ORIGINAL RESEARCH

Microbiology and Antimicrobial Susceptibility in Adult Dacryocystitis

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Purpose: To investigate the microbiology and antimicrobial susceptibility of dacryocystitis in adults and identify the changing trends over time in Taiwan.

Methods: This is a single-centered, retrospective study. We retrospectively reviewed adult patients with dacryocystitis from January 2012 to December 2021 in a tertiary medical center in Taiwan. The pathogens and in vitro antimicrobial susceptibility of the pus cultures from the lacrimal sac were collected.

Results: Thirty-five cultures in acute and 211 cultures in chronic dacryocystitis were collected. Of the 220 isolates, a similar proportion of gram-positive (44%) and gram-negative (43%) aerobes were demonstrated in chronic dacryocystitis and more gram-negative aerobes (50%) than gram-positive aerobes (41%) in acute dacryocystitis. The most common pathogens were methicillin-resistant *Staphylococcus aureus* (MRSA; 28.1%) and *Pseudomonas aeruginosa* (28.1%) in acute dacryocystitis, while coagulase-negative *Staphylococci* was the most common micro-organism in chronic dacryocystitis. The effective antibiotics for gram-positive aerobes were vancomycin (100%), moxifloxacin (88%) and trimethoprim/sulfamethoxazole (78%). Meropenem (95%), amikacin (93%), and levofloxacin (91%) were sensitive to more than 90% of gram-negative aerobes in current study. High resistant species were also isolated in our cohort.

Conclusion: More gram-negative pathogens and more resistant species are rising in adult dacryocystitis. Understanding the bacteriology and antimicrobial susceptibility of the region is crucial for the empirical antibiotic selection in clinical practice. **Keywords:** dacryocystitis, antibiotic, microbiology

Introduction

Dacryocystitis is an inflammation of the lacrimal sac, usually results from nasolacrimal duct obstruction (NLDO). The obstruction of lacrimal system may lead to stasis of tears and accumulation of desquamated cells as well as mucoid secretions, consequently, create a fertile environment for secondary bacterial infection or chronic inflammation.

Dacryocystitis is typically categorized into acute or chronic forms. Acute dacryocystitis, an acute inflammation of the lacrimal sac, is usually presenting with erythematous, swelling and tenderness of the overlying tissue of lacrimal sac area. Chronic dacryocystitis is a more common and indolent form of the lacrimal sac inflammation with presentation of epiphora, mucoid discharge and chronic conjunctivitis. A few studies had attempted to analyze and conclude the different microbiology spectrum between acute and chronic dacryocystitis, and yet various outcomes demonstrated,^{1–3} which may result from the different geographic distribution of microbials and the distinct antibiotic culture of the medical systems. Besides, the more accessible medical resources and the application of broad-spectrum antibiotic may change the microbiology and its drug susceptibility.¹ In the late 20th century, more gram-positive bacteria were isolated in both acute and chronic dacryocystitis, with over 60% pathogens being gram-positive pathogens.^{4–6} However, more gram-negative organisms and methicillin-resistant *Staphylococcus aureus* (MRSA) have been isolated in lacrimal sac infections in recent years.^{2,7}

This study aims to investigate the microbiology and antimicrobial susceptibility of dacryocystitis in adults from 2012 to 2021 in southern Taiwan, and to identify the changing trends in bacteriology and drug resistance over time.

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Materials and Methods

We retrospectively reviewed medical records of patients with acute or chronic dacryocystitis from January 2012 to December 2021 at a single tertiary medical center, Kaohsiung Medical University Hospital. Patients were diagnosed with acute or chronic dacryocystitis according to the clinical signs and symptoms. Acute dacryocystitis was diagnosed when patients presented with acute swelling, pain, and erythematous change of the lacrimal sac area. Chronic dacryocystitis was diagnosed as persistent epiphora and purulent regurgitation from the lacrimal drainage system during nasolacrimal duct irrigation. Patients with pus culture from the lacrimal system were enrolled. We excluded pediatric or infantile patients who were under 18 years of age, dacryocystitis or NLDO secondary to trauma, neoplasm, or foreign body occlusion and patients without a lacrimal pus culture.

All samples were collected from the lacrimal system under sterile conditions. In acute dacryocystitis, the lacrimal sac pus was obtained with pus aspiration through overlying skin from the lacrimal sac with a 19-gauze needle and a 5-cc sterile syringe. In chronic dacryocystitis, pus was collected from the punctum with irrigation of the lacrimal system or from the surgically excised lacrimal sac. The samples were cultured with the aerobic and anaerobic Copan swab transport system or culture media. Clinically significant growth of the pathogens and their antibiotic susceptibility tests were reported within 5–7 days of culture. The antibiotic susceptibility tests were presented as sensitive, resistant, and intermediate according to the Clinical and Laboratory Standards Institute standards.

If the pus culture showed no pathogens or if there were entirely different pathogens isolated with an interval of at least one month between the two cultures, it is considered a new infection despite involving the same participant.

This study was approved by the institutional review board of Kaohsiung Medical University Hospital (KMUHIRB-E(I)-20220219) and in accordance with the ethical standards of the Declaration of Helsinki. Due to the retrospective manner, the informed consents from individual participants were waived. Nevertheless, the database was kept anonymized during data collection, and the analyses were conducted using the same encrypted computer.

Results

One hundred ninety-five dacryocystitis patients with lacrimal pus cultures were involved in current study. We excluded five patients under 18 years old, five trauma-related dacryocystitis, one dacryocystitis secondary to neoplasm, and one with foreign body in the lacrimal system. Thus, the final enrolled cases were 183 patients. There were 134 females (74%) and 49 males (26%). Thirty-five patients (19.1%) with 35 pus cultures had acute dacryocystitis, while 148 patients (80.9%) with a total of 211 pus cultures were diagnosed with chronic dacryocystitis. Five cultures in acute dacryocystitis yielded no growth of pathogen, resulting the total positive culture rate of 80.8%. Polymicrobial infections were observed in one pus culture (2.9%) in acute dacryocystitis, and 21 pus cultures (10%) in chronic dacryocystitis.

Of the 35 cultures in acute dacryocystitis, 13 (40.6%) gram-positive aerobes, 16 (50%) gram-negative aerobes and three (9.4%) anaerobic pathogens were isolated. Of 211 cultures in chronic dacryocystitis, 188 pathogens were isolated, including 84 (44.2%) gram-positive aerobes, 80 (42.6%) gram-negative aerobes, and 25 (12.8%) anaerobic pathogens. The isolated micro-organisms were demonstrated in Table 1. There were similar proportion of gram-positive and gram-negative aerobes in chronic dacryocystitis, and slightly more gram-negative isolates in acute dacryocystitis. More anaerobic pathogens were isolated in chronic dacryocystitis than in acute dacryocystitis (13.30% vs. 9.38%). MRSA (28.1%) and *Pseudomonas aeruginosa* (28.1%) were the most isolated pathogens followed by *Citrobacter koseri* (9.4%), methicillin-sensitive MSSA (6.3%), *Escherichia coli* (6.3%) and coagulase-negative *staphylococci* (CoNS) (6.3%) in acute dacryocystitis. In chronic dacryocystitis, CoNS (19.2%) was the most isolated micro-organisms, followed by *Pseudomonas aeruginosa* (13.3%), MRSA (8.5%), and α -hemolytic *Streptococcus* (5.9%).

The susceptibilities of antibiotics commonly used in our practice were shown in Tables 2–4. The most sensitive antibiotics to gram-positive aerobes were vancomycin (100%), moxifloxacin (88%) and trimethoprim/sulfamethoxazole (78%). Cefazolin (31%), oxacillin (31%), erythromycin (29%) and ampicillin/sulbactam (amp/sul) (33%) only yielded an around 30% sensitive rate to gram-positive isolates. Meropenem (95%), amikacin (93%), and levofloxacin (91%) were sensitive to more than 90% of gram-negative aerobes, while amp/sul (37%) and piperacillin (50%) had less sensitivity to

	Chronic Dacryocystitis N = 188	Acute Dacryocystitis N = 32	Overall Dacryocystitis N = 220
Gram-positive aerobes	83 (44.15%)	13 (40.63%)	96 (43.64%)
Staphylococcus aureus	24 (12.77%)	II (34.38%)	35 (15.91%)
MRSA	16 (8.51%)	9 (28.13%)	25 (11.36%)
MSSA	8 (4.26%)	2 (6.25%)	10 (4.55%)
Coagulase-negative Staphylococci	36 (19.15%)	2 (6.25%)	38 (17.27%)
α -hemolytic Streptococcus	II (5.85%)	0	II (5.00%)
β -hemolytic Streptococcus	6 (3.19%)	0	6 (2.73%)
Other gram-positive isolates	6 (3.19%)	0	6 (2.73%)
Gram-negative aerobes	80 (42.55%)	16 (50.00%)	96 (43.64%)
Pseudomonas aeruginosa	25 (13.30%)	9 (28.13%)	34 (15.45%)
Citrobacter koseri	9 (4.79%)	3 (9.38%)	12 (5.45%)
Escherichia coli	9 (4.79%)	2 (6.25%)	II (5.00%)
Stenotrophomonas maltophilia	9 (4.79%)	0	9 (4.09%)
Enterobacter species	5 (2.66%)	I (3.I3%)	6 (2.73%)
Klebsiella pneumoniae	5 (2.66%)	I (3.I3%)	6 (2.73%)
Acinetobacter species	5 (2.66%)	0	5 (2.27%)
Achromobacter xylosoxidans	2 (1.06%)	0	2 (0.91%)
Morganella morganii	2 (1.06%)	0	2 (0.91%)
Other gram-negative isolates	9 (4.79%)	0	9 (4.09%)
Anaerobic isolates	25 (13.30%)	3 (9.38%)	28 (12.73%)
Propionibacterium acnes	8 (4.26%)	0	8 (3.64%)
Bacteroides species	7 (3.72%)	0	7 (3.18%)
Gemella morbillorum	2 (1.06%)	0	2 (0.91%)
Parvimonas micra	2 (1.06%)	0	2 (0.91%)
Fusobacterium species	2 (1.06%)	0	2 (0.91%)
Actinomyces odontolyticus	l (0.53%)	I (3.I3%)	2 (0.91%)
Finegoldia magna	I (0.53%)	I (3.I3%)	2 (0.91%)
Peptostreptococcus species	0	I (3.I3%)	l (0.45%)
Capnocytophaga species	I (0.53%)	0	l (0.45%)
Micromonas micros	I (0.53%)		l (0.45%)

Table I	Microbiology	of Acute	and	Chronic	Dacr	yoc	ystitis
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Abbreviations: MRSA, methicillin-resistant Staphylococcus aureus; MSSA, methicillin-sensitive Staphylococcus aureus.

Table 2 Antimicrobial Susceptibility of the Gram-Positive Aerobes

	Cefazolin	Erythromycin	Moxifloxacin	Oxacillin	Amp/Sul	Tri/Sul	Vancomycin
Staphylococcus aureus							
MRSA	0/25 (0%)	2/25 (8%)	21/25 (84%)	0/25 (0%)	0/25 (0%)	23/25 (92%)	25/25 (100%)
MSSA	10/10 (100%)	2/10 (20%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)	10/10 (100%)
Coagulase-negative Staphylococci	12/38 (32%)	14/38 (37%)	33/38 (87%)	12/38 (32%)	12/38 (32%)	29/38 (76%)	38/38 (100%)
α-hemolytic Streptococcus	-	4/11 (36%)	6/7 (86%)	-	-	0/7 (0%)	11/11 (100%)
β -hemolytic Streptococcus	-	3/3 (100%)	-	-	3/3 (100%)	-	3/3 (100%)
Other gram-positive isolates	1/2 (50%)	1/3 (33%)	2/2 (100%)	1/2 (50%)	I/3 (33%)	2/2 (100%)	3/3 (100%)
Total gram-positive aerobes	23/75 (31%)	26/90 (29%)	72/82 (88%)	23/75 (31%)	26/79 (33%)	64/82 (78%)	90/90 (100%)

Abbreviations: MRSA, methicillin-resistant Staphylococcus aureus; MSSA, methicillin-sensitive Staphylococcus aureus; Amp/Sul, ampicillin/sulbactam; Tri/Sul, trimethoprim/ sulfamethoxazole.

Table 3 Antimicrobia	Susceptibility	of the	Gram-Negative Aerobes
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	Amp/Sul	Tri/Sul	Ceftazidime	Amikacin	Gentamicin	Levofloxacin	Meropenem	Piperacillin
Pseudomonas aeruginosa	-	-	33/34 (97%)	34/34 (100%)	32/34 (94%)	34/34 (100%)	15/15 (100%)	3/3 (100%)
Citrobacter koseri	4/12 (33%)	12/12 (100%)	/ (100%)	12/12 (100%)	12/12 (100%)	12/12 (100%)	7/7 (100%)	0/3 (0%)
Escherichia coli	3/11 (27%)	4/11 (36%)	8/11 (73%)	10/11 (91%)	8/11 (73%)	6/11 (55%)	4/4 (100%)	0/1 (0%)
Stenotrophomonas maltophilia	-	6/9 (67%)	_	-	-	9/9 (100%)	-	-
Enterobacter species	0/6 (0%)	4/6 (67%)	5/6 (83%)	6/6 (100%)	6/6 (100%)	6/6 (100%)	4/4 (100%)	2/2 (100%)
Klebsiella pneumoniae	5/6 (83%)	5/6 (83%)	5/6 (83%)	6/6 (100%)	5/6 (83%)	6/6 (100%)	3/3 (100%)	-
Acinetobacter species	4/5 (80%)	2/5 (40%)	3/5 (60%)	4/5 (80%)	4/5 (80%)	3/5 (60%)	3/3 (100%)	-
Achromobacter xylosoxidans	-	2/2 (100%)	2/2 (100%)	0/2 (0%)	0/2 (0%)	0/2 (0%)	1/2 (50%)	-
Morganella morganii	0/2 (0%)	2/2 (100%)	1/2 (50%)	2/2 (100%)	2/2 (100%)	2/2 (100%)	1/1 (100%)	0/1 (0%)
Other gram-negative isolates	1/4 (25%)	7/7 (100%)	6/8 (75%)	6/8 (75%)	5/8 (63%)	8/8 (100%)	4/5 (80%)	1/2 (50%)
Total gram-negative aerobes	17/46 (37%)	44/60 (73%)	74/85 (87%)	80/86 (93%)	74/86 (86%)	86/95 (91%)	42/44 (95%)	6/12 (50%)

Abbreviations: Amp/Sul, ampicillin/sulbactam; Tri/Sul, trimethoprim/sulfamethoxazole.

	Amp/Sul	Meropenem	Metronidazole
Propionibacterium acnes	7/7 (100%)	4/4 (100%)	0/7 (0%)
Bacteroides species	5/7 (71%)	7/7 (100%)	7/7 (100%)
Gemella morbillorum	2/2 (100%)	2/2 (100%)	1/2 (50%)
Parvimonas micra	2/2 (100%)	2/2 (100%)	2/2 (100%)
Fusobacterium species	2/2 (100%)	2/2 (100%)	2/2 (100%)
Actinomyces odontolyticus	2/2 (100%)	2/2 (100%)	0/2 (0%)
Finegoldia magna	2/2 (100%)	2/2 (100%)	2/2 (100%)
Peptostreptococcus species	1/1 (100%)	1/1 (100%)	1/1 (100%)
Capnocytophaga species	1/1 (100%)	1/1 (100%)	0/1 (0%)
Micromonas micros	1/1 (100%)	1/1 (100%)	1/1 (100%)
Total anaerobes	25/27 (93%)	24/24 (100%)	16/27 (59%)

Table 4 Antimicrobial Susceptibility of the Anaerobes

Abbreviation: Amp/Sul, ampicillin/sulbactam.

the gram-negative micro-organisms. In anaerobes, meropenem (100%) was the most sensitive antimicrobial agent, while metronidazole (59%) seemed to be the most resistant drug.

Discussion

Dacryocystitis is the most common infection of the lacrimal system mainly secondary to NLDO. In this study, there was a trend of female predominance (72%) in dacryocystitis, which is compatible to previous studies,^{1, 8, 9} and in concordance with the female preponderance in NLDO.¹⁰ It might be a result of smaller diameter of nasolacrimal duct in women,¹¹ or the hormonal change in postmenopausal females.¹² More chronic dacryocystitis was presented than the clinically acute one, which may imply the chronic structural change in the lacrimal system as its main pathophysiology.^{8, 13}

The common causative pathogens of dacryocystitis are changing over time. *Streptococcus pneumoniae* was once the most common species in the 1930s, but gradually replaced by *Staphylococci* (*Staphylococcus epidermidis* and *Staphylococcus aureus*) in the late 20th century.^{4, 5} The gram-positive pathogens remained to be the leading pathogens then, which was responsible for around 60% of the isolates in the 1980–1990s.^{4–6} However, recent bacteriologic analysis in dacryocystitis revealed an increasing incidence of gram-negative bacteria, especially the *Pseudomonas* species.^{1, 3, 7, 14} In the current study, there were similar proportion of gram-positive and gram-negative isolates in dacryocystitis, which supported the observation of an increasing number of gram-negative pathogens infection in recent studies.^{3, 7}

Stenotrophomonas maltophilia was a rare causative pathogen in dacryocystitis.¹⁵ It is mostly seen in immunocompromised patients, and highly resistant to majority of β -lactam antibiotics; as a result, it presented mostly as a nosocomial infection. This pathogen was reported in chronic dacryocystitis in one case (2.5%) in Briscoe's study and four cases (<1%) in Chaudhry et al^{16, 17} Further case reports demonstrated *Stenotrophomonas maltophilia* as a responsible micro-organism in chronic dacryocystitis in different age and various immune status around the 2010s.^{18, 19} In our study, we reported nine cases (4.79%) of *Stenotrophomonas*, all isolated from chronic dacryocystitis, which was the highest incidence among present literatures. The relatively high incidence of *Stenotrophomonas* highlights the emerging change that the rare, highly resistant gram-negative pathogens are rising recently.

The prevalence of pathogens responsible for acute or chronic dacryocystitis differed. The predominant microorganisms in acute dacryocystitis were *Staphylococcus aureus* (34.38%) and *Pseudomonas aeruginosa* (28.13%) in acute dacryocystitis, whereas CoNS (19.15%) was the most common pathogen in chronic dacryocystitis. The results were similar to that of reported in Bharathi et al,¹ since infections of highly virulent pathogens (*Staphylococcus aureus* and *Pseudomonas*) are more likely to present acutely, while a less virulent pathogen (CoNS) usually cause an indolent form of dacryocystitis. Higher frequency of MRSA was observed within the acute group, as reported in Mills et al,²⁰ may result from the more fulminant characteristic and antimicrobial resistance to first-line antibiotics.

The overall polymicrobial infection rate was 10.43% which was within the range of previous reported incident rates in adults with dacryocystitis (5–23%).^{3, 21} More polymicrobial micro-organisms were cultured from chronic dacryocystitis.

Moreover, more anaerobes were isolated from chronic dacryocystitis. The most common anaerobes in current study were *Propionibacterium acne* and anaerobic gram-negative bacilli (*Bacteroides* species and *Fusobacterium* species). These microorganisms constituted the normal floral in oral and skin flora.²²

More antimicrobial-resistant isolates were taking place nowadays. MRSA accounted for more than half of the *Staphylococcus aureus* in either acute or chronic dacryocystitis in current study. The increased frequency of MRSA was reported not only in dacryocystitis but all infectious diseases.^{20, 23, 24} Furthermore, all *Streptococcal pneumoniae* were resistant to erythromycin in our study, which was consistent with the increasing trend of erythromycin-resistant *pneumococci* in Asian countries over these years, and nearly total resistance (96.4%) in Zhou's study in 2010.²⁵ We reported a proportion of *Stenotrophomonas maltophilia*, which was strongly resistant to multiple broad-spectrum antibiotics due to its β -lactamases, efflux pumps for quinolone agents, and aminoglycoside acetyl transferases.^{18, 19}

Vancomycin (100%) remained to be the most effective antibiotic for gram-positive pathogens as previously reported.^{26, 27} The third generation quinolones such as moxifloxacin or gatifloxacin also possessed a high sensitivity to gram-positive aerobes.²⁷ Trimethoprim/sulfamethoxazole may be a reasonable choice for gram-positive and gram-negative aerobes with over 70% sensitivity rate in our study. Additionally, it was relatively sensitive to *Stenotrophomonas*, which is resistant to a broad spectrum of antibiotics.¹⁹ Of gram-negative aerobes, more antimicrobials yielded an over 90% sensitivity rate other than some resistance to piperacillin (50%). Cefazolin, oxacillin, erythromycin and amp/sul had a low sensitivity rate.^{26, 27}

Chen et al reported a significantly decreased sensitivity of erythromycin in gram-positive pathogens over time. They also reported no significant decreased in sensitivity of cefazolin (68.3%), sulfamethoxazole (79.3%), gatifloxacin (86.5%), and the same as our result, 100% sensitivity to vancomycin. In the susceptibility tests for gram-negative pathogens, they reported 74.6% sensitivity to gentamicin, 85% to ciprofloxacin, 92% to tobramycin, 92% to ceftazidime and 99.5% to gatifloxacin.²⁷ In our investigation, we observed a higher resistance to cefazolin and erythromycin among gram-positive pathogens than that shown in Chen's results. A small-scaled microbiology study for dacryocystitis in the same center in Taiwan was conducted from April 1995 to June 1998.²⁸ There were 50% sensitivity to erythromycin, 75% to ampicillin/sulbactam and 100% to vancomycin in gram-positive micro-organisms. Additionally, sensitivity rates were 50% for ampicillin/sulbactam, 77.8% for gentamicin, 100% for amikacin and piperacillin in gram-negative pathogens. Longitudinally, the sensitivities of erythromycin, ampicillin/sulbactam and piperacillin exhibited a decline when comparing to the results of the present study.

There were some limitations in current study. First, relatively small sample size was included in our study. This may result from the less culture performed clinically especially in acute dacryocystitis, since some clinicians might avoid immediate aspiration of the pus from lacrimal sac to avoid further fistula formation. Moreover, we did not exclude patients with previous antibiotic treatment since most patients had been treated before referral to our hospital, a tertiary medical center. There may be a bias that more resistant pathogens than those in the community might be presented in current study. Furthermore, the limitation of the retrospective manner should be recognized. Inevitably, there were missing data, and the initial treatment of each patient was barely identified if it was from other medical institutions and not recorded in the chart.

Conclusion

This study echoes to a trend that more gram-negative pathogens and more resistant species are rising in adult dacryocystitis. CoNS remains to be the leading pathogen in chronic dacryocystitis, but more *Pseudomonas* species perceived. More virulent species such as *Pseudomonas* and *Staphylococcus aureus* are more common in acute dacryocystitis. We identified MRSA more than MSSA, as well as a proportion of *Stenotrophomonas* suggest the high resistant micro-organisms are emerging. This study disclosed the causative pathogens and the drug susceptibility in dacryocystitis and provide a reference for empirical antibiotics selection.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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