

Drift in the bacteriology of chronic suppurative otitis media and methicillin-resistant *Staphylococcus aureus* as an emerging pathogen: an experience

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Abstract

Background: Chronic suppurative otitis media (CSOM) is a condition of the middle ear, which is characterized by persistent or recurrent discharge. Many studies done in CSOM have found the predominance of Gram negatives in the ear discharge, with *Pseudomonas* and *Proteus* species as the most commonly identified aerobic organisms. Gram positives [*Staphylococcus aureus*, methicillin-resistant *S. aureus* (MRSA)] are found but are less common.

Objective: To study the aerobic culture and sensitivity results of pediatric patients with CSOM attending the outpatient department, with special emphasis on MRSA.

Materials and Methods: One hundred-fifteen pediatric patients with CSOM who fulfilled the inclusion and exclusion criteria were prospectively studied. They showed chronic ear discharge and had not received antibiotics for the previous 7 days. Swabs were taken from the middle ear under microscope and cultured for only aerobic bacteria. The antimicrobial susceptibility testing was performed using an agar disk diffusion method according to the guidelines of Clinical and Laboratory Standards Institute.

Result: The male subjects were commonly involved. There were 113 positive cultures for organisms from the 115 patients. The most common organism was *Staphylococcus* seen in 65% of patients [35% methicillin-sensitive *Staphylococcus aureus* (MSSA) and 30% MRSA], followed by *Pseudomonas* sp. 13%, and *Escherichia coli* in 7%. The majority of *Staphylococcus* sp. were MSSA (53%), followed by MRSA (44%). Gram positives were seen in 65% of cases, while gram negatives in 31% of cases. We noticed a drift in bacteriology from gram negatives to gram positives. MRSA were sensitive to linezolid, vancomycin, and clindamycin, whereas resistant to azithromycin, cefuroxime, and ciprofloxacin. The majority of MRSA were seen in patients with central perforation with ossicular discontinuity. The percentage of MRSA seen in our study was quite high.

Conclusion: In this study, we can see a drift in bacteriology of CSOM from gram negative to gram positive, and MRSA is emerging as an important pathogen in CSOM. Empirical antibiotics should be directed to gram positives, and especially, MRSA should be taken into consideration.

KEY WORDS: CSOM, bacteriology, MRSA, drift, gram positives

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Introduction

Chronic suppurative otitis media (CSOM) is the stage of ear disease in which there is chronic inflammation of the middle ear and mastoid and in which a nonintact tympanic membrane is present. Mastoiditis is invariably a part of the pathological process. The best illustrative expression is chronic otitis media with perforation, discharge, and mastoiditis;

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however, it is not used in general. The term cholesteatoma with CSOM is found to be pertinent in the presence of cholesteatoma.^[1] CSOM is a commonly encountered infection of the middle ear in all parts of world. It is a state in which the middle ear exhibits persistent or recurrent discharge.

Untreated cases of CSOM can lead to a wide range of problems such as persistent otorrhea, mastoiditis, labyrinthitis, and facial nerve paralysis to more serious intracranial abscesses or thromboses;^[2] so, the knowledge of the local pattern of infection is essential to enable efficacious treatment of this disorder.

The microbiology cultures result in a lot of, frequently multiple, organisms, and these differ based on climate, patient population, and whether antibiotics have or have not been recently used. Many studies done in CSOM have found the predominance of gram negatives in the ear discharge, with *Pseudomonas* and *Proteus* species as the most commonly identified aerobic organisms, while *Bacteroides* and *Peptococcus/Peptostreptococcus* sp. are the most commonly found anaerobes. Gram positives [*S. aureus*, methicillin-resistant *Staphylococcus aureus* (MRSA)] are found but less common.^[2] There have been reports of unusual organisms such as *Mycobacterium tuberculosis*, *M. chelonae*, *M. avium* complex, *Actinomyces* species, and *Candida* species.

Identification and detection of MRSA and extended spectrum beta-lactamase producers are also important before the treatment of CSOM cases.

MRSA is a common hospital pathogen found worldwide. Community-acquired (CA) MRSA, was reported first in the United States in 1995.^[3] A considerable proportion of outpatient strains of MRSA come from ear discharge found in otolaryngology practices.^[3]

It is difficult to do cultures in all patients with CSOM, because culture and sensitivity facilities are costly and not available in rural and some urban areas of developing countries. On the basis of the result, antibiotics are prescribed empirically depending on the predominance of gram negatives in the ear discharge; empirical antibiotics should have more activity against gram negatives.

At peripheral health centers, empirical antibiotics against gram negatives such as ciprofloxacin, levofloxacin, and cefpodoxime are prescribed, but there are many failures to these empirical antibiotics leading to continuation of discharge from ear. Keeping this fact in mind, a clinical study was done at our tertiary center to study the culture and sensitivity of organisms in a set of patients with CSOM who were either referred to us from peripheral center or came directly to us. This study was difficult, because, nowadays, almost all patients with discharge in the ear are given antibiotics at peripheral centers and are referred to tertiary center once there is failure to their empirical treatment. Gram positives predominated in our set of patients, and there was drift in bacteriology from *Pseudomonas* sp. to *S. aureus*.

Materials and Methods

This study was done on outpatient basis in the Department of Ear, Nose and Throat, Head and Neck surgery of Government Medical College Srinagar, Kashmir, India, from March 2013 to March 2015. One hundred-fifteen pediatric patients were prospectively studied with the following inclusion and exclusion criteria. An informed consent was obtained from all the patients, but ethical approval was not necessary in this observational study.

Inclusion Criteria

- Pediatric patients.
- All the patients who revealed chronic suppurative otitis media with active purulent discharge at the time of collection of samples.
- Both the safe and unsafe ears were studied.

Exclusion Criteria

- Patients who had received either oral or topical antibiotics in the preceding 7 days.
- Patients with comorbid conditions such as diabetes, tuberculosis, or immunodeficiency.
- Patients older than 16 years.
- Patients with history of trauma to the ear.

Detailed clinical history regarding the age, sex, duration of discharge, and antibiotic treatment was taken. Excess discharge was mopped out from external auditory canal, and it was cleaned by spirit for 2 days before taking the sample of discharge from the middle ear. Ear discharge was then collected from them under aseptic precautions under a microscope using sterile single use Mini-tip Culture swabs with the aid of an aural speculum.

All the care was taken to avoid surface contamination, and the swabs were transported to the Microbiology section of the Hospital for further processing. Only the swabs were processed for aerobic bacteria.

All the organisms isolated were identified by morphological, cultural, and biochemical characteristics. Anaerobic organisms and fungi were not cultured in this study.

The material was inoculated on duplicate blood agar, chocolate agar, McConkey's agar, and mannitol salt agar for aerobic bacteria. The antimicrobial susceptibility testing was performed using an agar disk diffusion method according to the guidelines of Clinical and Laboratory Standards Institute.

Result

The male subjects were seen more commonly than the female subjects (79% vs. 21%). The most common age group affected was 9–12 years (43%), followed by 13–16 years (31%) [Table 1].

Table 1: Age and sex distribution of patients

| Age group (years) | Number of patients | Males | Females | Percentage |
|-------------------|--------------------|----------|----------|------------|
| 0–4 | 10 | 6 | 4 | 9 |
| 5–8 | 20 | 15 | 5 | 17 |
| 9–12 | 50 | 40 | 10 | 43 |
| 13–16 | 35 | 30 | 5 | 31 |
| Total | 115 | 91 (79%) | 24 (21%) | |

Table 2: Otoscopic findings in the safe and unsafe ears

| | Number of patients | Percentage |
|--|--------------------|------------|
| Patients with safe ear, <i>n</i> = 80 (70%) | | |
| Central perforation only | 22 | 27 |
| Central perforation with ossicular necrosis | 26 | 3 |
| Central perforation with tympanosclerosis | 6 | 9 |
| Central perforation with granulations/polypoidal middle ear mucosa | 26 | 32 |
| Patients with unsafe ear, <i>n</i> = 35 (30%) | | |
| Granulations only | 6 | 17 |
| Cholesteatoma only | 4 | 11 |
| Cholesteatoma with granulations | 18 | 52 |
| Aural polyp | 3 | 9 |
| Marginal perforation | 4 | 11 |

Table 3: Distribution of organisms in safe and unsafe ears

| Safe ear, <i>n</i> = 80 | Unsafe ear, <i>n</i> = 35 |
|--|---|
| 65 <i>Staphylococcus</i> ; 1 no growth; 14 negatives | 10 <i>Staphylococcus</i> ; 2 mixed; 1 no growth; 22 negatives |

Table 4: Organisms in pus culture

| | Number of patients | Percentage |
|---|--------------------|------------|
| Gram-positive organism (<i>n</i> = 75) (65%) | | |
| MRSA | 33 | 44 |
| MSSA | 40 | 53 |
| Coagulase-negative <i>Staphylococcus</i> | 2 | 3 |
| Gram-negative organism (<i>n</i> = 36) (31%) | | |
| <i>Pseudomonas</i> | 16 | 45 |
| <i>Proteus</i> | 4 | 12 |
| <i>Klebsiella</i> | 4 | 11 |
| <i>Escherichia coli</i> | 8 | 22 |
| <i>Haemophilus influenzae</i> | 2 | 5 |
| <i>Citrobacter</i> | 2 | 5 |
| Mixed organism (<i>n</i> = 2) (2%) | | |
| <i>Pseudomonas</i> + MSSA | 2 | 2 |
| No growth | 2 | 2 |

MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.

Table 5: Correlation between otoscopic findings and organism

| Otosopic finding (n) | Organisms present | Number | |
|---|--|--------|---|
| Safe ear | | | |
| Central perforation only | MSSA | 22 | |
| Central perforation with ossicular necrosis | MRSA | 26 | |
| Central perforation with tympanosclerosis (6) | MSSA | 3 | |
| | Coagulase negative | 1 | |
| | <i>Proteus</i> sp. | 1 | |
| | <i>Klebsiella</i> sp. | 1 | |
| | Central perforation with granulations (26) | MRSA | 3 |
| | | MSSA | 9 |
| Coagulase negative | | 1 | |
| No growth | | 1 | |
| <i>Pseudomonas</i> sp. | | 6 | |
| <i>Klebsiella</i> sp. | | 1 | |
| <i>Escherichia coli</i> | | 4 | |
| <i>Proteus</i> sp. | 1 | | |
| Unsafe ear | | | |
| Granulations only (6) | MSSA | 4 | |
| | <i>Citrobacter</i> sp. | 2 | |
| Cholesteatoma only (4) | <i>Pseudomonas</i> sp. | 2 | |
| | <i>Proteus</i> sp. | 2 | |
| Cholesteatoma with granulations (18) | MRSA | 4 | |
| | <i>Pseudomonas</i> sp. | 8 | |
| | <i>Klebsiella</i> sp. | 2 | |
| | <i>Escherichia coli</i> | 2 | |
| | Mixed | 2 | |
| Aural polyp (3) | <i>Escherichia coli</i> | 2 | |
| | <i>Haemophilus influenzae</i> | 1 | |
| Marginal perforation (4) | MSSA | 2 | |
| | <i>Haemophilus influenzae</i> | 1 | |
| | No growth | 1 | |

MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.

Table 6: Antibiotic sensitivity pattern of major isolates

| | Amikacin | Clinda- mycin | Cipro- floxacin | Amoxi- clav | Chloram- phenicol | Linezolid | Vanco- mycin | Azithro- mycin | Cefurox- ime |
|---------------------------------|----------|------------------|--------------------|----------------|----------------------|-----------|-----------------|-------------------|-----------------|
| MSSA (n = 40) | | | | | | | | | |
| Sensitive | 30 | 35 | 10 | 36 | 20 | 37 | 36 | 31 | 32 |
| Resistant | 10 | 5 | 30 | 4 | 20 | 3 | 4 | 9 | 2 |
| MRSA (n = 33) | | | | | | | | | |
| Sensitive | 25 | 31 | 6 | 2 | 3 | 32 | 31 | 3 | 3 |
| Resistant | 8 | 2 | 27 | 31 | 30 | 1 | 2 | 30 | 30 |
| <i>Pseudomonas</i> sp. (n = 16) | | | | | | | | | |
| Sensitive | 14 | 4 | 12 | 3 | 8 | 3 | 2 | 1 | 2 |
| Resistant | 2 | 10 | 4 | 13 | 8 | 13 | 14 | 15 | 14 |

Safe ear was observed in 70% patients, while unsafe ear in 30% patients. Central perforation with ossicular necrosis and with granulations/polypoidal tissue was the most common otoscopic findings in safe ear. Cholesteatoma with granulations was the most common otoscopic finding in the unsafe ears [Table 2].

The majority of patients with safe ears showed *S. aureus* (65 cases) growth on the culture, while the majority of patients with unsafe ears showed gram negative growths on the culture [Table 3].

The most common organism was *S. aureus* observed in 65% of patients (35% methicillin-sensitive *Staphylococcus aureus* (MSSA) and 30% MRSA) followed by *Pseudomonas* in 13% and *Escherichia coli* in 7%. The majority of *Staphylococcus* sp. were MSSA (53% of *S. aureus*), followed by MRSA (44% of *S. aureus*). Gram positives were seen in 65% of cases, while gram negatives in 31% of cases. No growth and mixed aerobic growth were seen in 2% of the cases. The majority of gram positives were MSSA (40), followed by MRSA (33). The majority of gram negatives were *Pseudomonas* sp. (16), followed by *E. coli* (8) [Table 4].

The majority of gram positives (65/75) were seen in the safe ears. The majority of MRSA (29/33) were seen in patients with central perforation with ossicular necrosis. Only four MRSA were present in unsafe ears. The majority of gram negatives were *Pseudomonas* sp. and the majority of them were found in cholesteatoma with granulations group. About 81% of safe ears showed gram positives, while 63% of unsafe ears showed gram negatives [Table 5].

MSSA in our study were sensitive to linezolid (92.5%), amoxiclav (90%), vancomycin (90%), cefuroxime (80%), and amikacin (45%), while most of the MRSA were sensitive to linezolid (97%), clindamycin (94%), vancomycin (94%), and amikacin (76%). Most of the *Pseudomonas* sp. in our study were sensitive to amikacin (87%) and ciprofloxacin (75%), while most of them were resistant to amoxiclav, linezolid, vancomycin, and azithromycin [Table 6].

Discussion

CSOM and its complications are among the most common conditions seen by otologists and general practitioners. It can lead to thickening of the middle ear mucosa, mucosal polyps, and cholesteatoma. CSOM is a common cause of hearing impairment, disability, and poor scholastic performance and can occasionally lead to fatal intracranial infections and acute mastoiditis, especially, in resource-poor countries.^[4]

There are different methods of obtaining the samples for culturing organisms causing CSOM. These include cotton wool swab collection of discharge from the external auditory canal, needle aspiration of the middle ear (tympanocentesis), and suction aspiration of the discharge from the middle ear through the tympanic membrane perforation.^[5] The best method

is tympanocentesis from the intact tympanic membrane; but it loses its utility once the tympanic membrane ruptures and the discharge from middle ear comes in external auditory canal. The discharge in the external auditory canal mixes with the preexisting normal flora of external auditory canal, and the identification of the real culprit organism is difficult. Under such circumstances, the cultures that are taken from the external ear by cotton swab may not reveal true microorganism, and sometimes, the culture can mislead us. Taking all the things into consideration, we first cleaned the external auditory canal by spirit swab for 2 days, and on the third day, we took the cultures using ear speculum under the microscope from the middle ear, minimizing the contamination from external auditory canal to a large extent.

The high prevalence of CSOM in this study was in the age group of 9–12 years with 43% of cases, followed by the age group of 13–16 years with 31% of cases. This is in correlation with the study done by Vijaya,^[6] Sinha *et al.*,^[7] and Gupta *et al.*^[8] In contrast, Loy *et al.*^[2] showed a higher incidence in the patients aged between 30 and 40 years of age.

Gender analysis showed that the incidence of CSOM was more common in male (79%) than in the female subjects (21%), which is in accordance with the studies done by Gulati,^[9] Moshi and Minja,^[10] Ahmad *et al.*,^[11] and Vijaya^[6] who reported male predominance. In contrast, Prakash *et al.*^[12] and Loy *et al.*,^[2] have reported female predominance in their studies. The possible reason for a high male predominance in our study could be, because our society is a bit traditional and conservative where men have the privilege when compared with women in being taken to tertiary centers for treatment from far away rural health centers.

This study included patients with both the safe and unsafe ears, but most studies on bacteriology have taken only patients with safe ears. The majority of our patients were with safe ears (70%). The most common otoscopic findings were central perforation with ossicular necrosis and granulations/polypoidal mucosa (23% each), followed by cholesteatoma with granulations (16%). Marginal perforation was found in 3.4% of cases, while the study on bacteriology of CSOM by Nikakhlagh *et al.*^[13] found the most common type of tympanic membrane perforation was marginal (48%), followed by attic (28%) and central perforations (24%).

Two of 115 (1.7%) patients in our study were culture negative. This low percentage of negative culture rate is in contrast to that reported by Vijaya (5.28%),^[6] Sinha *et al.* (9.8%),^[7] and Asiri and Bangar (19.5%).^[14] The reason for the low percentage of culture negative in this study is because we ensured before taking the samples from the ears, all topical and oral antibiotics should have been stopped 1 week prior. Negative cultures can be attributed to nonbacterial growth, anaerobic growth, and prior antibiotic therapy.

We found that the majority of patients in our study (65%) revealed gram positives, while only 31% revealed gram negatives. The most common organism cultured in our study was

Staphylococcus sp. present in 65% of patients (35% MSSA and 30% MRSA), followed by *Pseudomonas* sp. in 13%, and *E. coli* in 7%. The majority of *Staphylococcus* sp. were MSSA (53%), followed by MRSA (44%). Our findings are in contrast to other similar studies done by Loy et al.,^[2] Sharma et al.,^[5] Indudharan et al.,^[15] Kumar et al.,^[16] and Goyal et al.,^[17] who have revealed *Pseudomonas* sp. as the predominant organism. Kenna et al.^[18] and Chandrasekhar et al.,^[19] in their studies, found *Pseudomonas* sp. as the predominant organism in 67% and 46.5% cultures, respectively.

E. coli was seen in 7% of cases in this study, while Gulati^[9] cultured *E. coli* in 21.75%. *Citrobacter* sp. was isolated in 1.7% cases in our study, while Chandrasekhar et al.^[19] isolated *Citrobacter* sp. in 11.5% of cases. We found polymicrobial culture in two cases, and, in general, 5% to 10% of the infections are found to be poly microbial,^[13] often demonstrating a combination of gram-negative organisms and *S. aureus*. We did not culture anaerobes, but it has been seen that the anaerobes make up (20%–50%) of the isolates in CSOM and tend to be associated with cholesteatoma.^[2]

MRSA could be designated as either community-acquired, healthcare-associated, or nosocomial in origin. However, the definite designation of MRSA strains as community-acquired or healthcare-associated requires both the rigorous epidemiological and molecular analyses. Community-associated methicillin-resistant *Staphylococcus aureus* has been recognized as another substantial public health threat caused by *S. aureus*.^[3] The genetic basis of the methicillin resistance of MRSA is the presence of the *mecA* gene, which encodes the low-affinity penicillin binding protein 2a.^[3]

MRSA was seen in 30% of our patients, which is quite high in comparison with the studies by Park et al.,^[20] who found the prevalence of MRSA in CSOM was 4.9% and by Archana and Sree Harsha^[21] who found *S. aureus* in 45 (37.5%) patients was the predominant isolate, of which six (5%) isolates were MRSA. This alarming high percentage of MRSA demands that MRSA cannot be ignored in bacteriology of CSOM and shows that the spectrum of bacteriology has shifted from the classical gram negatives. MRSA is emerging as an important organism in ear discharge.

The majority of gram positives (65/75) were seen in the safe ears, while the majority of gram negatives (*Pseudomonas*) were found in unsafe ears. We found that MRSA were seen in the safe type CSOM with ossicular necrosis in the majority (29/33) of cases, but we do not know whether this is just by chance or there is a definite association between MRSA and ossicular erosion. More studies are needed to confirm our peculiar findings.

Thus, we see in this study, a drift in bacteriology of CSOM from gram negative to gram positive, and this drift significantly tells us that our population has different bacteriology than reported worldwide in different studies, and we need to prescribe empirical antibiotics taking this drift into consideration.

MSSA in our study were sensitive to linezolid (92.5%), amoxiclav (90%), vancomycin (90%), cefuroxime (80%), and amikacin (45%), while most of the MRSA were sensitive to

linezolid (97%), clindamycin (94%), vancomycin (94%), and amikacin (76%). In a study by Archana and Sree Harsha,^[21] antibiotic susceptibility of MSSA showed that 80% were sensitive to gentamicin and chloramphenicol, 70% to ciprofloxacin, 60% to clindamycin, 62% to cotrimoxazole, and 41% to erythromycin. All the MRSA isolates were sensitive to vancomycin, linezolid, tetracycline, doxycycline; 33% isolates to gentamicin, ciprofloxacin, clindamycin, cotrimoxazole; and 17% isolates to erythromycin.

Most of the *Pseudomonas* sp. in our study were sensitive to amikacin (87%) and ciprofloxacin (75%). While most of them were resistant to amoxiclav, linezolid, vancomycin, and azithromycin. In a study done by Loy et al.,^[2] *Pseudomonas aeruginosa* was shown to be sensitive to ceftazidime, ciprofloxacin, piperacillin, and amikacin. In another study by Ayson et al.,^[22] *P. aeruginosa* was resistant to penicillin in 64.3% of cases, and ciprofloxacin was active against *Pseudomonas* sp. in 85.7%.

Because we found that *S. aureus* is the most common culprit in the patients of this study, MSSA and MRSA are equally responsible, and gram negatives are not commonly involved, we now believe that empirical antibiotics if prescribed to patients should cover gram positives (*S. aureus*) and if possible MRSA. In our set of patients, we now believe that amoxiclav, linezolid, azithromycin, and clindamycin are the drugs of choice replacing the traditional drugs such as ciprofloxacin and third-generation cephalosporin. In cholesteatoma, anaerobes are seen in some patients; we should administer metronidazole or tinidazole to few such selected patients to cover the anaerobes. Because MRSA is seen in a significant number of patients, due consideration should be given to it while prescribing empirical drugs to patients with CSOM. These observations may not hold true to all areas, because bacteriology and sensitivity can change from region to region.

Conclusion

In conclusion, a variety of bacteria are responsible for CSOM. We found gram positives (*S. aureus*) as the predominant organisms, followed by *P. aeruginosa*. Mixed isolates were found in only two patients. MSSA was the most common gram positive organism (53%), followed by MRSA (40%). Overall MRSA was seen in 29% of the patients. The majority of the MRSA were seen in patients with central perforation with ossicular discontinuity. The percentage of MRSA seen in our study was quite high. In this study, we can see a drift in bacteriology of CSOM from gram negative to gram positive, and MRSA is emerging as an important pathogen in CSOM. Proper selection of empirical antibiotics helps in preventing drug resistance and clearing of infection. Hence, isolation of bacteria and sensitivity study are important for all CSOM cases for a particular region. We believe empirical antibiotics should be directed to gram positives and, especially, MRSA should be taken into consideration. The changing pattern of

causative agents and their antibiotic susceptibility should be constantly monitored to prevent the emergence and spread of resistant pathogens.

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