Bacteriological profile and antibiotic resistance in cases of chronic otitis media and its clinical implications

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INTRODUCTION

Chronic otitis media (COM) is defined as chronic inflammation of middle ear and mastoid cavity that may present with recurrent ear discharges or otorrhoea through a tympanic perforation.1 COM is prevalent worldwide maximally affecting the developing or underdeveloped countries especially in areas of poor socio-economic standards owing to factors such as malnutrition, overcrowding and poor hygiene.2 Due to its recurrent nature and the development of resistant pathogenic organisms, control of infection in COM now poses a greatest therapeutic challenge. Often, the primary care physicians, who first see these patients rely on empirical antibiotic therapy. Irrational and unethical use of antibiotics has led to high resistance patterns and increase in burden of the disease and its complications. This has been confirmed by various studies which have brought out the changes in bacterial flora and their resistance patterns in COM in the last decade.3,4

The objective of this cross sectional prospective study on COM was to study the etiological bacterial diversity and their antibiotic resistance pattern with the aim of...
developing effective treatment protocols to reduce the morbidity from the disease. The study was conducted as a cohort study at a tertiary care centre in the National capital region of India. To the best of our knowledge no such study data is available from this region.

METHODS

Place of study: ENT Department in a tertiary care referral centre in New Delhi

Period of study: July 16 to June 17

Type of study: Prospective cross sectional observational study

Inclusion criteria

All cases of COM both mucosal and squamous, who reported to the ENT OPD of a tertiary care defence hospital between Jul 16 to Jun 17, with history of ear discharge of more than 3 months, were included in the study. Only samples growing aerobic bacterial organisms were included in the study.

Exclusion criteria

Cases exhibited antibiotic either systemic or topical in the ear in last 2 weeks or patients who had clinical evidence of otomycosis, otitis externa, or or acute otitis media.

Sample collection

Cotton tipped swab was taken from each patient and sent for bacteriological culture and antibiotic sensitivity pattern. All care was taken to avoid surface contamination and the swabs were taken to the microbiology laboratory for further bacteriological processing. Non bacterial flora such as fungi and anaerobic organisms were not included in the present study.

Statistical analysis

The frequency and prevalence of organisms was determined and expressed in percentage. Mean and ratio proportion was calculated for analysis using Statistical Package for Social Sciences (SPSS) version 20.

RESULTS

A total of 500 samples were collected during the period of study from cases of COM both mucosal type (74.2%) and squamous type (25.8%). In our study, age group of patients ranged from 0 to 80 years (mean age - 31.26 years). Maximum incidence of COM was observed in patients of 16–35 years age group (171/500). The sex ratio obtained was female to male ratio preponderance was 1.4:1 (Table 1).

Table 1: Age and sex pattern in cases of COM.

| Age group (in yrs) | Total no of cases |
|--------------------|------------------|
| <5                 | 12               |
| 5-15 yrs           | 92               |
| 16-35 yrs          | 171              |
| 36-50              | 117              |
| >50                | 108              |
|                    | 500              |

| Gender             |                  |
|--------------------|------------------|
| Male               | 206              |
| Female             | 294              |

A positive bacterial growth on culture was obtained in 466/500 (93.2%) of the samples. Out of these, 454 showed growth of a single bacterium only. In remaining 12 samples, mixed growth was obtained. No growth was seen in 34 patients (6.8%). *Pseudomonas aeruginosa* was the predominant organism 261/466 (56%) followed by *Staphylococcus aureus* (Table 2).

Other bacteria isolated were *Proteus* spp. (4.08%), *Klebsiella pneumoniae* (6%), *Escherichia coli* (6%), *Acinetobacter* (1.72%) and *Streptococcus viridans* (2.14%). Among the *Staphylococci* species, *Staph aureus* was detected in 110 cases, and Coagulase negative Staph (CoNS) in 2 cases.

The sensitivity patterns of organisms isolated are shown in Table 3. *Pseudomonas* showed 100% resistance to Ampicillin and Amoxycillin-Clavulanic acid combination, both considered 1st line antibiotics in COM. Moderate degree of resistance was seen in other Aminoglycosides (162/261 for Gentamycin and 171/261 to Amikacin). 3rd and 4th generation Cephaloporins also showed certain degree of resistance pattern (Ceftriazone 41/261 and Cefepime 27/261 resistance). However there was 100% sensitive to Colistin.

*Staph.aureus* showed high degree of resistance to Benzylpenicillin and Triamethoprim/Sulphamethoxazol combination, with moderate resistance to Ciproflloxacin and Levofloxacin. However there was 100% sensitivity to Linezolid and Vancomycin (Table 4).
Table 3: Details of bacteriology and sensitivity pattern in cases of COM

| Antimicrobial                  | Pseudomonas - S | Pseudomonas - R | Klebsiella - S | Klebsiella - R | Proteus - S | Proteus - R | E. Coli - S | E. Coli - R | Acinetobacter - S | Acinetobacter - R | Streptococci S | Streptococci R |
|-------------------------------|-----------------|-----------------|----------------|----------------|--------------|--------------|-------------|-------------|-------------------|-------------------|-----------------|-----------------|
| Ampicillin                    | 0               | 261             | 0              | 28             | 0            | 19           | 0           | 28          | 0                 | 18                | 10              | 0               |
| Amoxy-clav                    | 0               | 261             | 7              | 21             | 0            | 19           | 0           | 28          | 0                 | 18                | 5               | 5               |
| Piperacillin/Tazobactam       | 234             | 27              | 26             | 2              | 19           | 0            | 28          | 0           | 18                | 0                 | 10              | 0               |
| Cefuroxime                    | 199             | 62              | 26             | 2              | 19           | 0            | 28          | 0           | 0                 | 0                 | 10              | 0               |
| Ceftriazone                   | 220             | 41              | 26             | 2              | 19           | 0            | 28          | 0           | 0                 | 0                 | 10              | 0               |
| Cefoperazone/Sulbactam        | 198             | 63              | 26             | 2              | 19           | 0            | 19          | 9           | 9                 | 9                 | 10              | 0               |
| Cefepime                      | 224             | 37              | 26             | 2              | 19           | 0            | 28          | 0           | 0                 | 0                 | 10              | 0               |
| Imipenem                      | 234             | 27              | 26             | 2              | 19           | 0            | 28          | 0           | 18                | 0                 | 10              | 0               |
| Meropenem                     | 225             | 36              | 26             | 2              | 19           | 0            | 19          | 9           | 18                | 0                 | 10              | 0               |
| Amikacin                      | 90              | 171             | 26             | 2              | 19           | 0            | 15          | 13          | 9                 | 9                 | 7               | 3               |
| Gentamycin                    | 99              | 162             | 26             | 2              | 6            | 13           | 6           | 22          | 9                 | 9                 | 6               | 4               |
| Nalidixic acid                | 9               | 252             | 26             | 2              | 4            | 15           | 1           | 27          | 0                 | 18                | 3               | 7               |
| Ciprofloxacillin              | 72              | 189             | 26             | 2              | 5            | 14           | 1           | 27          | 0                 | 18                | 5               | 5               |
| Tigecycline                   | 252             | 9               | 26             | 2              | 19           | 0            | 19          | 9           | 0                 | 18                | 8               | 2               |
| Nitrofurantoin                | 30              | 231             | 0              | 28             | 1            | 18           | 19          | 9           | 0                 | 18                | 3               | 7               |
| Colistin                      | 261             | 0               | 28             | 0              | 19           | 0            | 28          | 0           | 18                | 0                 | 10              | 0               |
| Trimethoprim/Sulphamethoxazole| 0               | 261             | 28             | 0              | 1            | 18           | 1          | 27          | 0                 | 18                | 3               | 7               |

*S- Sensitive, R- Resistant.

Table 3: Sensitivity pattern of *Staphylococcus* species.

| Antimicrobial                  | Staph aureus - S | Staph aureus- R | CONS -S | CONS -R |
|-------------------------------|------------------|-----------------|---------|---------|
| Cefoxetin screen              | 80               | 30              | 2       | 0       |
| Benzylpenicillin              | 0                | 110             | 1       | 1       |
| Oxacillin                     | 33               | 77              | 2       | 0       |
| Ciprofloxacin                 | 7                | 103             | 2       | 0       |
| Levofloxacillin               | 7                | 103             | 2       | 0       |
| Gentamycin                    | 68               | 42              | 2       | 0       |
| Erytheromycin                 | 23               | 87              | 2       | 0       |
| Clindamycin                   | 100              | 10              | 2       | 0       |
| Linezolid                     | 110              | 0               | 2       | 0       |
| Daptomycin                    | 110              | 0               | 2       | 0       |
| Telcoplanin                   | 108              | 2               | 2       | 0       |
| Vancomycin                    | 110              | 0               | 2       | 0       |
| Tetracycline                  | 15               | 95              | 2       | 0       |
| Tigecycline                   | 107              | 3               | 1       | 1       |
| Nitrofurantoin                | 83               | 27              | 1       | 1       |
| Rifampicin                    | 98               | 12              | 2       | 0       |
| Trimethoprim/Sulfamethoxazole | 6                | 104             | 0       | 2       |

CoNS – Coagulase negative *Staphylococcus* S- Sensitive R- Resistant.
DISCUSSION

World Health Organization has listed antibiotic resistance as a growing global problem which poses a major threat to health.\(^1\) Higher incidence of COM is common in cases due to the malnutrition, overcrowding and poor hygiene and hence is more commonly seen to occur in communities from poor socio-economic standards.\(^2\) Both gram positive and gram negative organisms contribute to the bacteriological profile of COM infection. Proper antibiotic profile is essential for timely treatment as also to reduce the menace of antibiotic resistance. This study was therefore undertaken to define the organism profile and their resistance pattern to commonly administered antibiotics in cases of COM in a select cohort in the NCR of India.

A positive bacterial growth on culture was obtained in 466/500 (93.2%) of the samples. Pure mono-microbial cultures were obtained in 454 (90.8%) samples. Where as in remaining 12 (2.4%) patients mixed growth was obtained. No growth was seen in 34 patients (6.8%). Various studies have showed varying results on the numbers of positive culture.\(^3,4\) Poorey and lyer in their study reported pure growth from 82% cases, mixed growth from 10%, and no growth in 8%. Prakash Rajat al, showed lesser frequency (57.84%) of mono microbial growth.\(^3\) Varying and complex host, environment and patient profile may affect outcome of results in these cases.

In our study, 6.8% of the cultures did not yield any microbial growths which is similar to findings in other reports in which negative cultures in their studies.\(^6,7\) Such negative cultures may have been as a result of the modification of the bacterial flora in the affected ears by prior empirical antibiotic therapy.

Most studies revealed the disease to be prevalent in the younger age group.\(^3,8\) However in our study, young adults were also equally affected. Mean age in our study was about 31 years. Similar results were recorded by Varunika et al and Sharma et al.\(^9,10\)

Our study showed the disease to be common in females than males, in the ratio 1.4:1. Similar reports were obtained in the findings of other authors while Poorey et al reported the ratio to be more towards males.\(^3,5,11\)

Pseudomonas was the commonest organism in our study followed by Staph aureus. Similar results were obtained by others studies.\(^9,12-15\) Whereas certain reports have cited Staphylococcus aureus as the most predominant organism in COM.\(^3,16\) Other bacteria isolated in our study were Proteus spp. (4.07%), Klebsiella pneumoniae (6%), Escherichia coli (6%), Acinetobacter (1.72%) and Streptococcus viridans (2.14%).

The variations in bacteria isolation rates of different organisms reported by different workers may be as an effect of inappropriate antibiotic uses, climatic and other geographical factors.\(^17\) This therefore, highlights the importance of bacterial antibiotic culture sensitivity in cases of COM. Empirical use of antibiotics should be avoided and specific therapy tailor made to individual cases should be encouraged for effective antibiotic use and disease control.

Pseudomonas, infection of the middle ear cleft is generally not attributed due to invasion via the auditory tube as it is not a usual inhabitant of the upper respiratory tract. Source of infection is considered to be access via a perforation in the tympani membrane in such cases.\(^15\) High frequency of bacteria isolated in faeces such as E. coli, Klebsiella and water borne bacteria like Pseudomonas indicates that individuals with poor hygiene are at high-risk of acquiring such infections.

Based on the antibiogram, there was high resistance to Ampicillin, Amoxycillin/Clavulanic acid and Trimethoprim/ Sulphamethoxazole combinations across complete spectrum of bacterial isolates. Pseudomonas showed 100% sensitivity to Colistin and High Sensitivity to Piperacillin/ Tazobactam (225/252). It showed complete 100% resistance pattern to Ampicillin, Amoxycillin/Clavulanic acid and Trimethoprim/ Sulphamethoxazole and also a high resistance to Aminoglycosides. This is in variance with other studies such as Prakash et al who showed good response of Amikacin to Pseudomonas.\(^3\) This shows development of increase in resistance patterns of the organism maybe as a result of rampant misuse of these antibiotics over time. The mechanism of resistance is believed to be mediated by formation of biofilms by these organisms.\(^18\)

Staphylococcus species showed high susceptibility to Linezolid, Vancomycin and Teicoplanin. However there was high resistance to penicillin group in our study. Similar results were obtained by other studies.\(^9,19\) CoNS were isolated in 2 cases. All were isolated as mixed infections with Staph aureus. Although generally considered nonpathogenic, they may be associated in cases of immune compromised hosts wherein they then become pathogenic and can be cause of infection either singly or in combination with other organisms.\(^20\) In our study all the CONS were in combination with Staph aureus (mixed infection).

Antibiotic commonly used as ear drops preparations such as ciprofloxacine and gentamycin, showed high resistance pattern to the microorganisms in our study. Earlier similar studies showed common antibiotic ear drops to have high sensitivity to implicated bacteria in COM.\(^3,21\) Rampant misuse of these antibiotic drugs may have led to this high resistant state today, which is a cause for worry.

CONCLUSION

There have been rapid changes in the microbial pattern in cases of COM and their antibiotic sensitivity has been
changing over time with high levels of resistance to commonly used antibiotics. Periodical assessment of microbiological profile is therefore essential for making effective protocols for cases of COM in a particular geographical location.

ACKNOWLEDGMENTS

The authors would like to thank the Department of Microbiology, Base Hospital Delhi Cantt, for all the help in providing the antibiograms for the research paper.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Mallick A, Sharma H, Mishra AK, Maggon NV, Sethi A. Bacteriological profile and antibiotic resistance in cases of chronic otitis media and its clinical implications. Int J Otorhinolaryngol Head Neck Surg 2018;4:918-22.