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Original Article

Prevalence of Multi-Drug Resistance Bacteria among Adult Chronic Dacryocystitis Cases in Rajshahi Medical College Hospital

*Afroze T[1], Alam MS[2], Salam MU[3], Rahman N[4], Tasnim A[5], Ferdose J[6], Razzaque S[7]

Abstract:

Background: Chronic dacryocystitis is a common ophthalmological problem in Bangladesh. Clinicians need to prescribe antibiotics to patients as an early conservative treatment protocol and, for prevention of post-operative soft tissue infections. But in most of the cases, the empiric antibiotic therapy shows treatment failure and, consequent development of complications, which might be due to emergence and spread of Multi-Drug-Resistant (MDR) organisms.

Objectives: The objective of this study was to detect the prevalence rates of MDR organisms among adult chronic dacryocystitis cases, so that preventive measures can be undertaken in advance to stop its further spread.

Methods: A cross sectional descriptive type of study was carried out in the ophthalmology inpatient department of Rajshahi Medical College Hospital (RMCH), a tertiary care government teaching hospital, from January to December, 2017. One hundred diagnosed cases of chronic dacryocystitis undergoing DCR operation were selected and lacrimal sac swabs were collected from each of them. Isolation and identification of bacteria and their antibiotic sensitivity tests were done by standard procedures in the microbiology laboratory of the college. MDR bacteria were detected according to CDC (Centers for Disease Control and Prevention) and ECDC (European Centre for Disease Prevention and Control) guidelines.

Results: Of the 100 swabs, 73% were culture-positive and, of them, 72.59% were gram-positive and the rest were gram-negative. None of the gram-positive isolates were MDR, but 70% of the gram-negative isolates were MDR.

Conclusion: This study provided an early insight into the prevalence of MDR organisms among chronic dacryocystitis cases in the RMCH. The results might be beneficial for the therapeutic approach and prevention of MDR spreading in the ophthalmology wards of all hospitals.

Keywords: chronic dacryocystitis, bacterial agents, MDR, multi drug resistance.

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Introduction:

Dacryocystitis is an inflammation of the lacrimal sac.[1] Bangladesh, India and, other surrounding countries, due to their tropical disposition and also, due to the low socio-economic and poor personal hygiene status of the people, have high prevalence rates (around 19.5 cases per 10,000) of this condition.[2] Chronic dacryocystitis is more common than acute dacryocystitis.[3] It has the highest bed occupancy rates in the ophthalmology wards after cataracts.[4] Although the definitive treatment of chronic dacryocystitis is surgery, pre-treatment with antibiotics is important for good outcomes, as the chances of post-operative soft tissue infections are high and, can increase up to five times in the absence of antibiotic treatment.[5] However, studies have proved that causative organisms of chronic dacryocystitis are variable according to regional variations. Bacterial causatives account for 61-95% of the infections. Their susceptibility patterns also exhibit regional differences.[6]

1. Dr. Tamanna Afroze Assistant Professor Department of Microbiology, Udayan Dental College, Rajshahi.
2. Dr. Md. Shah Alam Professor, Department of Microbiology, Barind Medical College, Rajshahi.
3. Dr. Mahjuba Umme Salam Professor and Head, Department of Medicine, Sylhet Women's Medical College, Sylhet
4. Dr. Nahreen Rahman Assistant Professor, Department of Microbiology, Rajshahi Medical College, Rajshahi.
5. Dr. Anika Tasnim Assistant Professor, Department of Microbiology, Delta Medical College, Dhaka.
6. Dr. Jannatul Ferdose, Medical Officer, Department of Pathology and Microbiology, NIDCH, Dhaka
7. Dr. Sabrina Razzaque, Assistant Professor, Department of Dental Pharmacology, Udayan Dental College, Rajshahi

Corresponding author: Dr. Tamanna Afroze,
Assistant professor, Dept. of Microbiology,
Udayan Dental College, Rajshahi.
Email: drtamanna86@gmail.com

Unfortunately, as sufficient information about the susceptibility pattern of organisms in Bangladesh is lacking, antibiotics are prescribed on an empiric basis in the majority of the cases. This has resulted in the emergence and spread of antimicrobial resistance (AMR) among the causative bacteria.

AMR is currently one of the most critical public health threats throughout the world. According to CDC (Centers for Disease Control and Prevention), 70, 0000 people die each year globally from AMR. South and Southeast Asia are considered as hotspots for AMR and, Bangladesh is an important contributor in this region.[7,8] A systematic review of 46 studies done in the country in 2019 revealed that antibiotic resistance of tested bacteria is quite high and commonly prescribed first-line antibiotics are almost all ineffective. Long before this study, in 2003, a study in Chittagong showed that all patients with enteric fever were resistant to second-line antibiotic therapy.[8] Another study in 2019 found that 53% of the bacteria isolated from respiratory tract infections, wound infections, enteric fever, and diarrhea from various tertiary hospitals of Dhaka city between 2015 to 2019 were MDR.[9] The CDC and the ECDC (European Centers for Disease Control and Prevention) have defined MDR as acquired non-susceptibility to at least one agent in three or more antimicrobial categories.[10] MDR bacteria are mainly associated with nosocomial infections. However, some MDR bacteria are also responsible for some community-acquired infections.[11] Chronic dacryocystitis is a community-acquired infection. According to the ICDDR,B (International Center for Diarrhoeal Disease Research, Bangladesh) report, the community environment of Bangladesh is ideal for spreading of MDR bacteria for many reasons.[12] Moreover, the final operative procedure compels the patient to stay in the hospital for a long period of time. This in turn increases the risk of acquiring MDR bacteria from hospitals because they are quite prevalent in hospitals and their spread from more prevalent wards like surgery, and ICU to less prevalent wards like eye wards is common.

In the past, many studies have been conducted to see the prevalence of MDR bacteria in common infections like urinary tract infections, wound infections, respiratory tract infections, enteric fever, diarrhea, etc. and, the antibiotic choices have been updated and adopted accordingly. But, despite chronic dacryocystitis being a common ophthalmological infection, few such study has been conducted on it. As a result, the possibility of treatment failure with complications continues to increase.

Considering the above situation, this study was designed to see the prevalence of MDR bacteria among adult chronic dacryocystitis cases in Rajshahi Medical College Hospital with a view to prevent treatment failure and complications with an updated antibiotic profile in in this condition. Also, important preventive measures can be taken in advance to reduce the prevalence of MDR bacteria in the eye ward.

Materials and method:

Study design, time frame and location

A cross sectional descriptive type of observational study was carried out in the ophthalmology inpatient department of Rajshahi Medical College Hospital (RMCH), a tertiary care government teaching hospital of northern Bangladesh, from January to December, 2017.

Ethical clearance

Informed written consent was taken from every patient before enrollment for the study. The study protocol was approved by the Institutional Ethical Committee.

Study population and sample collection

By purposive sampling, 100 consecutive diagnosed cases of chronic dacryocystitis admitted into the ophthalmology ward of the RMCH, for DCR operation, were selected. Non-consenting patients and, those who had received antibiotics within the last 7 days were excluded from the study. Lacrimal sac swab was collected with a sterile swab stick from each enrolled case prior operative procedure with the help of the attending ophthalmologist. The swabs were then placed in a sterile capped tube for transfer to the microbiology laboratory of the college without delay.

Microbiological analysis

Collected samples (lacrimal swab) were inoculated into appropriate culture media (nutrient agar, blood agar, MacConkey agar and, chocolate agar) for bacteriological culture under aerobic condition. Isolated bacteria were identified by standard biochemical methods. Antibiotics were selected mainly according to the Clinical and Laboratory Standards Institute (CLSI) guidelines, 2017 and in a few cases it was done according to clinician's preference. Sensitivity tests were performed by modified Kirby-Bauer disc diffusion method. To identify MDR bacteria according to the CDC (Centers for Disease Control and Prevention) and the ECDC (European Centre for Disease Prevention and Control) guidelines, the antibiotic categories for gram positive cocci (Table a), *Enterobacteriaceae* (Table b) and, Pseudomonas (Table c) were included in the study.

Table a: For gram-positive cocci-

Category	Name of category	Included antibiotics
A	aminoglycosides	Gentamycin, tobramycin, amikacin
B	anti-staphylococcal β-lactams	Oxacillin
C	fluoroquinolones	Ciprofloxacin, moxifloxacin
D	glycopeptides	Vancomycin
E	macrolides	Azithromycin
F	phenicols	Chloramphenicol
G	tetracyclines	Tetracycline

Table b: For Enterobacteriaceae-

Category	Name of category	Included antibiotics
A	aminoglycosides	Gentamycin, tobramycin, amikacin
B	anti-pseudomonal penicillins + β-lactamase inhibitors	Piperacillin-tazobactum
C	non-extended spectrum cephalosporins: 1st and 2nd generations	Cefuroxim
D	extended spectrum cephalosporins: 3rd and 4th generations	Cefepime
E	fluoroquinolones	Ciprofloxacin, moxifloxacin
F	penicillins + β-lactamase inhibitors	Amoxiclav
G	phenicols	Chloramphenicol
H	tetracyclines	Tetracyclin

Table c: For Pseudomonas-

Category	Name of category	Included antibiotics
A	aminoglycosides	Gentamycin, tobramycin, amikacin
B	antipseudomonal cephalosporins	Cefepime
C	antipseudomonal fluoroquinolones	Ciprofloxacin
D	antipseudomonal penicillins + β-lactamase inhibitors	Piperacillin-tazobactum

Operational definition of MDR isolate

Multidrug-resistant isolate is defined as one that is resistant to at least one antibiotic belonging to three or more classes of drug.

Results:

Of the 100 collected samples of lacrimal sac swab from 100 different patients, 73 yielded growth of microbes [Table I]. Of these 73 isolates, 53(72.59%) were gram-positive and the rest (20) were gram-negative [Table II]. *Staphylococcus epidermidis* was the predominant (39.73%) gram-positive isolate followed by *Staphylococcus aureus* (30.12%) and, *Streptococcus pyogenes* (2.74%). *Pseudomonas aeruginosa* was the most frequent (13.7%) gram-negative isolate followed by *Escherichia coli* (9.6%) and, *Klebsiella pneumoniae* (4.12%) [Table III]. None of the gram-positive isolates were MDR. However, 14 (70%) isolates, all belonging to the gram-negative class were MDR.

Of the isolated *S. epidermidis,* 20 (68.96%) were resistant to at least one group of the tested antimicrobials. Seven (24.13%) isolates were resistant to two groups of antimicrobials. The highest (31%) resistance was observed against 'C' group (fluoroquinolones) of antimicrobials. However, no resistance was observed against 'B' (anti-staphylococcal β-lactams) and, 'D' (glycopeptides) categories of antimicrobials. [Table IV]

S. aureus isolates exhibited full susceptibility (Figure 1-a) to 'B', 'D' and, 'F' (phenicols) categories of antimicrobials. But 63.64% of the isolates showed resistance against at least one of the antimicrobial categories. Of the resistant isolates 28.6% were resistant to two antimicrobial categories. They showed high resistance against 'C' and, 'E' (macrolides) categories- at rates 50.0% and 42.9% respectively [Table V]. One of the 2 isolates of *St. pyogenes* showed resistance to group 'B' category of antimicrobials. [Table VI]

Among the *Enterobacteriaceae* microbes, 6 isolates- *E. coli* 4 (57.1%) and *Klebsiella spp.* 2 (66.67%) exhibited MDR. Two of the E.coli isolates (Figure 1-b) were resistant to all 8 categories of tested drugs and, three of them were resistant to 6 categories. Two isolated *Klebsiella* were found to be MDR. [Table VII]

All 10 (100%) *P. aeruginosa* isolates were resistant to at least one antimicrobial category and of them 8 (80%) were MDR. [Table VIII]

Figure 1: a- antibiogram of *S. aureus*, **b-** antibiogram of *E.coli*

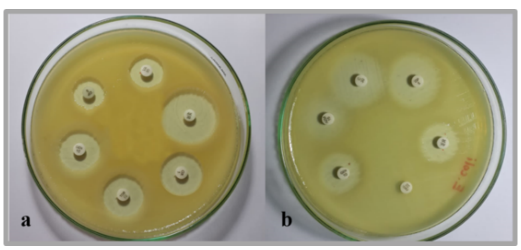

Table I: Culture positivity of collected samples (n=100)

Culture positivity	Number	Percentage
Culture positive	73	73%
Culture negative	27	27%
Total	100	100%

Table II: Gram staining variety of isolated organisms (n=73)

Gram stain	Number	Percentage
Gram-positive	53	72.59%
Gram-negative	20	27.42%
Total	73	100%

Table III: isolated organisms from cases (n=73)

Gram stain	Organism	Number	Percentage
Gram-positive	*S. epidermidis*	29	39.73%
	S. aureus	22	30.12%
	St. pyogenes	2	2.74%
Gram-negative	*P. aeruginosa*	10	13.7%
	E. coli	7	9.6%
	Klebsiella spp.	3	4.12%
Total		73	100%

Table IV: Resistance pattern of *S. epidermidis* to different antibiotic categories (R= Resistant, N= No**)**

Isolated number of S. epidermidis	Antibiotic category							Number of resistant category	MDR	Total number of MDR
	A	B	C	D	E	F	G			
1	R		R					2	N	
3			R					1	N	
4					R			1	N	
5	R				R			2	N	
6			R		R			2	N	
7	R						R	2	N	
8					R			1	N	
9			R					1	N	
10			R					1	N	
11			R					1	N	
13	R		R					2	N	
18						R		1	N	
21						R		1	N	
22						R		1	N	
24						R		1	N	
25	R						R	2	N	
26			R			R		2	N	
27			R					1	N	
28	R							1	N	
29						R		1	N	

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Table V: Resistance pattern of *S. aureus* to different antibiotic categories (R= Resistant, N= No**)**

Isolated number of *S. aureus*	Antibiotic category							Number of resistant category	MDR	Total number of MDR
	A	B	C	D	E	F	G			
1					R			1	N	-
3			R		R			2	N	
4			R					1	N	
6					R			1	N	
7			R					1	N	
8					R			1	N	
12			R					1	N	
13	R						R	2	N	
14			R		R			2	N	
16	R							1	N	
17			R					1	N	
19			R		R			2	N	
20	R							1	N	
21							R	1	N	

Table VI: Drug resistance pattern of *St. pyogenes* in different antibiotic categories
(R= Resistant, Y= yes, N= no**)**

Isolated number of *St. pyogenes*	Antibiotic category							Number of resistant category	MDR	Total number of MDR
	A	B	C	D	E	F	G			
1		R						1	N	-
2								-	N	-

Table VII: Resistance pattern of Enterobacteriaceae (*E. coli* and *Klebsiella*) to different antimicrobial categories (R= Resistant, Y= Yes, N= No**)**

Isolated number of Enterobacteriaceae	Antibiotic category								Number of resistant category	MDR	Total number of MDR
	A	B	C	D	E	F	G	H			
E1		R	R	R	R	R		R	6	Y	4
E2			R	R	R	R			4	Y	
E3					R				1	N	
E4	R	R	R	R	R	R			6	Y	
E5			R			R			2	N	
E6	R	R	R	R	R	R	R	R	8	Y	
E7	R							R	2	N	
K1			R	R					2	N	2
K2	R	R	R	R		R	R		6	Y	
K3	R	R	R	R	R	R	R	R	8	Y	

Table VIII: Resistance pattern of *Pseudomonas aeruginosa* to different antimicrobial categories
(R= Resistant, Y= Yes, N= No**)**

Isolated number of enterobacteriaceae	Number of resistant category				Number of resistant category	MDR	Total number of MDR
	A	B	C	D			8
P1			R		1	N	
P2	R	R	R		3	Y	
P3	R				1	N	
P4	R	R	R	R	4	Y	
P5	R	R	R		3	Y	
P6	R	R	R		3	Y	
P7	R	R	R	R	4	Y	
P8	R	R	R	R	4	Y	
P9	R	R	R	R	4	Y	
P10	R	R	R	R	4	Y	

Discussions:

Though surgical intervention is the mainstay of treatment of chronic dacryocystitis, appropriate pre-operative antibiotic treatment raises success rates.[5] AMR and, more importantly MDR, is the key factor influencing the effectiveness of antibiotics.[11,12] In the index study, out of 100 lacrimal sac swabs from chronic dacryocystitis patients, none of the 53 gram-positive isolates showed MDR. But 70% of the gram-negative isolates exhibited resistance to 3 or more categories of the tested antibiotics.

Simulating studies conducted in Ethiopia, Nepal and, India showed a gram-positive preponderance (>70%) among the study samples.[13,14,15] In the Ethiopian study, Streptococcus pneumoniae was the top (23%) gram-positive isolate with more than 90% sensitivity to chloramphenicol. Haemophilus influenzae (9.9%), on the other hand, was the most common gram-negative organism with highest susceptibility to tetracycline.[13] The study in Nepal revealed a 14.13% of mixed growth in the test samples and, coagulase-negative *Staphylococcus aureus* was the most predominant growth in the mixed isolates. This study, and also another Indian study, demonstrated an excellent antimicrobial susceptibility to chloramphenicol and nalidixic acid. Other antimicrobial agents showing susceptibility were the quinolones (ofloxacin, ciprofloxacin) and, the cephalosporins (cefazolin, cefixime).[14,15] In an Egyptian study on 25 chronic dacryocystitis patients, *Klebsiella* was the leading gram-negative infection, and according to this study, gatifloxacin and amikacin were the implied antibiotics of choice.[16] However, none of these studies aimed at exploring MDR prevalence among the isolates. Shahraki et al found that chloramphenicol was the most sensitive and co-trimoxazole was the most resistant of the antibiotics used.[17] A gram-negative preponderance was found among acute dacryocystitis patients in Tehran in a study conducted by Eshraghi et al and also in a few other studies.[18,19] High rates of culture-positive samples among the chronic dacryocystitis patients in the index study and, in other Asian and African studies may be due to the low living standards and, poor personal hygiene of the people in these parts of the globe.[20,21]As the bacterial infection prevalence is high, the AMR prevalence is also expected to be high these continents. The greater prevalence of gram-positive bacterial infection among chronic dacryocystitis patients in the most of the studies may be due to the nasal and conjunctival normal flora entering into the lacrimal apparatus in presence of obstruction of the nasolacrimal duct.[6,22]

The researchers in this study could not include all antimicrobial categories recommended by the CDC and the ECDC guidelines, due to logistic constraints. That might be a cause of no MDR among the gram-positive isolates. Even with the preferred limited category that they have worked with, it had not been possible to include all antibiotics due to limited time, material and workplace range. However, the 70% prevalence of MDR among the gram-negative isolates in this study was quite high. In general, gram-negative bacteria exhibit greater AMR than the gram-positive because of their unique outer membrane and high transformation rate. [23,24]

The index study did not find any fungal growth in the samples, but other studies did.[16]Although, no MDR isolates were detected among gram-positive organisms, but considering its high prevalence rates in different community acquired infections,[25] more studies are to be conducted among chronic dacryocystitis patients to demonstrate that this finding is reproducible before taking it as a recommendation. On the other hand, the high prevalence rate of MDR isolates among gram-negative organisms in this study imposes a warning in advance to deal with chronic dacryocystitis infections seriously. This finding, too, needs further validation with larger-scale studies for validation. Therefore, as preventive measures, improved hygiene and sanitation should be maintained and self antibiotic medication without indication should be minimized at the community level. At the hospital level, empiric antibiotic therapy, long hospital stay of patients before operation should be avoided. Besides, the eye wards should be kept away from other wards where MDR organisms are might be prevalent. The government and all other related sectors should act in co-ordination, and keeping in line with the WHO (World Health organization) and CDC recommended strategies and plans to treat and prevent the spread of MDR bacteria.

Conclusion:

This study provides an insight into the prevalence and pattern of MDR organisms among chronic dacryocystitis cases in a northern medical college hospital of Bangladesh. The results might be beneficial for the therapeutic approach and prevention of MDR spreading in the ophthalmology wards of all hospitals. However, nation-wide and larger-scale studies are necessary for making valid recommendations.

Limitations: It was a single center study, so may not represent a universal scenario. It was also a very small-scale study. Larger studies are necessary to draw authentic inferences.

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