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# Bacterial profiles and antibiotic susceptibility pattern in patients with chronic dacryocystitis

## Kronik dakriyosistitli hastalarda bakteri profili ve antibiyotik duyarlılık paterni

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**Abstract**

Aim: Dacryocystitis is an infection of the lacrimal apparatus, and without appropriate treatment, it can lead to serious complications such as orbital cellulitis and meningitis. In this study, we aimed to determine the frequency and antibiotic susceptibility of the bacterial pathogens in chronic dacryocystitis.

Methods: This cross-sectional study included 60 patients diagnosed with chronic dacryocystitis in the Ophthalmology department of Karabuk Training and Research Hospital between December 2019 and February 2020. Aerobic culture tests were performed using swab samples obtained from the lacrimal punctum of the patients. Identification and antibiotic susceptibility of isolates were determined using Phoenix-100™ (Becton Dickinson, Sparks, MD, USA) fully automated system.

Results: In total, 43 of 60 (71.7%) of patients were females, and the mean age was 56.78 (12.67) years. Aerobic bacteria were isolated from 51 (85%) of 60 samples. The most common pathogens were *Pseudomonas aeruginosa* (45%), *Staphylococcus epidermidis* (15.7%), and *Staphylococcus aureus* (11.8%) respectively. The most effective antibiotics against Gram-negative bacteria were aminoglycosides with a susceptibility of >90%. Gentamicin was also active against 85.7% of Gram-positive bacteria. Although in-vitro efficacy of ciprofloxacin was 81.5% against Gram-negative bacteria, it was mildly active against Gram-positive bacteria (52.5%). Methicillin resistance was detected in 33% of *Staphylococcus* species.

Conclusion: In our region, aminoglycosides may be preferred instead of fluoroquinolones for the empirical treatment of chronic dacryocystitis. However, since our study is single-centered and small-sized, these findings should be supported by large-scale studies in the future.

**Keywords:** Dacryocystitis, *Corynebacterium striatum*, *Pseudomonas aeruginosa*, Antibiotic, Ciprofloxacin, Gentamicin

**Öz**

Amaç: Dakriyosistit lakrimal aparatusun enfeksiyonu olup, uygun şekilde tedavi edilmezse orbital sellülit, menenjit gibi ciddi komplikasyonlara yol açabilir. Bu çalışmada kronik dakriyosistitte, bakteriyel patojenlerin sıklığını ve antibiyotik duyarlılık profilini saptamayı amaçladık.

Yöntemler: Bu kesitsel çalışmaya Aralık 2019- Şubat 2020 tarihleri arasında Karabük Eğitim ve Araştırma Hastanesi Göz hastalıkları bölümünde kronik dakriyosistit tanısı almış 60 hasta dahil edilmiştir. Hastaların punktumundan alınan sürüntü örneklerinden aerop kültür yapılmıştır. İzolatların identifikasyonu ve antibiyotik duyarlılığı Phoenix-100 (Becton Dickinson,MD, PA,USA) tam otomatize sistemle saptanmıştır.

Bulgular: Kronik dakriyosistitli toplam 60 hastanın 43'ü (%71,7) kadın olup yaş ortalaması 56,78 (12,67) idi. Altmış örneğin 51 inde aerop bakteri üredi (%85). En sık izole edilen patojenler *Pseudomonas aeruginosa* (%45), *Staphylococcus epidermidis* (15,7) ve *Staphylococcus aureus* (%11,8) idi. Gram negatif bakterilere en etkili antibiyotikler aminoglikozidler olup, duyarlılık %90'ın üzerinde idi. Gentamisin, Gram-pozitif bakterilere de %85,7 oranında etkili idi. Siprofloksasinin etkinliği Gram- negatiflerde %81,5 iken, Gram-pozitif bakterilere düşük etkili idi (%52,5). Stafilokok türlerinin %33' ünde ise metisilin direnci saptandı.

Sonuç: Yöremizde kronik dakriyosistitin ampirik tedavisinde florokinolonlar yerine aminoglikozidler tercih edilebilir. Bununla birlikte, çalışmamız tek merkezli ve küçük boyutlu olduğundan, bu bulgular gelecekte büyük ölçekli çalışmalarla desteklenmelidir.

**Anahtar kelimeler:** Dakriyosistit, *Corynebacterium striatum*, *Pseudomonas aeruginosa*, Antibiyotik, Gentamisin, Siprofloksasin

## Introduction

Dacryocystitis is the most common inflammatory disease of the lacrimal system. It may occur due to primary or secondary obstructions. Primary obstruction is usually idiopathic, whereas secondary obstruction occurs as a result of infection, trauma or neoplasm [1,2].

In acute dacryocystitis, obstruction of the lacrimal sac leads to the accumulation of tears, predisposing for infection. Clinical symptoms include pain, swelling, and redness in the lacrimal sac region [2]. In chronic dacryocystitis, there is chronic inflammation of the lacrimal sac, connective tissue, and nasal mucosa associated with dilation of the lacrimal sac due to nasolacrimal duct stenosis [1,3]. Also, there is no sign of infection; however, compression of the inflamed sac results in discharge of purulent material from the lacrimal punctum [4]. Insufficient lacrimal drainage leads to the colonization of microorganisms, leading to infection in the lacrimal sac. In previous studies, it has been shown that inflammation and fibrosis occur secondary to bacterial colonization in the lumen of the lacrimal sac in chronic cases [1,5]. Chronic dacryocystitis poses a potential risk of infection to the cornea and other neighboring tissues [6]. Without proper treatment, it can lead to life-threatening complications including orbital cellulitis, cavernous sinus thrombosis, and meningitis [2]. Although treatment guidelines recommend bacterial culture testing in patients with dacryocystitis, empirical antibiotic treatment is generally preferred [6,7]. However, the microbial spectrum of chronic dacryocystitis may change over time and lead to treatment failures [2,8]. Therefore, identification and antibiotic susceptibilities of microorganisms should be determined in patients with dacryocystitis.

In this study, we aimed to contribute to the empirical antibiotic treatment options by determining the frequency and in vitro antibiotic susceptibility profiles of bacterial pathogens in patients with chronic dacryocystitis.

## Materials and methods

This cross-sectional study included 60 patients who were admitted to the ophthalmology department of Karabuk Training and Research Hospital between December 2019 and February 2020 and diagnosed with chronic dacryocystitis. Patients who underwent surgery for dacryocystitis, who were treated using topical or systemic antibiotics within the last 10 days, or those not wanting to participate in this study were excluded. Informed consent was obtained from all patients before the study. This study was performed in accordance with the principles stated in the Declaration of Helsinki and approved by the Karabuk University Non-Interventional Ethics Committee (Date: 12/8/2019; No:2019/60).

Nasolacrimal duct irrigation was performed using sterile saline by inserting a lavage cannula from the lower punctum of the patients. Swab samples were obtained from the fluid and pus draining from the lower and upper puncti, transferred onto the Stuart transport medium (COPAN, Brescia, Italy), sent to the microbiology laboratory, inoculated onto 5% sheep blood agar (RTA laboratories, Kocaeli, Turkey), chocolate agar (RTA), and eosin methylene blue agar (RTA) and then incubated at 35 °C for 24–48 hours under aerobic conditions. Identification and antibiotic susceptibility testing of the isolates were performed using BD -Phoenix 100 (Becton Dickinson Diagnostic Systems, Sparks, MD, USA) fully automated system. Kirby–Bauer disc diffusion method was used for *Corynebacterium striatum*. Antibiotic susceptibility results were evaluated according to the European Committee on Antimicrobial Susceptibility Testing guidelines [9]. *Escherichia coli* ATCC 25922 and *Staphylococcus aureus* ATCC 29213 were used as quality control strains.

**Statistical analysis**

Statistical analysis of the data was performed using Minitab 17 (Minitab, Inc., PA, USA) program. Descriptive statistics were expressed as number, percentage, and mean (standard deviation: SD). Anderson–Darling test was used to determine whether the data were normally distributed. Two-sample t-test was used to compare continuous variables. Pearson chi-square or Fisher's exact test were used for evaluation of categorical variables. A *P*-value $\leq 0.05$ was considered statistically significant at 95% confidence interval.

## Results

The mean age of patients was 56.78 (12.67) years. Among 60 patients, 43 (71.7%) were females and 17 (28.3%) were males. The mean ages of females and males were similar with 55.67(13.59) years and 59.59 (9.79) years, respectively *(P*=0.221). Bacterial growth was detected in 51 (85%) of 60 samples, of which 37 (72.5%) were isolated from females and 14 (27.5%) from males. Gram negative bacterial growth was detected in 21 of 37 females and 6 of 14 males, while 8 males and 16 females were found to have Gram positive bacterial growth. There was no significant difference between gender and bacterial species (Gram-positive/Gram-negative) (*P*=0.375). The distribution of bacterial pathogens isolated from the samples are presented in Table 1. Among 51 isolates, 27 (53%) were Gram-negative and 24 (47%) were Gram-positive bacteria. The most common pathogens were *Pseudomonas aeruginosa* (45%), followed by *S. epidermidis* (15.7%), and *S. aureus* (11.8%). Twenty-three (85.2%) of 27 Gram-negative bacteria were *P. aeruginosa* and 4 other isolates were *Enterobacterales* species (spp.) (2 *Klebsiella pneumonia*e and 2 *Proteus mirabilis*). Antibiotic susceptibilities of Gram-negative strains are presented in Table 2. They were susceptible to more than 80% of all evaluated antibiotics. The most active antibiotics were amikacin, gentamicin, and netilmicin, with susceptibility rates of 96.3%, 92.6%, and 92.6%, respectively. The lowest susceptibility was detected for ciprofloxacin (81.5%). In other words, approximately 20% of the Gram-negative isolates were resistant to ciprofloxacin.

Antibiotic susceptibility rates of Gram-positive bacteria are shown in Table 3. Eighteen (75%) of 24 Gram-positive bacteria were *Staphylococcus* spp., 6 of which (33.3%) were resistant to methicillin. Four of the methicillin-resistant strains were coagulase-negative staphylococcus (CNS) and 2 were *S. aureus*. The most effective antibiotics were vancomycin, trimethoprim/sulfamethoxazole (TMP-SMX), and gentamicin, with susceptibility rates of 100%, 95.2%, and 85.8%, respectively. On the other hand, almost half of the isolates

(47.6%) were resistant to ciprofloxacin, levofloxacin, and erythromycin.

Table 1: Distribution of bacterial pathogens isolated from patients with chronic dacryocystitis (n=51)

| Bacterial species | n (%) |
|---|---|
| Gram-negative bacteria | |
| *Pseudomonas aeruginosa* | 23(45) |
| *Klebsiella pneumoniae* | 2(3.9) |
| *Proteus mirabilis* | 2(3.9) |
| Gram-positive bacteria | |
| *Staphylococcus* species | 18(35.3) |
| *S.epidermidis* | 8(15.6) |
| *S. aureus* | 6(11.8) |
| *S.schleiferi* | 3(5.9) |
| *S. saprophiticus* | 1(2) |
| *Corynebacterium striatum* | 3(5.9) |
| *Streptococcus pyogenes* | 3(5.9) |
| Total | 51(100) |

Table 2: Antibiotic susceptibilities of Gram-negative bacterial strains (n=27)

| | *P.aeruginosa* (n=23) | Enterobacterales spp. (n=4) | Total % (susceptible/total) |
|---|---|---|---|
| Amikacin | 23 | 3 | 96.3 (26/27) |
| Netilmicin | 22 | 3 | 92.6 (25/27) |
| Gentamicin | 22 | 3 | 92.6 (25/27) |
| Ciprofloxacin | 20 | 2 | 81.5 (22/27) |
| Cefepime | 22 | 2 | 88.9 (24/27) |
| Ceftazidime | 22 | 2 | 88.9 (24/27) |
| TZP | 21 | 3 | 88.9 (24/27) |
| TMP-SMX | * | 3 | |
| Levofloxacin | * | 2 | |
| Moxifloxacin | * | 2 | |

TZP: Piperacillin-tazobactam, TMP-SMX: Trimethoprim-sulfamethoxazole, * no EUCAST recommendation

Table 3: Antibiotic susceptibilities of Gram-positive bacterial strains (n=24)

| Antibiotic | CNS (n=12) | *S.aureus* (n=6) | *S.pyogenes* (n=3) | *C.striatum* (n=3) | Total % (susceptible/total) |
|---|---|---|---|---|---|
| Ciprofloxacin | 6 | 4 | * | 1 | 52.4 (11/21) |
| Clindamycin | 10 | 5 | 3 | 1 | 79.2 (19/24) |
| Erythromycin | 5 | 3 | 3 | * | 52.4 (11/21) |
| Gentamicin | 10 | 5 | * | 3 | 85.8 (18/21) |
| Levofloxacin | 6 | 3 | 2 | * | 52.4 (11/21) |
| Tetracycline | 4 | 6 | 3 | 2 | 62.5 (15/24) |
| Tobramycin | 6 | 6 | * | * | 66.6 (12/18) |
| TMP-SMX | 10 | 5 | ** | * | 83.3 (15/18) |
| Vancomycin | 12 | 6 | 3 | 3 | 100 (24/24) |
| Moxifloxacin | 8 | 4 | 2 | 2 | 66.6 (16/24) |
| Methicillin (Oxacillin) | 8 | 4 | ** | ** | 66.6 (12/18) |

CNS: coagulase-negative staphylococcus, TMP-SMX: Trimethoprim-sulfamethoxazole, * no EUCAST recommendation, ** not applicable

## Discussion

Dacryocystitis is the most common infection of lacrimal apparatus with unknown etiology. In the literature, it has been reported that female gender is a risk factor for the development of dacryocystitis [9]. Narrower nasolacrimal canal in females compared to males and hormonal changes may play a role [9-11]. Indeed, in our study, 70% of patients were females. In previous studies, 63.3%–78% of patients with dacryocystitis were reportedly females [2,9,10,12].

In this study, we have included 60 patients with chronic dacryocystitis. To prevent the development of a possible infection in neighboring tissues, dacryocystitis should be treated for a sufficient period of time with effective antibiotics. It is important to define the current microbiological profile, because the causative agents can change over time. Although Gram-positive bacteria have been reported as a common cause in many studies, Gram-negative bacteria were isolated more frequently in this study. In fact, Gram-negative bacteria are increasingly reported as the cause of chronic dacryocystitis [13,14]. For instance, Briscoe et al. [14] have reported that 25 of 41 bacteria (61%) isolated from 39 patients with dacryocystitis were Gram-negative, with the most frequently isolated species being *P. aeruginosa* (22%), similar to our study. In a study from Turkey conducted by Gümüşsoy et al. [12] in 150 samples obtained from 50 patients with chronic dacryocystitis, *P. aeruginosa* (10.8%) was the most frequently isolated Gram-negative pathogen. In the literature, the frequency of *Pseudomonas* spp. in patients with dacryocystitis has been reported in highly varying rates between 9.6% and 61% [1,2,9,14]. This may be due to regional differences and preferences of antibiotic prescription. In addition, overuse of antibiotics in patients with chronic dacryocystitis can lead to the selection of resistant strains. *Pseudomonas* aeruginosa is one of the opportunistic pathogens occurring particularly in hospitalized patients with chronic diseases who have had long-term antibiotic treatments. The fact that *P. aeruginosa* is naturally resistant to many routinely used antibiotics and that antimicrobial resistance is increasing limits the treatment options. Indeed, Infectious Diseases Society of America (IDSA) grouped six bacterial species in 2009 with the acronym ESKAPE [16], *Enterococcus faecium*, *S. aureus*, *K. pneumoniae*, *Acinetobacter baumanni*, *P. aeruginosa*, and *Enterobacter* spp., all of which show multidrug resistance and can escape via different resistance mechanisms from the biocidal effect of antibiotics. However, IDSA does not recommend antibiotics with local antibiotic resistance above 20% in empirical treatment [20]. Thus, empirical treatment protocols should be established according to the regional antibiotic resistance profiles.

In this study, the susceptibility of Gram-negative isolates to aminoglycoside antibiotics was over 90%. Similarly, 93%–99% susceptibility to amikacin [18-20] and 75%–91% susceptibility to gentamicin [12,18,19] have been reported in various studies in Turkey. In our study, Gram-negative strains were 81.5% susceptible to ciprofloxacin. In the national ARMOR surveillance study conducted in the USA, ciprofloxacin susceptibility was 94.9 % in 389 ocular *P. aeruginos*a strains [21]. Turkey-based studies have reported that susceptibility to ciprofloxacin was 51%–70% [12,22,23]. In this study, ciprofloxacin resistance (18.5%) was close to the empirical treatment limit (20%). Hence, aminoglycosides should be preferred instead of quinolones against infections caused by Gram-negative bacteria. Besides, 88.9% susceptibility was detected against cefepime, ceftazidime, and piperacillin/tazobactam. However, these antibiotics are not available in topical form and can only be administered parenterally, which makes them less preferred in the treatment of dacryocystitis in our region.

In this study, *Staphylococcus* spp. (35.2%, 18/51) were the second most common isolates. In previous studies, *Staphylococcus* spp. had been reported as the causative pathogens in dacryocystitis with a frequency ranging from 39%–75% [12,14,24,25]. In our study, 6 (33.3%) of 18 *Staphylococcus* strains were resistant to methicillin. Among these 6 strains, 4 were methicillin resistant CNS, and 2 were methicillin resistant *S. aureus* (MRSA). MRSA was first described in the United Kingdom In 1961 [26]. Recently, MRSA prevalence is below 5% in Nordic countries, but it is 25%–50% in southeast Europe. In Turkey, it has been reported as 30% [27]. Mills et al. [1] reported that the rate of MRSA in dacryocystitis cases is 21.7%. This rate was 20% in a study by Chung et al. [2] and 42.2% in the ARMOR surveillance study [21]. In this study, the most effective antibiotics for *Staphylococcus* spp. were vancomycin,

gentamicin, clindamycin, and TMP-SMX. Almost half of the strains were resistant (47.6%) to ciprofloxacin, which is commonly used. Fluoroquinolones, which are broad-spectrum antibiotics effective against many Gram-positive and Gram-negative bacteria, are often prescribed in ocular infections owing to their availability in both oral and eye drops forms, good ocular penetration, and low toxicity [26,28]. Ciprofloxacin, which is a second-generation quinolone derivative, has greater efficacy against Gram-negative microorganisms, whereas limited efficacy of ciprofloxacin has been demonstrated against Gram-positive bacteria [28]. It was approved for the topical treatment of bacterial corneal ulcers in 1990 [26]. Compared with ciprofloxacin, moxifloxacin, which is a fourth-generation quinolone, has been reported to have a broader efficacy against Gram-positive pathogens [28]. In this study, the susceptibility rates to ciprofloxacin and moxifloxacin were 52.4% and 66.6% respectively. In the literature, ciprofloxacin susceptibility of *Staphylococcus* spp. ranged from 60.2%–93.8% [15,21,23,26]. Moreover, a trend of increase in resistance of ocular pathogens against fluoroquinolones has been emphasized [26,28]. The ARMOR surveillance study reported that ciprofloxacin resistance of *S. aureus* strains was 39.8%, whereas this rate was 76.1% in MRSA. In addition, moxifloxacin resistance was 56.8% among MRSA strains [21]. In this study, the susceptibility of Gram-positive bacteria against gentamicin was 85.8%. In the literature, susceptibility rates of gentamicin have been reported as 79.1%–90.9% [12,23,29,30]. Although gentamicin has been frequently used in ocular infections for a long time, the resistance rate is still low, therefore, it can be preferred instead of quinolones in empirical treatment of ocular infections.

In the present study, three *C. striatum* were isolated as ocular pathogens. All strains were susceptible to vancomycin and gentamicin, but one strain was resistant to ciprofloxacin and erythromycin. Antibiotic resistance is gradually increasing in *C. striatum* strains. In the literature, among clinical *C. striatum* isolates, resistance to gentamicin and ciprofloxacin were 7.2%–75% [31-34] and 83%–100% [31.32, 35], respectively. In ocular *Corynebacterium* isolates, ciprofloxacin resistance has been reported as 50% [3,36]. *Corynebacterium* spp. are inhabitants of the skin and mucous membranes which can cause opportunistic infections. Resistance to fluoroquinolones in *Corynebacterium* spp. is caused by point mutations occurring in the gyrase gene. After exposure to fluoroquinolones, spontaneous mutations have reportedly occurred in skin and mucous membrane colonizers such as *Corynebacterium* spp., with the consequential emergence of quinolone-resistant strains [37]. Therefore, gentamicin may be preferred instead of ciprofloxacin in infections of *C. striatum*.

**Limitations**

This study has some limitations. It is a single-center study with a small sample size; therefore, our study results cannot be generalized. In addition, only aerobic culture testing was performed, and the presence of anaerobic bacteria was not investigated.

**Conclusions**

In this study, *P. aeruginosa* and *S. epidermidis* are most frequently isolated pathogens from patients with chronic dacryocystitis. Based on our study results, aminoglycoside antibiotics are highly effective against both Gram-negative and Gram-positive bacteria; however, quinolones showed reduced efficacy against Gram-positive bacteria. Thus, in our region, in patients with chronic dacryocystitis, aminoglycosides may be preferred instead of quinolones for empirical antibiotic treatment. On the other hand, these study results are preliminary, so they should be supported by large-scale studies. Bacterial profiles and antibiotic susceptibility can change over time in patients with chronic dacryocystitis. They should be monitored with active surveillance.

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