Serum Specific IgE Levels Allergen semi-quantitative screening and detection system (MEDIWISS Analytic GmbH, Moers, Germany) was used to assay the serum specific IgE of specific 10 inhaled allergens in accordance with the manufacturer's instructions and all serological tests were carried out by professional laboratory technicians. The grading of results followed the international standards[24] and was divided into 0-6 grades: grade 0, <0.35 IU/mL; grade 1, 0.35 to 0.70 IU/mL; grade 2, 0.70 to 3.5 IU/mL; grade 3, 3.5 to 17.5 IU/mL; grade 4, 17.5 to 50 IU/mL; grade 5, 50-100 IU/mL; grade 6, 100 IU/mL.

Statistical Analysis Statistical analyses were performed using IBM SPSS Statistics (Version 26.0, New York, USA). Because the measurement data did not meet the normal distribution confirmed by the Shapiro-Wilk test, the nonparametric Mann-Whitney *U* test was used for the comparison between different groups, presented as median (interquartile range, IQR). Chi-square test was used for comparison between groups for ordinary enumeration data, and the nonparametric Mann-Whitney *U* test was used for comparison between groups for enumeration data of different grouping levels, expressed in the form of *n* (%). The correlation between measurement data was performed using Spearman rank correlation analysis. All tests were two-tailed and $P<0.05$ was considered significant.

Table 1 Participant demographic information and clinical characteristics

Parameters	PBC+SAC (*n*=38)	PBC controls (*n*=35)	*P*
Age (y)	59.60±10.69	58.72±11.13	0.629
Females	34 (89.47%)	32 (91.43%)	0.713
Allergic rhinitis	23 (60.53%)	3 (8.57%)	<0.001

PBC: Primary biliary cholangitis; SAC: Seasonal allergic conjunctivitis.

RESULTS

Participants A total of 73 eligible participants was recruited into the two groups based on ophthalmic consultation results. The mean ages of the 38 PBC+SAC patients (34 females) and 35 PBC controls (32 females) were 59.60±10.69 and 58.72±11.13y, respectively ($P=0.629$). There were no sex differences between both the groups ($P=0.713$). All the participants recruited were Chinese. The demographic data were summarized in Table 1, and the clinical data of serum-specific IgE grade for ten inhalant allergens in PBC+SAC group were showed in Table 2.

Analysis of Ophthalmic Examinations Ocular clinical measurements are presented in Table 3. Among participants fulfilling the TFOS DEWS II diagnostic criteria for dry eye, the prevalence of dry eye [25 (65.79%) *vs* 10 (28.57%)] between the two groups was statistically significant ($P=0.002$). At the same time, there were also significant differences in OSDI score, NIBUT, Upper MGL grade, and CFS score between PBC+SAC patients and PBC controls (all $P<0.001$), where PBC+SAC patients exhibited shorter NIBUT (median 4.16s *vs* 6.88s) than that of the PBC control group and higher OSDI score (median 34.3 *vs* 21.2), worse upper MGL grade, and CFS score (median 1 *vs* 0). However, there were no statistical differences in TMH, tear film LLT grade, Schirmer I test, and lower MGL grade between the two groups (all $P>0.05$). Meibomian gland morphology was also significantly altered in PBC+SAC patients (Figure 1). Thinning and distortion of the ducts were demonstrated in 60.53% *vs* 31.43% and 73.68% *vs* 25.71% in the two groups, respectively (all $P<0.05$), while without notable changes in dilatation (5.26% *vs* 2.86%, $P>0.05$).

Table 2 Serum-specific IgE grade for inhalant allergens in PBC+SAC group *n* (%)

Allergen	Positive cases	Serum-specific IgE grade					
		Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Grade 6
Mugwort	32 (84.21)	1 (3.13)	5 (15.63)	5 (15.63)	7 (21.88)	13 (40.63)	1 (3.13)
Mixed tree	15 (39.47)	2 (13.33)	6 (40.00)	4 (26.67)	3 (20.00)	0	0
Ragweed	13 (34.21)	2 (15.38)	6 (46.15)	3 (23.08)	1 (7.69)	1 (7.69)	0
Cat hair	12 (31.58)	1 (8.33)	4 (33.33)	2 (16.67)	3 (25.00)	2 (16.67)	0
Hops	9 (23.68)	1 (11.11)	4 (44.44)	4 (44.44)	0	0	0
Dog dander	5 (13.16)	1 (20.00)	1 (20.00)	1 (20.00)	1 (20.00)	1 (20.00)	0
House dust	4 (10.53)	1 (25.00)	2 (50.00)	1 (25.00)	0	0	0
Mold	2 (5.26)	2 (100.00)	0	0	0	0	0
Mixed dust mite	1 (2.63)	1 (100.00)	0	0	0	0	0
Cockroach	1 (2.63)	0	1 (100.00)	0	0	0	0

PBC: Primary biliary cholangitis; SAC: Seasonal allergic conjunctivitis.

Table 3 Tear film and ocular surface characteristics of participants in PBC+SAC and PBC control group

Parameters	PBC+SAC (*n*=38)	PBC controls (*n*=35)	*P*
TFOS DEWS II dry eye criteria	25 (65.79%)	10 (28.57%)	0.002
OSDI score	34.3 (26.05, 43.6)	21.2 (15.15, 31.2)	<0.001
Tear meniscus height (mm)	0.16 (0.11, 0.25)	0.17 (0.10, 0.27)	0.689
Non-invasive tear film breakup time (s)	4.16 (2.52, 6.48)	6.88 (4.81, 9.28)	<0.001
Tear film lipid layer thickness			0.112
Grade 1	1 (2.63%)	1 (2.86%)	
Grade 2	6 (15.79%)	5 (14.29%)	
Grade 3	15 (39.47%)	12 (34.29%)	
Grade 4	10(26.32%)	12 (34.29%)	
Grade 5	5 (13.16%)	5 (14.29%)	
Grade 6	1 (2.63%)	0	
Schirmer I test (mm/5min)	9 (8, 12.25)	9 (7, 12)	0.675
Corneal fluorescein staining score	1 (0, 1)	0 (0, 0.25)	<0.001
Upper meibomian gland loss grade			<0.001
Grade 0	11 (28.95%)	17 (48.57%)	
Grade 1	25 (65.79%)	18 (51.43%)	
Grade 2	2 (5.26%)	0	
Lower meibomian gland loss grade			0.595
Grade 0	18 (47.37%)	18 (51.43%)	
Grade 1	18 (47.37%)	16 (45.71%)	
Grade 2	2 (5.26%)	1 (2.86%)	
Thinning	23 (60.53%)	11 (31.43%)	0.004
Dilatation	2 (5.26%)	1 (2.86%)	0.762
Distortion	28 (73.68%)	9 (25.71%)	0.001

PBC: Primary biliary cholangitis; SAC: Seasonal allergic conjunctivitis; OSDI: Ocular Surface Disease Index.

Connection between TOSS and Ocular Parameters

The correlation analysis between TOSS and various ocular indicators in PBC+SAC group are presented in Table 4. A significant positive correlation was detected between TOSS and OSDI score (P<0.001, r=0.484). There was no significant correlation between TOSS and the remaining indicators.

DISCUSSION

This case-control analysis yields a principal and novel finding: a diagnosis of allergic conjunctivitis is associated with a significantly more severe ocular surface phenotype in patients with PBC. Pruritus and sicca symptoms represent two of the most prevalent and clinically impactful extrahepatic manifestations of PBC. When these systemic symptoms manifest in the ocular surface, they translate into clinically distinct but potentially interrelated conditions–allergic conjunctivitis and dry eye–that should not be overlooked in the

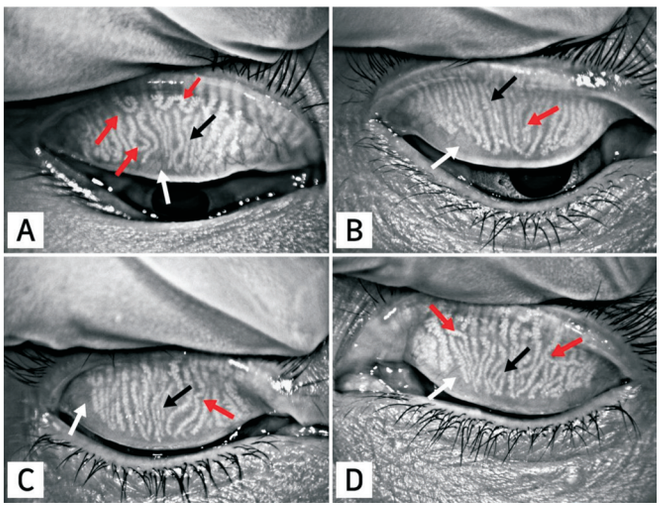

Figure 1 Morphological alterations in meibomian glands of patients with PBC complicated by SAC Representative infrared meibography images illustrate characteristic ductal changes in PBC+SAC patients, including thinning (black arrows), distortion (red arrows), and gland loss (white arrows). A: A 51-year-old female, OSDI=47.92, TMH=0.17 mm, NIBUT=3.78s, LLT=grade 3, Schirmer I=7 mm/5min; B: A 59-year-old female, OSDI=39.58, TMH=0.16 mm, NIBUT=4.01s, LLT=grade 2, Schirmer I=6 mm/5min; C: A 61-year-old female, OSDI=42.5, TMH=0.17 mm, NIBUT=3.87s, LLT=grade 3, Schirmer I=8 mm/5min; D: A 53-year-old female, OSDI=27.78, TMH=0.19 mm, NIBUT=2.29s, LLT=grade 2, Schirmer I=6 mm/5min. PBC: Primary biliary cholangitis; SAC: Seasonal allergic conjunctivitis; OSDI: Ocular Surface Disease Index; TMH: Tear meniscus height; NIBUT: Noninvasive breakup time; LLT: Lipid layer thickness.

Table 4 Correlation analysis of TOSS with other ocular surface parameters in PBC+SAC group

Parameters	TOSS	
	r	*P*
OSDI score	0.484	<0.001
Tear meniscus height	0.191	0.127
Non-invasive tear film breakup time	0.100	0.429
Upper meibomian gland loss grade	-0.071	0.576
Lower meibomian gland loss grade	-0.129	0.306
Schirmer I test	-0.199	0.113
Corneal fluorescein staining score	-0.103	0.413

PBC: Primary biliary cholangitis; SAC: Seasonal allergic conjunctivitis; TOSS: Total ocular symptom score; OSDI: Ocular Surface Disease Index.

comprehensive management of PBC patients.

Our study demonstrates that PBC patients with SAC exhibit a higher prevalence of dry eye, worse subjective symptomology, greater tear film instability, and more pronounced corneal epitheliopathy and meibomian gland alterations compared to PBC controls without ocular allergy. The significant positive correlation between allergic symptom severity (TOSS) and dry eye discomfort (OSDI) within the comorbid group further underscores a synergistic symptomatic burden. These results position SAC not as an incidental finding in PBC but as a critical disease modifier, transforming the classic autoimmune-driven aqueous-deficient dry eye into a more complex and severe “dry eye-allergy” comorbid phenotype. To the best of our knowledge, for the first time, we accurately reported a 65.79% prevalence of dry eye in PBC complicated by SAC adult patients based on the TFOS DEWS II dry eye diagnostic criteria, which is higher than that previously reported by Hom *et al*[8]. They found that the overlap between itchiness and dryness was 57.7% of the self-reported itchiness patients and 45.3% of the self-reported dryness patients according to the validated questionnaire.

Our findings must be interpreted within the broader context of PBC as a prototypical autoimmune liver disease. The hepatic pathology in PBC is characterized by a loss of self-tolerance and immune-mediated destruction of cholangiocytes[25]. The ocular surface, as an immunologically active site, often mirrors this systemic autoimmune dysregulation[26]. The novel insight from our study is that this autoimmune-primed, vulnerable ocular surface provides a fertile ground for exacerbated damage upon exposure to additional inflammatory triggers. The classic IgE-mediated type I hypersensitivity of SAC introduces a potent cascade of inflammatory mediators–including histamine, leukotrienes, and cytokines–that directly disrupt tear film stability, increase epithelial permeability, and induce neurogenic inflammation[27]. The convergence of the chronic, cell-mediated autoimmune response of PBC and the acute, humorally-mediated allergic response of SAC likely creates a self-perpetuating cycle of inflammation, accounting for the significantly worse clinical outcomes we observed in the comorbid group.

The observed exacerbation of meibomian gland morphology in PBC patients with SAC provides a compelling anatomical correlate for this immune cross-talk. While PBC itself is linked to sicca syndrome, the significantly higher upper eyelid meibomian gland loss and the increased prevalence of ductal distortion and thinning in the comorbid group suggest a pathology beyond simple comorbidity. Chronic allergic inflammation can induce peri-glandular fibrosis and direct cytotoxic effects on meibocytes[28]. This process may be amplified in the context of PBC, where a shared underlying immune dysregulation, particularly impaired regulatory T cell function and a propensity for Th2 polarization, could create a microenvironment that simultaneously drives autoantibody production and facilitates allergic sensitization and effector responses[29]. This mechanistic overlap suggests that the meibomian gland is not a passive bystander but an active target in the compounded immune attack, leading to accelerated glandular dropout and qualitative tear deficiency, which further destabilizes the tear film.

Interestingly, even though the morphology of meibomian gland was altered and tear film instability was present, we did not observe significant changes in tear film LLT grading, unlike previous studies by Suzuki *et al*[30] which noted an unexpected thickened LLT in adult SAC patients and Yang *et al*[31] which revealed a significant decreased LLT in pediatric AC patients. This discrepancy may be due to different ethnic groups and different measuring instruments, we measured semi-quantitative with DED-3H, while they used the semi-quantitative DR-1 tear film lipid layer interferometry system (Kowa, Tokyo, Japan) and the quantitative LipiView interferometer (TearScience, Morrisville, NC), respectively, and more studies should focus on this aspect.

The strong correlation between TOSS and OSDI scores in PBC patients with SAC, in the absence of similar correlations with objective signs like NIBUT, is highly instructive. It highlights that the patient's symptomatic experience is a complex amalgam of allergic pruritus and dry eye discomfort, which may be neurologically linked through sensitization of corneal and conjunctival nerves[32]. From a clinical standpoint, this correlation is profoundly practical: in a PBC plus SAC patient, a high TOSS score should alert the clinician to the likelihood of significant, concomitant dry eye symptoms, necessitating a comprehensive ocular surface workup beyond allergy management.

It is noteworthy that allergic rhinitis was significantly more prevalent in the PBC+SAC group. While AR may contribute to systemic inflammation and potentially influence ocular symptoms, we believe the observed ocular surface changes are primarily driven by local allergic conjunctivitis, given the direct correlation between ocular allergy severity (TOSS) and dry eye symptoms (OSDI), and the presence of objective signs of SAC. Future studies with larger cohorts could stratify patients by AR status to further delineate its independent contribution.

The clinical implications of our study are immediate and significant. They advocate for a paradigm shift in the management of PBC patients, from a reactive to a proactive and integrated model. Ophthalmologists and hepatologists should collaborate to implement routine screening for ocular allergy in PBC patients, particularly those with poorly controlled dry eye symptoms or significant ocular pruritus. The therapeutic strategy must correspondingly evolve. While lubricants address the deficiency, they do not target the inflammation. For persistent cases, introducing broader anti-inflammatory agents such as topical calcineurin inhibitors or T-cell targeted immunomodulators like cyclosporine may be necessary to suppress the shared underlying immune dysregulation.

Our study has several limitations. Its retrospective and case-control design robustly establish an association but cannot infer causality or temporal sequence. Prospective longitudinal cohorts are needed to confirm that the onset of SAC accelerates ocular surface damage in PBC. The recruitment from a single tertiary hepatology center may introduce a referral bias, potentially selecting for a more severe PBC phenotype. Furthermore, while we documented detailed morphological changes in the meibomian glands, we did not quantitatively assess meibum quality or expressibility, which could provide additional functional insights. Future research should employ conjunctival transcriptomics or cytology to delineate the precise molecular interplay between autoimmune and allergic pathways on the ocular surface in PBC. Ultimately, interventional trials are crucial to determine if early and aggressive control of allergic inflammation can alter the long-term progression of dry eye in this vulnerable population.

In conclusion, this study elucidates that comorbid allergic conjunctivitis acts as a significant modifier of ocular surface disease in PBC, transforming it into a more severe, symptomatic, and anatomically diffuse condition. The recognition that systemic pruritus and sicca symptoms in PBC may have clinically significant ocular correlates in the form of allergic conjunctivitis and dry eye demands heightened clinical vigilance. By framing PBC within the wider spectrum of autoimmune liver diseases and highlighting its interaction with allergic pathways, we provide a more holistic understanding of its extrahepatic manifestations. Recognizing this compounded burden is essential for developing integrated, multidisciplinary care strategies aimed at preserving visual function and improving the quality of life for patients navigating the complex interplay of systemic autoimmunity and ocular surface disease.

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