

# Clinical characteristics of patients with conjunctivochalasis

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**Purpose:** To evaluate the clinical characteristics of patients with conjunctivochalasis (CCh).

**Methods and materials:** This retrospective study enrolled 30 subjects diagnosed with conjunctivochalasis. Complete ophthalmic examination, including visual acuity assessment, slit-lamp examination, applanation tonometry, dilated funduscopy, tear break-up time, Schirmer 1 test, and fluorescein staining were performed in all patients. Age, sex, laterality, ocular history, symptoms, and clinical findings were recorded.

**Results:** The study included 50 eyes from 30 cases. Ages ranged from 45 to 80 years, with a mean age of  $65 \pm 10$  years. CChs grading were as follows: 30 (60%) eyes with grade 1 CCh; 15 (30%) eyes with grade 2 CCh; and five (10%) eyes with grade 3 CCh. CCh was located in the inferior bulbar conjunctiva in 45 (90%) eyes, and in the remaining five (10%) CCh was located in the superior bulbar conjunctiva. Ten (33.3%) patients had no symptoms. Dryness, eye pain, redness, blurry vision, tired eye feeling, and epiphora were the symptoms encountered in the remaining twenty (63.6%) patients. Altered tear meniscus was noted in all cases. The mean tear break-up time was 7.6 seconds. The mean Schirmer 1 test score was 7 mm. Pinguecula was found in ten patients.

**Conclusion:** Dryness, eye pain, redness, blurry vision, and epiphora were the main symptoms in patients with CCh. Dryness, eye pain, and blurry vision were worsened during downgaze and blinking. So CCh should be taken into consideration in the differential diagnosis of chronic ocular irritation and epiphora.

**Keywords:** ocular irritation, epiphora, dryness, eye pain, blurry vision

## Introduction

Conjunctivochalasis (CCh) is an ocular surface condition defined as a redundant loose nonedematous inferior bulbar conjunctiva. CCh is most often located between the globe and the lower eyelid, but CCh is not always limited to the inferior bulbar conjunctiva; it can be found in the superior and even within 360 degree of the bulbar conjunctiva.<sup>1</sup> Several reports regarding the etiology of CCh have been published,<sup>2-4</sup> but the exact etiology is still not well understood. Aging, ocular movement, ocular surface inflammation, and delayed tear clearance have been demonstrated as etiological factors.<sup>1-24</sup> Patients with CCh are generally asymptomatic; in cases where the patient is symptomatic, symptoms include tearing, foreign body sensation, redness, subconjunctival hemorrhage, eye pain, and blurriness, especially in downgaze. It is important to remember this condition in the differential diagnosis of chronic ocular irritation and epiphora. This study aimed to evaluate the clinical characteristics of patients with CCh.

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## Methods

A total of 50 eyes of 30 patients with CCh were recruited in this study. The study was a retrospective chart review of the patients. Written informed consents were obtained from all patients. CCh diagnosis was based on slit-lamp examination. CCh was graded according to the grading system proposed by Hoh et al.<sup>25</sup> The details of the grading criteria were as follows: grade 0, no persistent fold; grade 1, a single small fold; grade 2, two or more folds, but not higher than the tear meniscus; and grade 3, multiple folds and higher than the tear meniscus (Table 1).

Complete ophthalmic examination, including visual acuity assessment, slit-lamp examination, applanation tonometry, dilated funduscopy, tear film stability test, Schirmer 1 test, and vital staining with fluorescein were performed in all patients. Tear film stability assessed with the fluorescein tear break-up time (BUT), measured the interval in seconds between a complete blink and the first appearing dry spot or discontinuity in the precorneal film. Obliteration or disruption of the tear meniscus was noted. Schirmer 1 test was performed with Schirmer filter paper without anesthesia. A 5 mm curved portion of Schirmer filter paper was placed on the outer third of the lower eyelid. After 5 minutes, the amount of wetting measured from the edge of the lid was noted as the Schirmer 1 test wetting score. Values smaller than 5 mm were considered as aqueous tear deficiency.

Fluorescein dye was used for ocular surface staining. After fluorescein staining, the cornea was examined using slit-lamp evaluation with a yellow barrier filter and cobalt blue illumination. The pattern of fluorescein was recorded according to whether it was located at the interpalpebral exposure zone or the non-exposure zone. Age, sex, laterality, ocular history, symptoms, and clinical findings were recorded. Patients with a history of previous ocular surgery and chronic ocular diseases were excluded. None of these patients had any evidence of ocular infection or abnormal blinking.

## Results

The study included 50 eyes of 30 cases. Sixteen of the cases were female (53.3%) and 14 (46.6%) were male. Ages ranged from 45 to 80 years with a mean of age  $65 \pm 10$  years. Ten

(33.3%) cases had unilateral involvement while 20 (66.6%) had bilateral involvement. In unilateral cases, right eye involvement was noted in five (50%) cases and left eye was involved in five (50%) cases. CChs grading were as follows: 30 (60%) eyes with grade 1 CCh, 15 (30%) eyes with grade 2 CCh, and five (10%) eyes with grade 3 CCh. CCh was found in the inferior bulbar conjunctiva in 45 eyes (90%) and in the remaining five (10%) eyes, CCh was found in the superior bulbar conjunctiva. Conjunctival folds were distributed in 25 (50%) temporal, 15 (30%) nasal, and five (10%) central (6 o'clock) bulbar aspects of inferior bulbar conjunctiva; the remaining folds (five; 10%) were in nasal and in central bulbar aspects of the superior bulbar conjunctiva. Demographics, grading of CCh, and conjunctival folds distribution are shown in Table 2.

Ten (33.3%) patients had no symptoms. Dryness was the most common symptom found in all the patients. Fifteen (50%) patients suffered dryness. Dryness was more prominent in the morning, when patients were just awakening. Seven patients had eye pain, eight had several degrees of redness, five had blurry vision, and four had tired eye feeling in addition to dryness. Frequent blinking aggravated the dryness and blurry vision. Five (16.7%) patients with CCh complained of epiphora. Altered tear meniscus was noted in all cases. The mean BUT was 7.6 seconds. BUT was found to be lowest in grade 3 cases. Conjunctival staining with fluorescein was found in 40 (80%) eyes. In 40 eyes, conjunctival staining was found in the non-exposure zone, CCh area. In 15 of 40 eyes, corneal staining was also found at the non-exposure zone. Schirmer 1 test results were higher

**Table 2** Demographics: grading of CCh and conjunctival folds distribution

Demographics	Grade 1 CCh	Grade 2 CCh	Grade 3 CCh
Age, years (mean)	60	65	70
Sex			
Female	8	6	2
Male	10	3	1
Laterality			
Unilateral	6	3	1
Bilateral	12	6	2
Folds distribution (eyes)			
Inferior			
Temporal	14	9	2
Nasal	10	4	1
Central	4	1	0
Superior			
Temporal	0	0	0
Nasal	1	1	1
Central	1	0	1

**Table 1** Classification of CCh using the lid-parallel folds method grading of CCh

Grade	Number of folds and relationship to the tear meniscus height
0	No persistent fold
1	Single small fold
2	More than two folds and not higher than the tear meniscus
3	Multiple folds and higher than the tear meniscus

**Abbreviation:** CCh, conjunctivochalasis.

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**Table 3** Symptoms and clinical findings in patients with CCh

	Grade 1 CCh	Grade 2 CCh	Grade 3 CCh
Symptoms (patients)			
Dryness	7	7	1
Eye pain	0	5	2
Blurry vision	0	3	2
Epiphora	0	4	1
Redness	4	3	1
Findings (eyes)			
BUT	10	7	6
Schirmer I test	8	7	6
Conjunctival staining	20	15	5
Corneal staining	4	8	3

**Abbreviations:** CCh, conjunctivochalasis; BUT, tear break-up time.

than 5 mm in all cases. The mean Schirmer I test score was 7 mm. Lid margin inflammation was recorded in five eyes. History of subconjunctival hemorrhage was noted in four patients. Pinguecula was found in ten patients. Symptoms and clinical findings encountered are given in Table 3.

## Discussion

Laxity of the conjunctiva in quiet eyes was first reported by Middlemore<sup>26</sup> in 1835 followed by Ferradas<sup>27</sup> in 1879 and by Elschnig<sup>4</sup> in 1908. Elschnig<sup>4</sup> described this condition as nonedematous loose conjunctiva. In 1921, Braunschweig<sup>5</sup> introduced the term “lippenartige Falten” (lip-like folds) for these conjunctival pleats. Hughes<sup>1</sup> initially introduced the term conjunctivochalasis in 1942. CCh has been described as an age-dependent condition in several reports.<sup>1,2,29–32</sup> Zhang et al<sup>29</sup> estimated a prevalence of 44.08% in a senile Chinese population, while Mimura et al<sup>30</sup> noted an even higher prevalence (75.5%) in a hospital-based Japanese population. In another study, Gumus and Pflugfelder<sup>32</sup> stated that Fourier-domain optical coherence tomography confirmed increased incidence of CCh in the older age group. Similarly, the mean age was 65±10 years in this study.

Besides being more prevalent in the elderly, CCh is usually bilateral. In this study, 66.6% of eyes with CCh revealed a bilateral involvement. Mimura<sup>30</sup> reported that the mean grade of conjunctivochalasis was higher in female patients than in male patients. There was a female predominance in this report but there was no sex dominance in the mean grade of CCh. The location of CCh is most frequently found in the nasal and temporal regions of inferior conjunctiva versus middle zone of inferior conjunctiva or superior conjunctiva.<sup>1,2</sup> In an epidemiologic study<sup>31</sup> the authors found that CCh is usually located on the nasal and temporal side (944 eyes, 53.58%); Mimura et al<sup>30</sup> also reported that the mean grade of CCh was higher for the temporal conjunctiva

than the nasal conjunctiva. Similar to these reports, in the present study, 50% of conjunctival folds were distributed in temporal aspects of the conjunctiva, while 36% of conjunctival folds were distributed in the nasal aspects of the conjunctiva.

Previous eye surgery, age, and eyelid issues (blepharitis and meibomian gland secretion) were reported as associated conditions.<sup>1,2</sup> Contact lens wear (gas permeable more so than soft contact lenses), hyperopia, and short axial length were also found as risk factors for CCh.<sup>33–35</sup> In this study, five patients were wearing soft contact lenses for hyperopic correction. In 2012, Mimura et al<sup>36</sup> suggested that CCh may be associated with pinguecula. The authors aimed to assess the relationship between the prevalence and severity of CCh and pinguecula in a large consecutive series of 1,061 patients. They found that pinguecula was independently associated with CCh. In this study, pinguecula was recorded in ten patients.

In a recent study, patients with autoimmune thyroid disease (88%) presented with higher rates of CCh than the control group, thus establishing a possible association between thyroid disease and conjunctivochalasis.<sup>37</sup> Similarly superior limbic keratitis<sup>38</sup> and Ehler Danlos disease<sup>39</sup> were reported as in association with CCh. Further studies are required to explore relationships between systemic associations and CCh.

The exact mechanism of CCh is not known yet. Mechanical and inflammatory theories have been reported. Initially, a senile process related to conjunctival laxity was suggested in the 19th century. A gradual dissolution of the Tenon's capsule leads to an adhesion loss between the conjunctiva and the underlying sclera that combines with an age-related conjunctival thinning and stretching, causing CCh.<sup>1,2</sup> Eye movements were also suggested as a possible cause of CCh in 1921 when Braunschweig<sup>5</sup> noted that ductions often produced conjunctival displacement and laxity. Eye rubbing from irritation or allergy may also contribute to this laxity. Abnormalities in lid position were also suggested as an underlying etiology during the early 20th century.<sup>1,2</sup> Another hypothesis is that pressure from the eyelids may lead to impaired lymphatic drainage of the conjunctiva, which is supported by findings of lymphangiectasia, fragmentation of the elastic fibers, and no signs of inflammation on histopathology.<sup>40</sup> According to Watanabe et al's<sup>40</sup> histopathologic findings, mechanical forces between the lower lid and conjunctiva gradually affect the lymphatic flow. Chronic prolonged mechanical obstruction of lymphatic flow may result in lymphatic dilation and CCh. Similar to this finding, Zhang et al<sup>41</sup> investigated the relationship between the occurrence and development of CCh

and bulbar conjunctival lymphangiectasia. They found that the lamina propria of the bulbar conjunctiva in CCh specimens had mildly chronic inflammatory changes accompanied by a large number of lymphangiectasia.

In addition to these mechanical theories, histopathologic studies demonstrate elastosis, chronic nongranulomatous inflammation, fragmentation of the elastic fibers, and loss of collagen.<sup>13,42</sup> Zhang et al<sup>42</sup> found hyperplasia of conjunctival epithelium, decrease of elastic fiber, and chronic inflammation in specimens with CCh. The authors stated that the decrease of elastic fiber should be considered as a major cause of the changes in conjunctiva. In a prospective clinical and histopathological study of 29 specimens with CCh, Francis et al<sup>10</sup> showed that 22 of 29 specimens displayed normal conjunctival histology, while only four specimens showed inflammatory changes and three specimens showed elastosis. Fodor et al<sup>12</sup> found that inflammation plays a role in pathogenesis of CCh. In their report, the authors compared human leukocyte antigen (HLA-DR) expression of conjunctival epithelial cells in different grades of CCh. They found a significant increase ( $P < 0.005$ ) of HLA-DR expression in patients with severe CCh. But in mild and moderate cases HLA-DR expression was similar to normal controls. In another study of Fodor et al<sup>15</sup> the authors reported that tear osmolarity is elevated in only severe CCh; in mild and moderate cases, tear osmolarity was similar to normal controls. Zhang et al<sup>16</sup> compared tear protein between CCh and normal controls. They found that some apoptosis regulation proteins, apoptosis related proteins, and inflammatory proteins are in the CCh but not in normal controls. Erdogan-Poyraz et al<sup>17</sup> reported that inflammatory cytokine interleukin (IL)-6 and IL-8 levels were correlated with the severity of CCh. Guo et al<sup>18</sup> found that pentraxin 3 immunostaining was strongly positive in the subconjunctival stroma of CCh specimens. They stated that pentraxin 3 expression might partake in apoptosis and pathogenesis of CCh by upregulating expression of matrix metalloproteinase-1 (MMP-1) and matrix metalloproteinase-3 (MMP-3). In another study of Guo et al<sup>19</sup> the authors demonstrated that dysfunction of tumor necrosis factor-stimulated gene-6 might play a role in the pathogenesis of CCh by counteracting the transcription of MMP-1 and MMP-3 and the activation of MMP-1.

Acera et al<sup>20</sup> also found that pro-MMP-9 levels are significantly higher in CCh. Their results indicated that pro-MMP-9 levels decreased significantly after resection of CCh. In another study of Acera et al<sup>21</sup> the authors studied the concentration of IL-1beta, IL-6, and pro-matrix metalloproteinase (MMP) 9 in the tears of patients with different ocular surface diseases and examined the possible

relationship between the disorders and molecular inflammation. In this study, pro-MMP-9 levels in tears were elevated in all of the studied pathologies, especially in ocular allergy and CCh. However, IL-1beta and IL-6 were only found to be overexpressed in CCh. In a study of Li et al<sup>14</sup> the authors investigated the association of activity of MMPs and their tissue inhibitors in CCh specimens. They found that overexpression of MMP-1 and MMP-3 by CCh fibroblasts is correlated with their increased protein levels and proteolytic activities.

Ophthalmologists can often face patients with CCh in their routine daily practice. CCh is one of the most common misdiagnosed ocular surface diseases. The difficulty in diagnosing CCh is that the symptoms are nonspecific and the onset is insidious. CCh is generally asymptomatic; in symptomatic patients the clinical presentation can include irritation, tearing, blurry vision, and subconjunctival hemorrhage and exposure. Conjunctival folds lying along the inferior lid margin can destabilize the tear film, and disruption or aggravation of the tear film may cause irritation. These patients can be considered as dry eye patients. But the differentiation between CCh and dry eye can be easily made. Patients with either Aqueous tear deficiency (ATD) or CCh complain of dryness, but the dryness in ATD tends to be worse as the day progresses due to progressive exposure. In contrast, patients with CCh tend to be worse in the morning just after awakening. Patients with CCh complain of dryness especially in downgaze. This is because CCh folds are increased in downgaze. In contrast, ATD patients complain that the dryness tends to be worsened in upgaze because the interpalpebral exposure zone increases during upgaze. Frequent blinking results in spreading of the redundant conjunctiva and worsening of CCh at the 6 o'clock position, leading to aggravation of dryness. In contrast, increased blinking shortens the inter-blink interval, which stabilizes the tear film and improves the symptoms in ATD. Patients with ATD and CCh complain of similar dry eye symptoms; the aqueous tear secretion of the former is low, while that of the later may be normal. Although both ATD and CCh destabilize the tear film with a short tear-breakup time, a fluorescein-stained pattern is interrupted or obliterated by CCh, but not by ATD. Conjunctival or corneal staining can be seen in both ATD and CCh. The pattern of staining is located at the interpalpebral exposure zone in ATD and at the non-exposure zone in CCh.

Dryness was the main symptom in this study. Although the most common symptom found in this study was dryness, none of the patients had ATD. The mean Schirmer 1 test score was 7 mm. Dryness was more prominent in

the morning just after awakening. Altered tear meniscus was noted in all cases. The mean BUT was 7.6 seconds. BUT was found to be lowest in grade 3 cases. Conjunctival staining with fluorescein was found in 80% of eyes. Conjunctival staining was found at the non-exposure zone CCh area. In 15 of 40 eyes with conjunctival staining, corneal staining was also found at the non-exposure zone. Dryness was worsened by downgaze and frequent blinking. In cases with nasal CCh, CCh can impede tear outflow through the inferior punctum, resulting in epiphora. Five patients in this study presented with epiphora. In all five patients, CChs were located at the nasal side, and all patients had open lacrimal passage. At advanced stages, complaints may include severe pain, subconjunctival hemorrhage, and blurry vision while reading. Both pain and blurry vision are aggravated during downgaze due to the increasing of the conjunctival folds. Anterior migration of the mucocutaneous junction can be another finding in patients with CCh. This was probably caused by overspill of aqueous tears due to obliteration of the tear meniscus. As a result, regional lid-margin inflammation ensues and is frequently mistaken for blepharitis. Lid-margin inflammation was recorded in five eyes in this study. But there was no evidence of meibomian gland dysfunction. The eyelid blinking can elicit friction over the loose conjunctiva, and can lead to subconjunctival hemorrhage and also superior limbic keratoconjunctivitis. Because of poor affixation of CCh conjunctiva onto the sclera, subconjunctival vessels are prone to rupture by blinking or rubbing. In this study, history of subconjunctival hemorrhage was noted in four patients, but none of the patients presented with superior limbic keratitis. Several degrees of redness and tired eye feeling were the other symptoms recorded in this study.

In management of CCh, treatment is not recommended if the patient is asymptomatic. For those patients with severe disease, medical therapy can be suggested. This often includes the use of surface lubricants, antihistamines, and topical corticosteroids. In mild cases, these medications can often relieve the symptoms. Topical steroids and/or tear lubricants were prescribed for the symptomatic patients in this study. These medications relieved the symptoms. In cases where medical management remains unsuccessful, surgical treatment becomes necessary. In this study, surgical management were recommended for the two patients with epiphora. Surgical management often involves the resection of the redundant tissue. Several methods have been described, including crescent resection with or without suture, suture fixation of the redundant conjunctiva to the globe, pinching the excess conjunctiva and performing bipolar cauterization,

conjunctivoplasty using a simple medial conjunctival resection, conjunctivoplasty with argon green laser, paste-pinch-cut conjunctivoplasty, conjunctival semiperitomy combined with gentle subconjunctival cauterization, and conjunctivoplasty with amniotic membrane transplantation with or without the use of fibrin tissue glue.<sup>43-54</sup>

In conclusion, the majority of patients with CCh have been diagnosed with the more common ocular surface disease conditions, such as dry eye, blepharitis, or allergic eye disease, prior to the correct diagnosis. So it is important to consider this pathology during the diagnostic work-up of chronic irritation and epiphora.

## Disclosure

The author reports no conflicts of interest in this work.

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