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Original Research Article

Are we ushering into the pre-antibiotic era: alarming trends of antibiotic resistance in chronic otitis media in a tertiary care hospital in Delhi, India

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ABSTRACT

Background: Chronic otitis media is an infection of the middle ear cleft for at least 12 weeks or more. It has a high prevalence rate in India pertaining to factors like malnutrition, overcrowding and poor hygiene. Thanks to greats like Paul Ehrlich and Alexander Fleming, Antimicrobials are a powerful and readily available form of treatment for this disease.
Methods: In this study we re-evaluated the changing trends in bacteriological profile of COM and the antibiotic sensitivity pattern to most of the currently available antibiotics in a tertiary care hospital in India.
Results: Most common pathogens found in our study were *Pseudomonas aeruginosa, Staphylococcus aureus, Proteus mirabilis, Proteus vulgaris, Enterococcus, Escherichia coli* and *Morganella morganii*. A declining pattern in the sensitivity towards commonly used antibiotics with an alarming increase in MRSA was observed.
Conclusions: The trends observed in our study warrant an urgent need for antibiotic policies, judicious use of antibiotics and vigilance in our hospitals.

Keywords: Antibiotic resistance, Chronic otitis media, Antimicrobials

INTRODUCTION

The world health organization defines chronic otitis media (COM) as ear discharge through a perforated tympanic membrane present for more than 12 weeks with chronic inflammation of the middle ear and mastoid cavity.[1] It is a major health problem in developing countries.[2] Inadequate treatment of CSOM can cause life-threatening intracranial and extracranial complications.

Thanks to greats like Paul Ehrlich and Alexander Fleming, Antimicrobials are a powerful and readily available form of treatment for the disease.[3]

Before the commencement of treatment, identification of the microorganisms responsible for the disease can help in selection of the most appropriate antibiotic. Based on the past studies *Proteus mirabilis, Pseudomonas aeruginosa*, and *Enterococcus* are commonly occurring organisms.

An increased virulence of the organism is seen due to bacterial factors such as Biofilm formation, Beta lactamase production, lipopolysacharide, metalloprotease production, colony swarming and capsule formation.[4]

However, excessive and indiscriminate use of antibiotics today topped with poor patient compliance and follow up have resulted in persistence of low-grade infections and an alarming increase in antibiotic resistance rapidly pushing us towards pre antibiotic era.[4-6]

In this study our objective was to re-evaluate the changing trends in bacteriological profile of CSOM and the antibiotic sensitivity pattern to most of the currently available antibiotics in a tertiary care hospital.

METHODS

We conducted a prospective study for a period of 1 year from April 2022-2023 in a tertiary care medical college and hospital of Delhi.

Sample size calculation and sampling technique

Calculated using:

Formula 1: Sample size for infinite population

$S=Z^2\times P\times(1-P)/M2$

Formula 2: Adjusted sample size

Adjusted sample size = (S)/1+(S−1)/Population

Where, S=sample size for infinite population, Z=Z score, P=population proportion (Assumed as 50% or 0.5), M=Margin of error, at CI=99%. SD=50%, margin of error 5%

Based on the prevalence of the disease the sample size was 130.

Data collection and sampling

All patients presenting with chronic or recurrent ear discharge of more than 12 weeks duration were included. Otoscopy and microscopy examination was performed followed by aural toileting. Sterile aural swabs were used to collect ear discharges from the middle ear after dry mopping the discharge in the external ear to avoid contamination of the samples.

Culture and identification

The samples were sent to the hospital's microbiology department to be inoculated onto Mac Conkey agar (MCA), blood Agar (BA), and chocolate agar plates. Antimicrobial sensitivity testing for aerobic isolates was carried out by Kirby Bauer disc diffusion method and results were interpreted. Most of our patients had received treatment at the lower centres but patients who had received antibiotics in the last seven days were excluded.

Data analysis

The data was entered and analyzed using SPSS statistical software package (version 20). The descriptive statistics and proportion of the findings were computed by percentages.

RESULTS

We studied a total of 131 cases with the most common pathogen being *Pseudomonas aeruginosa* in 36 cases (27.5%), *Staphylococcus aureus* in 32 cases (24.4%), A staggering 15 cases (around 11.45%) were found to have Methicillin resistant *Staphylococcus aureus, Proteus mirabilis* in 22 cases (16.8%), *Proteus vulgaris* in 12 cases (9.17%), *Enterococcus* in 7 cases (5.3%), *Escherichia coli* in 10 cases (7.6%) and *Morganella morganii* in 2 cases (1.5%).

Antibiotic sensitivity results

Pseudomonas aeruginosa

It was the most common pathogen in our study. It was sensitive to cefoperazone-sulbactam combination in 60% cases, intermediate in 10% cases and resistant in 30% cases. 65% cases showed resistance to Ciprofloxacin and, 8% showed intermediate sensitivity. 80% cases were resistant to Gentamicin.

It was sensitive to imipenem in 85% cases, intermediate sensitivity in 10%, and resistant in 5% cases. Piperacillin–Tazobactam showed sensitivity in 50% cases, intermediate sensitivity in 10% and resistance in 40%. cases colistin sensitivity was seen in 94.5% cases and only 2 cases i.e., 5.5% cases showed resistance to colistin as well.

Staphylococcus aureus

20 cases (62.5%) were sensitive to amoxicillin and 12 (37.5%) were resistant, out of the 12 resistant cases 7 were sensitive to amoxicillin with clavulanic acid and 5 were resistant. All 32 cases were sensitive to piperacillin tazobactam.

The 28 cases were sensitive to cefpodoxime and 4 were resistant. Only 8 cases were sensitive to ciprofloxacin and 24 (75%) were resistant, 16 cases were sensitive and 16 (50%) were resistant to cephoxitin, 30 cases were sensitive to clindamycin and 2 showed intermediate sensitivity.

The 29 (90.6%) cases were resistant to erythromycin and only 3 cases were sensitive. All cases were sensitive to linezolid and vancomycin.

Methicillin resistant Staphylococcus aureus

The 15 cases (around 11%) were found to have MRSA. All these cases (100%) were resistant to amoxicillin, ampicillin, oxacillin, cefpodoxime, piperacillin tazobactam and erythromycin i.e., 20% cases were sensitive to gentamicin and the rest were resistant. Seven i.e., around 47% cases were sensitive to Clindamycin and the rest were resistant. All 15 i.e., 100% cases were sensitive to linezolid, vancomycin, teicoplanin,

daptomycin, tetracycline and trimethoprim/ sulphamethoxazole.

Proteus mirabilis

The 14 (63.6%) were resistant to amoxicillin with clavulanic acid. All 22 (100%) cases were sensitive to piperacillin tazobactam, 16 cases were sensitive to cefuroxime and cefotaxime and 6 (27.3%) were resistant. 21 cases were sensitive to meropenem and 1 was resistant, 19 cases were sensitive to amikacin and 3 (13.6%) were resistant, 13 (59%) cases were resistant to gentamycin and 9 cases were sensitive. The 15 (68.2%) cases were resistant to ciprofloxacin and 7 were sensitive. All cases were resistant to colistin as *Proteus mirabilis* is intrinsically resistant to polymyxins.

Proteus vulgaris

Ten (83.3%) out of 12 cases were resistant to ampicillin. Eight cases were sensitive to piperacillin tazobactam and 4 (33.3%) were resistant. Seven were sensitive to gentamicin and 5 (41.6%) were resistant. All (100%) cases were resistant to polymyxin B. Ten were sensitive to levofloxacin and 2 were resistant. Nine were sensitive to ciprofloxacin, 1 showed intermediate sensitivity and 2 were resistant. 11 were sensitive to amikacin and 1 showed intermediate sensitivity, 11 cases showed resistance to ceftriaxone and 1 was sensitive and ten cases were resistant to cotrimoxazole and 2 were sensitive.

Escherichia coli

Enterococcus was found in 10 cases. 7 (70%) cases were resistant to amoxicillin with clavulanic acid and ampicillin. 60% (6 cases) resistance was seen towards cotrimoxazole and gentamicin. 4 cases (40%) were resistant to levofloxacin. 8 (80%) cases were found to be sensitive to polymyxin B.

Enterococcus

Enterococcus was found in 7 cases, 5 out of which existed as a mixed infection along with *Staphylococcus aureus*. All 7 cases were sensitive to ampicillin, cephoxitin, gentamicin, linezolid, polymyxin B and vancomycin. No resistance was observed in *Enterococcus* bacterial infections.

Morganella morganii

It was observed in 2 cases. Heavy antibiotic resistance was seen. Both cases were sensitive to piperacillin tazobactam, meropenem and amikacin. Intermediate towards ceftazidime and resistance towards cefotaxime, cefaperazone, sulbactam, imipenem, gentamicin, ciprofloxacin, levofloxacin, minocycline, tigecycline, colistin and trimethoprim/ sulfamethoxazole was seen.

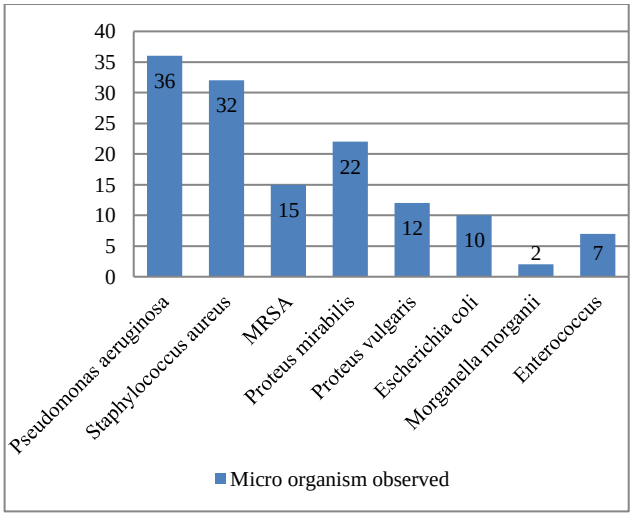

Figure 1: Micro-organism observed.

DISCUSSION:

COM is a major public health problem in India and an important cause of preventable hearing loss amounting to 13.8-36.2% burden of hearing loss.[4] It is a very persistent disease with great risk of irreversible complications.

Early microbiological diagnosis ensures prompt and effective treatment. Microbiology cultures yield many organisms which along with environmental factors depend largely on whether or not antibiotics have been recently used.

The first antibiotic, salvarsan came into effect in 1910. In time span extending just over 100 years, antibiotics have drastically changed modern medicine and extended the average human lifespan by about 23 years. The discovery of penicillin in 1928 started the golden age of antibiotic discovery that peaked in the mid-1950s.[3] Since then, a gradual decline in antibiotic discovery and development along with increasing drug resistance has led to the current antimicrobial resistance crisis.

In clinical practice bacterial cultures are not required in every discharging ear and multiple studies have proved that 90% to 100% of chronically discharging ears yield two or more isolates of both aerobic and anaerobic bacteria.[1,7] Bacterial cultures are especially recommended in cases recalcitrant infections or when bacterial resistance is suspected.

The microbiology profile in our study revealed that 96.2% of culture reports yielded a single pathogen whereas 3.8% cases were polymicrobial.

In general, gram-negative pathogens were significantly more common than gram positive pathogens in our study which is similar to multiple studies conducted in the past.[5,6] This finding indirectly points towards

nasopharynx not being the source of infection as these pathogens do not predominate this region.

Pseudomonas aeruginosa, an aerobic gram-negative pathogen was the most common pathogen in our study followed by *Staphylococcus aureus*. These findings were consistent with studies conducted by Shilpa et al, Kazeem et al and Wan Draman et al.[5,6,8] In a few other studies *S. aureus* was found to be the most common pathogen, followed by *P. aeruginosa*. A study by Bakari et al in Nigeria found *Klebsiella* spp. to be the most common followed by *Escherichia coli*.[9]

Unlike most studies conducted in India, we found a very high occurrence of MRSA (11%) in our study. This is consistent with a study conducted in South Korea and raises serious concerns over irrational use of antibiotics.[10] We also found 1.5% cases of *Morganella morganii*, a rare cause of otitis media. It is a rare opportunistic, facultatively anaerobic, gram-negative bacteria that mostly causes urinary tract and wound infections. It can be also be a cause for pathogenic brain abscess and its occurrence in chronic otitis media should be taken seriously.

Pseudomonas aeruginosa in our study showed heavy resistance towards fluroquinolones with 65% cases showing resistance and 8% showing intermediate sensitivity patterns to ciprofloxacin. Similar results were obtained with aminoglycosides with 80% resistance towards gentamicin. These findings are consistent with studies in the past where resistance pockets are seen for fluroquinlones and aminoglycosides.[11] A 40% resistance was seen towards piperacillin tazobactam, a broad-spectrum β-lactam antibiotic with 2 cases being resistant to colistin as well which is a cause for serious concern.

Among cases with *Staphylococcus aureus* 37.5% resistance was seen towards amoxicillin out of which 58.3% cases were sensitive to amoxicillin with clavulanic acid. Heavy resistance was seen towards fluroquinolones here as well with only 25% cases being sensitive to ciprofloxacin. A very high resistance was seen towards macrolides (90.6% resistance). Similar studies conducted in the past have shown declining sensitivity patterns towards fluoroquinolones and macrolides.[6,11] However, the study conducted by Samanth et al found Erythromycin to be effective in 62% cases.[4] We in our study found 11% cases to have MRSA. Methicillin-resistant *Staphylococcus aureus* should be considered when antibiotic treatment fails. 100 % cases of MRSA in our study were found to be resistant to amoxicillin, ampicillin, oxacillin, cefpodoxime, piperacillin tazobactam and erythromycin. Around 47% cases were sensitive to clindamycin and the rest were resistant. The 100% cases were sensitive to linezolid, vancomycin, Teicoplanin, daptomycin, tetracycline and trimethoprim/ sulphamethoxazole. These findings were similar to the study conducted by Moo et al.[12] Although most strains of MRSA respond drugs like linezolid and vancomycin, these drugs are expensive and associated with side effects. Vancomycin and teicoplanin consist of macromolecules and require IV administration and hospitalisation. Vancomycin can also induce anaphylactic reactions, clostridium difficile infections, hearing and vestibular disorders, neutropenia, and vasculitis.

Other common isolates in our study were *Proteus mirabilis, Proteus vulgaris* and *Escherichia coli* which is similar to various studies conducted in the past.[5,6,11] The 83.3% isolates of *Proteus vulgaris* in our study were resistant towards ampicillin and 33.3% towards piperacillin tazobactam. *Proteus mirabilis* showed an increased resistance towards cephalosporins with 27.3% cases being resistant to cefuroxime and cephoxitin. This is a cause for serious concern as it is intrinsically resistant to higher antibiotics like colistin and shows reduced sensitivity towards imipenem.

Two cases with *Morganella morganii* showed worrisome sensitivity patterns. Resistance was seen towards cefotaxime, cefaperazone, sulbactam, imipenem, gentamicin, ciprofloxacin, levofloxacin, minocycline, tigecycline, colistin and trimethoprim/ sulfamethoxazole. Studies have shown that *Morganella morganii* can harbour extended-spectrum β-lactamases and carbapenemases resulting in increased resistance to multiple antibiotics and a high mortality rate.[13] Both the patients in our study underwent hospitalization and received meropenem.

Limitations

Being a tertiary care centre all the patients that presented had undergone treatments at lower centres causing a change in the disease microbiology and resistance patterns.

CONCLUSION

Microbiological pattern and antibiotic sensitivity of chronic otitis media is constantly changing and a periodical review of the same is a must.

A declining pattern in the sensitivity towards commonly used antibiotics is alarming and warrants a strict antibiotic policy in our hospitals. A judicious and careful use of antibiotics is a must especially by junior doctors.

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