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Original Article

Antimicrobial Resistance in Patients with Chronic Ear Discharge Awaiting Surgery in Tertiary Care Hospital of Central India

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ABSTRACT

Introduction: The department of Otorhinolaryngology is a tertiary care facility located in central India. Since the hospital is a referral centre, it is possible that it will get long-term Chronic Suppurative Otitis Media (CSOM) patients who have previously been subjected to numerous antibiotics. Enhancing laboratory surveillance of antimicrobial resistance (AMR) has been recommended; this is a priority stated in the national and international action plans to combat AMR. The kind of bacterial infections present in CSOM and their patterns of AMR may also be useful in guiding treatment strategies.

Aims/ objective: To determine the antimicrobial resistance and sensitivity pattern among patients presenting with CSOM and awaiting surgery in a tertiary care hospital in central India.

Materials and Method: 108 patients presenting with CSOM and chronic ear discharge planned for surgery with bacterial infection were included in our study. Using a sterilized ear swab and strict aseptic procedures, an expert otolaryngologist collected pus from the auditory canals of CSOM patients and submitted the sample to the laboratory for microbiological testing. Following the standard guidelines for inoculating culture media, samples were directly injected into blood agar, chocolate agar, and MacConkey agar. The Kirby-Bauer disc diffusion method was used to assess the sensitivity to antibiotics of all isolated microorganisms. We have determined the findings with respect to the CLSI 2018 guidelines.

Results: *Pseudomonas aeruginosa* was most frequently identified pathogenic micro-organism in 45.37% of cases followed by *staphylococcus aureus* (37.96%). Most of the pseudomonas isolates were resistant to carbenicillin (62.07%) and ceftazidime (46.55%). Most of staphylococcus aureus isolates were resistant to ciprofloxacin (79.59%) followed by amoxicillin + clavulanate (55.1%). 63.27% of staph. aureus isolates were sensitive to cotrimoxazole. Resistance to more than or equal to 6 antibiotics was highest in *pseudomonas aeruginosa* and lowest in *proteus spp.*

Conclusion: There seems to be a positive correlation between over- utilization of antibiotics and antimicrobial resistance. It becomes imperative to investigate each patient of CSOM through microbiological culture and sensitivity. This will certainly help in solving the problem of delay in surgical cure due to antimicrobial resistance.

Keywords: Antibiotics, Chronic Ear Discharge, Ear Surgery, CSOM, Antimicrobial Resistance.

INTRODUCTION

A chronic inflammation or recurring infection of the middle ear cleft, which includes the mastoid air cells, middle ear, and Eustachian tube, is known as CSOM (chronic suppurative otitis media). [1,2] It is the infectious ear condition that affects children and young people the most frequently. [3] It is defined by ear discharge or chronic, sporadic, or recurrent otorrhea via a damaged tympanic membrane that lasts for at least two weeks. [4]

Chronic infection from resistant microbes that is not responding to antimicrobial therapy is one of the variables that causes surgical cure to be delayed. One of the most common reasons for young patients to need prescriptions for antibiotics is CSOM, which is primarily caused by bacteria. [5] A worldwide CSOM incidence of 4.7 percent was found in a meta-analysis that covered 15 of the 21 WHO regions. This translates to 31 million patients annually, of which 22.6 percent (7.6 million) affected are children under the age of five. An estimated 20,000 people pass away each year as a result of complications from CSOM. [6] Children with CSOM may experience hearing impairment and have poor academic performance. [7]

In underdeveloped nations, improper usage of antibiotics is frequently linked to CSOM. [8, 9] The absence of defined therapeutic guidelines, use of antibiotics without prescription, self-medication, and limited laboratory facility access could be the cause of this. Furthermore, the high price of second-line antibiotic may lead to the recurrent use of ineffective drugs, which could accelerate the emergence of antimicrobial resistance (AMR). [10] AMR has been demonstrated to be correlated with the improper usage of antibiotic. [8, 11]

All age groups are affected by ear infections, but children are more susceptible to them due to a short length of Eustachian tube, a more horizontal position, greater amount of flaccid cartilage, and immature immune system. [12] *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Escherichia Coli* and *Proteus* species are among the frequent micro-organisms identified in CSOM. [13] However, the kind of

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bacteria involved in CSOM varies depending on geographic location and climatic circumstances.[14, 15]

The main causes of the higher incidence of CSOM in underdeveloped countries are low socioeconomic position, unsanitary living circumstances, malnutrition, overcrowding, insufficient antibiotic therapy, incorrect drug selection, and mis-use of antimicrobials. [16] Compared to the urban community, the underprivileged rural community has a considerably greater incidence rate of CSOM. [17]

The department of Otorhinolaryngology is a tertiary care facility located in central India. Since the hospital is a referral centre, it is possible that it will get long-term CSOM patients who have previously been subjected to numerous antibiotics.

Enhancing laboratory surveillance of antimicrobial resistance (AMR) has been recommended; this is a priority stated in the national and international action plans to combat AMR. [18, 19] Such data is required to monitor the spread of antimicrobial resistance (AMR), support national, international, and local initiatives to combat AMR, and provide estimates of the overall burden of the problem. [20] The kind of bacterial infections present in CSOM and their patterns of AMR may also be useful in guiding treatment strategies. [21]

Evidence for antimicrobial resistance and sensitivity pattern is scarce in India as compared to European and American countries. So, this study was conducted to determine the antimicrobial resistance and sensitivity pattern among patients presenting with CSOM and awaiting surgery in a tertiary care hospital in central India.

MATERIALS AND METHODS

This was an observational and prospective study conducted in department of Otorhinolaryngology in a tertiary care hospital of central India from July 2022 to June 2023. The study was conducted after approval from institutional ethics committee and written informed consent was taken before recruiting the study participants into the study after giving and explaining them participant information sheet in their local language.

Inclusion Criteria: All patients of either sex aged between 12 to 60 years presenting with chronic suppurative otitis media and chronic ear discharge planned for surgery with bacterial infection as per culture results from ear swabs were included in our study.

Exclusion Criteria: The patients with acute infection of middle ear with duration of illness < 3 months or patients with history of traumatic perforations of the eardrum were excluded from this study.

Sampling Method

Consecutive sampling method was used and each patient of CSOM with ear discharge fulfilling our inclusion and exclusion criteria was enrolled in the study.

Methodology

Using a sterilized ear swab and strict aseptic procedures, an expert otolaryngologist collected pus from the auditory canals of CSOM patients and submitted the sample to the laboratory for microbiological testing. Following the standard guidelines for inoculating culture media, samples were directly injected into blood agar, chocolate agar, and MacConkey agar. Colonies were recognized by colony morphology and biochemical assays using conventional protocols after being sub-cultured for its purity. The Analytical Profile Index (API) isolation system (API-Biometrieux, Basingstoke, UK) was used for verifying the isolates. The Kirby-Bauer disc diffusion method was used to assess the sensitivity to antibiotics of all isolated microorganisms. Our setting has defined quality control requirements that are compliant with national guidelines and standard. We have determined the findings with resect to the CLSI 2018 guidelines. [22]

Relevant data from prescriptions and laboratory reports of the patients were collected using a proforma to extract relevant baseline demographic and clinical characteristics.

Statistical analysis

Demographic, antimicrobial resistance and drug sensitivity data collected from the enrolled patients were presented in a tabular form using Microsoft Excel 365 and transferred to Graph Pad version 8.4.3 for further statistical analysis. Descriptive analysis was done to express the findings in percentage and frequency and chi-square test was used to test statistical significance of difference between antimicrobial resistance pattern between different drugs.

RESULTS

A total of 108 patients diagnosed with CSOM with chronic ear discharge awaiting surgery with culture and sensitivity report of ear swabs were included in our analysis. Their baseline demographic and clinical characteristics is given in table 1.

Table 1: Baseline Demographic and Clinical Characteristics

Variables	Number of Patients	Percentage of Patients (n = 108)
Age		
12-20	24	22.22
21-40	69	63.89
41-60	15	13.89
Sex		
Male	58	53.70
Female	50	46.30
Ear Affected		
Unilateral	73	67.59
Bilateral	35	32.41
Type of CSOM		
Tubo-tympanic	94	87.04
Attico-antral	14	12.96

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Most of the patients belonged to age group of 21 to 40 years (63.89%). There were slightly a greater number of males as compared to female. Bilateral disease was found in 32.41% of cases and most of the cases were of tubo-tympanic CSOM (87.04%).

Table 2: Distribution of bacterial isolate among patients of CSOM

Organism Isolated	Number of Patients	Percentage of Patients (n=108)
Single Bacterial Isolates	98	90.74
Pseudomonas aeruginosa	49	45.37
Staphylococcus aureus	41	37.96
Proteus spp.	5	4.63
Klebsiella pneumoniae	3	2.78
Mixed Bacterial Isolates	10	9.26
P. aeruginosa and *S. aureus*	7	6.48
P. aeruginosa and *Proteus spp.*	2	1.85
Proteus spp. and *S. aureus*	1	0.93

Mixed bacterial isolates were found in 9.26% of cases. *Pseudomonas aeruginosa* was most frequently identified pathogenic micro-organism in 45.37% of cases followed by *staphylococcus aureus* (37.96%). Culture findings are summarized in Table 2.

Drug sensitivity for causative bacteria were tested for commonly indicated antibiotics that were feasible in our settings and are summarized in Table 3-6.

Table 3: Antimicrobial resistance and sensitivity pattern of *Pseudomonas aeruginosa* isolated from ear swab of CSOM patients (n = 58)

Antimicrobial	Sensitive	Resistant	P-Value
Piperacillin	53 (91.38)	5 (8.62)	<0.001
Gentamicin	42 (72.41)	16 (27.59)	
Amikacin	40 (68.97)	18 (31.03)	
Ceftazidime	31 (53.45)	27 (46.55)	
Carbenicillin	22 (37.93)	36 (62.07)	
Tobramycin	54 (93.1)	4 (6.9)	
Meropenem	55 (94.83)	3 (5.17)	
Aztreonam	51 (87.93)	7 (12.07)	

Most of the pseudomonas isolates were resistant to carbenicillin (62.07%) and ceftazidime (46.55%). Approximately 30% of *pseudomonas* isolated were resistant to aminoglycosides. More than 90% of *pseudomonas* isolated were sensitive to piperacillin, tobramycin and meropenem.

Table 4: Antimicrobial resistance and sensitivity pattern of *Staphylococcus aureus* isolated from ear swab of CSOM patients (n = 49)

Antimicrobial	Sensitive	Resistant	P-Value
Ampicillin	27 (55.1)	22 (44.9)	< 0.001
Methicillin	40 (81.63)	9 (18.37)	
Vancomycin	48 (97.96)	1 (2.04)	
Cotrimoxazole	**31 (63.27)**	**18 (36.73)**	
Ciprofloxacin	10 (20.41)	39 (79.59)	
Erythromycin	35 (71.43)	14 (28.57)	
Amoxicillin + Clavulanate	22 (44.9)	27 (55.1)	
Clindamycin	38 (77.55)	11 (22.45)	
Linezolid	48 (97.96)	1 (2.04)	
Cefazolin	24 (48.98)	25 (51.02)	

Most of staphylococcus aureus isolates were resistant to ciprofloxacin (79.59%) followed by amoxicillin + clavulanate (55.1%). 9 cases of methicillin resistant *staph. aureus* (MRSA) and 1 case of vancomycin resistant *staphylococcus aureus* (VRSA) were identified. 63.27% of staph. aureus isolates were sensitive to cotrimoxazole.

Table 5: Antimicrobial resistance and sensitivity pattern of *Proteus spp.* isolated from ear swab of CSOM patients (n = 8)

Antimicrobial	Sensitive	Resistant	P-Value
Piperacillin	7 (87.50)	1 (12.50)	0.25
Gentamicin	5 (62.50)	3 (37.50)	
Amikacin	6 (75.00)	2 (25.00)	
Ceftriaxone	3 (37.50)	5 (62.50)	
Carbenicillin	4 (50.00)	4 (50.00)	
Cotrimoxazole	3 (37.50)	5 (62.50)	
Levofloxacin	5 (62.50)	3 (37.50)	
Aztreonam	6 (75.00)	2 (25.00)	
Meropenem	7 (87.50)	1 (12.50)	

Proteus spp. isolates were most resistant to ceftriaxone and cotrimoxazole and least resistant to piperacillin and meropenem.

Klebsiella pneumoniae isolates were most resistant to aminoglycosides and amoxicillin + clavulanate and least resistant to tigecycline, colistin and meropenem.

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Table 6: Antimicrobial resistance and sensitivity pattern of *Klebsiella pneumoniae* isolated from ear swab of CSOM patients (n = 3)

Antimicrobial	Sensitive	Resistant	P-Value
Ampicillin	1 (33.33)	2 (66.66)	0.045
Piperacillin	2 (66.66)	1 (33.33)	
Cotrimoxazole	1 (33.33)	2 (66.66)	
Ciprofloxacin	2 (66.66)	1 (33.33)	
Gentamicin	0 (0.00)	3 (100.00)	
Amikacin	0 (0.00)	3 (100.00)	
Ceftriaxone	1 (33.33)	2 (66.66)	
Amoxicillin + Clavulanate	0 (0.00)	3 (100.00)	
Meropenem	3 (100.00)	0 (0.00)	
Aztreonam	2 (66.66)	1 (33.33)	
Colistin	3 (100.00)	0 (0.00)	
Tigecycline	3 (100.00)	0 (0.00)	

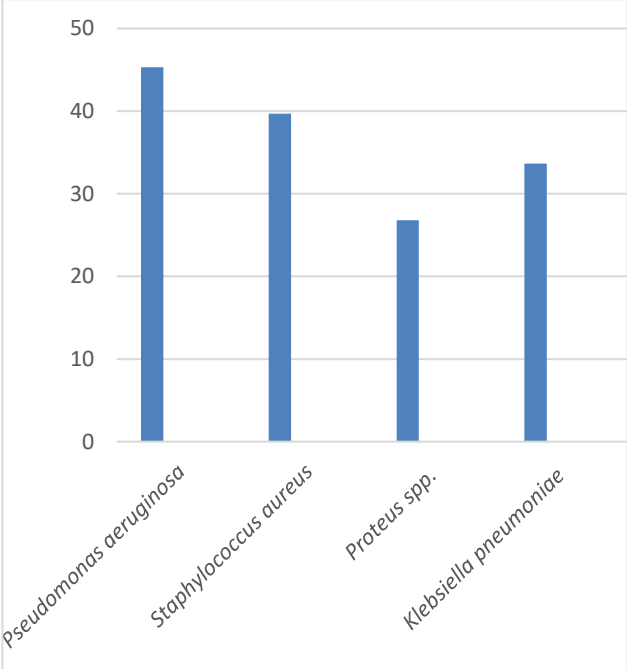

Figure 1: Percentage of Isolates with resistance to ≥ 6 antibiotics

Resistance to more than or equal to 6 antibiotics was highest in *pseudomonas aeruginosa* and lowest in *proteus spp.* (Figure 1).

DISCUSSION

The most frequent conditions that otologists, paediatricians, and general physicians see are CSOM and its associated problems. [23] It's a chronic illness with a high chance of permanent complications. Effective and suitable therapy will be assumed if all cases have early bacteriological diagnosis. [24]

The majority of the cases in the current study were between the ages of 21 and 40. The results of Kumar et al., Parween et al., and Deb et al. are not consistent with our findings.[25-27] Research by Saraswati et al. and Poorey et al. revealed that the majority of patients were under the age of twenty. [23, 27] In contrast, the largest number of patients in 21-30 years age group was recorded by Vishwanath et al. and Loy et al. [28, 29] In the current study, the male predominance was somewhat higher. This result was consistent with research by Hiremath et al., Deb et al., and Sharma et al. [26, 30, 31] Infections that were unilateral (67.59%) were more common than those that were bilateral (32.41%). These results were similar to those of studies by Sharma et al. and Kumar et al. [25, 32]

There are a number of reasons why *Pseudomonas aeruginosa* was the most common bacteria in the current study. According to Pollock et al., *Pseudomonas aeruginosa* is able to withstand competition from other bacteria because of its low nutritional needs, more AMR, and arsenal of antibacterial chemicals, which includes bacteriocin and pyocyanin.[33] Beyond these explanations, it adheres to the middle ear's damaged or necrotic epithelium using the pili. Once connected, the organism secretes lipopolysaccharides and proteases, which help it avoid the body's natural defences against infections. Additionally, the organism produces CSOM by flourishing in the external ear canal and acting as a pathogenic opportunistic microbe. *Pseudomonas aeruginosa* was similarly identified as the major organism in research by Vishwanath et al. (32.20%), Kumar et al. (46.00%), Deb et al. (79.00%) and Poorey et al. (35.20%). [23, 25, 26, 28]

Staphylococcus aureus was the next most frequently isolated bacterium (37.96%), which was similar to the findings of research by Deb et al. (20%) and Kumar et al. (33%). [25, 26] The number of cases of *Staphylococcus aureus* in the middle ear has grown due to a substantial number of antibiotic-resistant strains in the upper airways and external ear canal. Conversely, staphylococcus aureus (41.25%) was shown to be the most common causative pathogen in the research conducted by Prakash et al. [34]

Staphylococcus aureus proved to be the most sensitive pathogen to linezolid and vancomycin, with intermediate sensitivity to ampicillin and maximal sensitivity to clindamycin, erythromycin, and cotrimoxazole. On the other hand, ciprofloxacin showed the highest level of resistance, followed by amoxicillin + clavulanate. In a comparable manner staphylococcus aureus shown greatest susceptibility to erythromycin (75.00%), cotrimoxazole (95.00%), moderate susceptibility to ampicillin (55.00%), and ciprofloxacin (45.00%) in research by Vishwanath et al.[28] Half of the samples in a study by Deb et al. had resistance to fluoroquinolones.[16] On the other hand, *Staphylococcus aureus* shown susceptibility to ciprofloxacin (81%) and erythromycin (75%), according to research by Sharma et al.[32]

Since ciprofloxacin tends to be less ototoxic, more affordable, and more readily available in topical

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formulations, it is being over-utilized as a one of first line medication for the treatment of CSOM. [35] Studies have demonstrated sensitivity to the pathogens, but more recently, ciprofloxacin resistance to CSOM-causing microbes has increased, which is consistent with our findings.[36]

Piperacillin, tobramycin, and meropenem were found to be effective against over 90% of the pseudomonas isolates. In line with our findings, Vishwanath et al.'s study reports that *Pseudomonas aeruginosa* exhibited the highest sensitivity to piperacillin (97.3%), followed by gentamicin (73.00%), amikacin (78.40%), and ceftazidime (91.20%).[28] In contrast to the present study, Sharma et al. reported that *Pseudomonas aeruginosa* was susceptible to piperacillin (25.00%), gentamicin (30.00%).[30] The most efficient aminoglycosides were discovered to be gentamicin and amikacin; yet, the possibility of ototoxicity from using these preparations is still up for debate and precludes their regular use.

CONCLUSION

Ciprofloxacin and amoxicillin + clavulanate are most empirically prescribed antibiotics and this over-utilization has led to increase in antimicrobial resistance to these antibiotics. We have also noticed that there was surprisingly more sensitivity to co-trimoxazole which is under-utilized for more than a decade. So, there seems to be a positive correlation between utilization of antibiotics and antimicrobial resistance. As a result, in order to create a local antibiotic strategy for the responsible use of antibiotics, it becomes imperative to investigate each patient of CSOM through microbiological culture and sensitivity. This will certainly help in solving the problem of delay in surgical cure due to antimicrobial resistance.

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